



Grant Number: 2P51OD011107-54 REVISED
FAIN: P51OD011107

Principal Investigator(s):
Harris A Lewin

Project Title: California National Primate Research Center

Ahmad Hakim-Elahi
UNIVERSITY OF CALIFORNIA AT DAVIS
1850 Research Park Drive
Suite 300
Davis, CA 956186153

Award e-mailed to: awards@ucdavis.edu

Period Of Performance:

Budget Period: 05/19/2015 – 04/30/2016

Project Period: 05/01/1997 – 04/30/2018

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Regents of the University of California in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number P51OD011107. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website <http://grants.nih.gov/grants/policy/coi/> for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Gavin Wilkom
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 2P51OD011107-54 REVISED**Award Calculation (U.S. Dollars)**

Salaries and Wages	\$2,554,529
Fringe Benefits	\$1,095,594
Personnel Costs (Subtotal)	\$3,650,123
Consultant Services	\$96,621
Equipment	\$448,981
Supplies	\$3,724,338
Travel Costs	\$132,544
Alterations and Renovations	\$114,494
Other Costs	\$904,563

Federal Direct Costs	\$9,071,664
Federal F&A Costs	\$1,931,359
Approved Budget	\$11,003,023
Total Amount of Federal Funds Obligated (Federal Share)	\$11,003,023
Less Unobligated Balance	\$163,630
TOTAL FEDERAL AWARD AMOUNT	\$10,839,393

AMOUNT OF THIS ACTION (FEDERAL SHARE) \$0

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (54)	
GRANT NUMBER	TOTAL FEDERAL AWARD AMOUNT
2P51OD011107-54	\$10,839,393
3P51OD011107-54S1	\$499,700
3P51OD011107-54S2	\$249,144
TOTAL	\$11,588,237

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
54	\$10,839,393	\$11,588,237
55	\$11,183,961	\$11,183,961
56	\$11,181,581	\$11,181,581

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name: Research Infrastructure Programs
CFDA Number: 93.351
EIN: 1946036494A1
Document Number: POD011107J
PMS Account Type: P (Subaccount)
Fiscal Year: 2015

IC	CAN	2015	2016	2017
OD	8014499	\$10,729,106	\$11,073,674	\$11,071,294
AG	8470701	\$110,287	\$110,287	\$110,287

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:

PCC: CMP01 / **OC:** 414B / **Released:** WILKOMG 12/11/2015
Award Processed: 12/12/2015 12:00:29 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2P51OD011107-54 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III – TERMS AND CONDITIONS – 2P51OD011107-54 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- a. The grant program legislation and program regulation cited in this Notice of Award.
- b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
- c. 45 CFR Part 75.
- d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
- f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See <http://grants.nih.gov/grants/policy/awardconditions.htm> for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) P51OD011107. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: <http://publicaccess.nih.gov/>.

This award is funded by the following list of institutes. Any papers published under the auspices of this award must cite the funding support of all institutes.

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 2P51OD011107-54 REVISED

REVISION #2: Carryover Approval

Carryover

This revision reflects an authorized carryover of \$163,630 (\$133,359 direct costs and \$30,272 F&A costs) in accordance with the grantee's request dated 10/08/2015, and may be used for the requested purpose only.

All previous terms and conditions remain in effect.

REVISION #1 : This award is revised to address the following issue:

Change of Personnel

This revision acknowledges the departure of [Excluded by Requester] and approves the addition of Dr. [Excluded by Requester] in accordance with the grantee's request, dated June 2, 2015.

KEY PERSONNEL

In addition to the PI, the following individuals are named as key personnel (individuals who have effort that NCATS/ORIP staff is tracking):

[Excluded by Requester]

Written prior approval is required if any of the individual(s) named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

All previous terms and conditions remain in effect.

SUBJECT FOA

This award is subject to the conditions set forth in NIH Guide Notice PAR-14-226, which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link:

<http://grants.nih.gov/grants/guide/pa-files/PAR-14-226.html>

ORIP FUNDING PLAN FOR FY2015

This competing award reflects the NIH Fiscal Policy for Grant Awards for FY2015 (see NIH Guide Notice NOT-OD-15-050) and the implementation of the ORIP FY2015 grants funding policy:

http://dpcpsi.nih.gov/orip/rf/fyg_fp2015.

KEY PERSONNEL

In addition to the PI, the following individuals are named as key personnel (individuals who have effort that ORIP staff is tracking):

[Excluded by Requester]

Written prior approval is required if any of the individuals named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

RECYCLING FUTURE BUDGET PERIOD START DATES

In order to redistribute awards more evenly throughout the fiscal year, this grant has been issued with a 11.5-month initial budget period with 12 months of monetary support. The continuation award for this grant will cycle each year on May 1st. Information for where to submit reports may be found at: <http://grants.nih.gov/grants/submitapplication.htm>.

FRINGE BENEFITS

The requested budget has been reviewed and accepted by the ORIP. Fringe Benefit amounts reflect a slight variance from the F&A Rate Agreement dated 8/19/2013. The Fringe Benefits have been awarded at the requested level. The grantee may rebudget within the direct cost categories as necessary to adjust for the minimal increase and/or decrease in fringe benefit rates.

SALARY CAP

None of the funds in this award shall be used to pay the salary of an individual at a rate in excess of the current salary cap. Therefore, this award and/or future years are adjusted accordingly, if applicable. Current salary cap levels can be found at the following URL:

http://grants.nih.gov/grants/policy/salcap_summary.htm.

PRIOR APPROVAL REQUEST

Any prior approval request (e.g., changes to key personnel as noted on the award, changes in human and animal subjects requiring prior approval) must be submitted to the assigned Grants Management Specialist and Programmatic Official. Please refer to the NIH Grants Policy Statement for the activities and/or expenditures that require NIH approval at <http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf> Chapter 8.1

CO-FUND

This award reflects support from the ORIP in the amount of \$10,729,106 total costs and from the National Institute of Aging in the amount of \$110,287 total costs.

NON-COMPETING RENEWAL (NON-SNAP)

The NIH requires the use of the Research Performance Progress Report (RPPR) for all Type 5 progress reports. The RPPR and other documents applicable to this Non-SNAP grant are due the first of the month preceding the month in which the budget period ends (e.g., if the budget period ends 11/30, the due date is 10/1). Please see <http://grants.nih.gov/grants/rppr/index.htm> for additional information on the RPPR.

COMMUNICATIONS/PRESS RELEASE

If the grantee plans to issue a press release concerning the outcome of ORIP grant-supported research, it should notify Ms. Patricia Newman, ORIP Communications at 301-435-0744, in advance to allow for coordination.

The ORIP WWW home page is at <http://dpcpsi.nih.gov/orip/>

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Melissa Austin Williams

Email: Melissa.Austin@nih.gov **Phone:** (301) 402-7183 **Fax:** (301) 480-3777

Program Official: John D. Harding

Email: hardingj@mail.nih.gov **Phone:** 301-435-0776 **Fax:** 301-480-3819

SPREADSHEET SUMMARY

GRANT NUMBER: 2P51OD011107-54 REVISED

INSTITUTION: Regents of the University of California

Budget	Year 54	Year 55	Year 56
Salaries and Wages	\$2,554,529	\$2,605,889	\$2,605,889
Fringe Benefits	\$1,095,594	\$1,127,374	\$1,127,374
Personnel Costs (Subtotal)	\$3,650,123	\$3,733,263	\$3,733,263
Consultant Services	\$96,621	\$22,270	\$22,270
Equipment	\$448,981	\$477,966	\$516,186
Supplies	\$3,724,338	\$3,802,323	\$3,802,323
Travel Costs	\$132,544	\$136,520	\$136,520
Alterations and Renovations	\$114,494	\$121,800	\$81,200
Other Costs	\$904,563	\$931,700	\$931,700
TOTAL FEDERAL DC	\$9,071,664	\$9,225,842	\$9,223,462
TOTAL FEDERAL F&A	\$1,931,359	\$1,958,119	\$1,958,119
TOTAL COST	\$10,839,393	\$11,183,961	\$11,181,581

Facilities and Administrative Costs	Year 54	Year 55	Year 56
F&A Cost Rate 1	22.7%	22.7%	22.7%
F&A Cost Base 1	\$8,508,190	\$8,626,076	\$8,626,076
F&A Costs 1	\$1,931,359	\$1,958,119	\$1,958,119



Grant Number: 2P51OD011107-54
FAIN: P51OD011107

Principal Investigator(s):
Harris A Lewin

Project Title: California National Primate Research Center

Bunn, Alyssa
Contracts and Grants Analyst
1850 Research Park Drive
Suite 300
Davis, CA 956186153

Award e-mailed to: awards@ucdavis.edu

Period Of Performance:

Budget Period: 05/19/2015 – 04/30/2016

Project Period: 05/01/1997 – 04/30/2018

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of \$10,839,393 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Regents of the University of California in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number P51OD011107. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website <http://grants.nih.gov/grants/policy/coi/> for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Stacia H Fleisher
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 2P51OD011107-54**Award Calculation (U.S. Dollars)**

Salaries and Wages	\$2,529,989
Fringe Benefits	\$1,094,538
Consultant Services	\$21,621
Equipment	\$448,981
Supplies	\$3,691,576
Travel Costs	\$132,544
Alterations and Renovations	\$114,494
Other Costs	\$904,563

Federal Direct Costs	\$8,938,306
Federal F&A Costs	\$1,901,087
Approved Budget	\$10,839,393
Total Amount of Federal Funds Obligated (Federal Share)	\$10,839,393
TOTAL FEDERAL AWARD AMOUNT	\$10,839,393

AMOUNT OF THIS ACTION (FEDERAL SHARE) \$10,839,393

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
54	\$10,839,393	\$10,839,393
55	\$11,183,961	\$11,183,961
56	\$11,181,581	\$11,181,581

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name: Research Infrastructure Programs
CFDA Number: 93.351
EIN: 1946036494A1
Document Number: POD011107J
PMS Account Type: P (Subaccount)
Fiscal Year: 2015

IC	CAN	2015	2016	2017
OD	8014499	\$10,729,106	\$11,073,674	\$11,071,294
AG	8470701	\$110,287	\$110,287	\$110,287

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:

PCC: CMP01 / **OC:** 414B / **Released:** FLEISHERS 05/12/2015
Award Processed: 03/23/2015 01:36:12 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2P51OD011107-54

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III – TERMS AND CONDITIONS – 2P51OD011107-54

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- The grant program legislation and program regulation cited in this Notice of Award.
- Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.

- c. 45 CFR Part 75.
- d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
- f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the Central Contractor Registration. Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See <http://grants.nih.gov/grants/policy/awardconditions.htm> for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) P51OD011107. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: <http://publicaccess.nih.gov/>.

This award is funded by the following list of institutes. Any papers published under the auspices of this award must cite the funding support of all institutes.

Office Of The Director, National Institutes Of Health (OD) National Institute On Aging (NIA)

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 2P51OD011107-54

SUBJECT FOA

This award is subject to the conditions set forth in NIH Guide Notice PAR-14-226, which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link:

<http://grants.nih.gov/grants/guide/pa-files/PAR-14-226.html>

ORIP FUNDING PLAN FOR FY2015

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KEY PERSONNEL

In addition to the PI, the following individuals are named as key personnel (individuals who have effort that ORIP staff is tracking):

Excluded by Requester

Written prior approval is required if any of the individuals named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

RECYCLING FUTURE BUDGET PERIOD START DATES

In order to redistribute awards more evenly throughout the fiscal year, this grant has been issued with a 11.5-month initial budget period with 12 months of monetary support. The continuation award for this grant will cycle each year on May 1st. Information for where to submit reports may be found at: <http://grants.nih.gov/grants/submitapplication.htm>.

FRINGE BENEFITS

The requested budget has been reviewed and accepted by the ORIP. Fringe Benefit amounts reflect a slight variance from the F&A Rate Agreement dated 8/19/2013. The Fringe Benefits have been awarded at the requested level. The grantee may rebudget within the direct cost categories as necessary to adjust for the minimal increase and/or decrease in fringe benefit rates.

SALARY CAP

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NON-COMPETING RENEWAL (NON-SNAP)

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COMMUNICATIONS/PRESS RELEASE

If the grantee plans to issue a press release concerning the outcome of ORIP grant-supported research, it should notify Ms. Patricia Newman, ORIP Communications at 301-435-0744, in advance to allow for coordination.

The ORIP WWW home page is at <http://dpcpsi.nih.gov/orip/>

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Ruthann Rand
Email: randrudy@mail.nih.gov **Phone:** 301.451.4238 **Fax:** 301.480.3777

Program Official: John D. Harding
Email: hardingj@mail.nih.gov **Phone:** 301-435-0776 **Fax:** 301-480-3819

SPREADSHEET SUMMARY

GRANT NUMBER: 2P51OD011107-54

INSTITUTION: Regents of the University of California

Budget	Year 54	Year 55	Year 56
Salaries and Wages	\$2,529,989	\$2,605,889	\$2,605,889
Fringe Benefits	\$1,094,538	\$1,127,374	\$1,127,374
Consultant Services	\$21,621	\$22,270	\$22,270
Equipment	\$448,981	\$477,966	\$516,186
Supplies	\$3,691,576	\$3,802,323	\$3,802,323
Travel Costs	\$132,544	\$136,520	\$136,520
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Other Costs	\$904,563	\$931,700	\$931,700
TOTAL FEDERAL DC	\$8,938,306	\$9,225,842	\$9,223,462
TOTAL FEDERAL F&A	\$1,901,087	\$1,958,119	\$1,958,119
TOTAL COST	\$10,839,393	\$11,183,961	\$11,181,581

Facilities and Administrative Costs	Year 54	Year 55	Year 56
F&A Cost Rate 1	22.7%	22.7%	22.7%
F&A Cost Base 1	\$8,374,831	\$8,626,076	\$8,626,076
F&A Costs 1	\$1,901,087	\$1,958,119	\$1,958,119

PI: Lewin, Harris A	Title: California National Primate Research Center	
Received: 07/15/2014	FOA: PAR14-226	Council: 01/2015
Competition ID: FORMS-C	FOA Title: LIMITED COMPETITION: NATIONAL PRIMATE RESEARCH CENTERS (P51)	
2 P51 OD011107-54	Dual: AG,RI	Accession Number: 3719893
IPF: 577503	Organization: UNIVERSITY OF CALIFORNIA AT DAVIS	
Former Number:	Department:	
IRG/SRG: ZRG1 BBBP-J (55)P	AIDS: Y	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 54: 9,513,397 Year 55: 9,795,534 Year 56: 10,085,629 Year 57: 10,385,209 Year 58: 10,693,589	Animals: Y Humans: N Clinical Trial: N Current HS Code: 10 HESC: Y	New Investigator: N Early Stage Investigator: N
<i>Senior/Key Personnel:</i>	<i>Organization:</i>	<i>Role Category:</i>
Harris Lewin	UNIVERSITY OF CALIFORNIA DAVIS	PD/PI

Appendices

List of Affiliate and Visiting Scientists, Overall Sources of Support, Table of Employees and Effort

Additions for Review

Other	Lewin supp info	pdf file containing updated list of support letters
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APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE		State Application Identifier
1. TYPE OF SUBMISSION*		4.a. Federal Identifier OD011107
<input type="radio"/> Pre-application <input checked="" type="radio"/> Application <input type="radio"/> Changed/Corrected Application		b. Agency Routing Number
2. DATE SUBMITTED	Application Identifier	c. Previous Grants.gov Tracking Number
5. APPLICANT INFORMATION Organizational DUNS*: 0471200840000		
Legal Name*: UNIVERSITY OF CALIFORNIA DAVIS Department: Division: Street1*: UNIVERSITY OF CALIFORNIA DAVIS Street2*: OFFICE OF RESEARCH - SPONSORED PROGRAMS City*: DAVIS County: State*: CA: California Province: Country*: USA: UNITED STATES ZIP / Postal Code*: 956180000		
Person to be contacted on matters involving this application Prefix: First Name*: Alyssa Middle Name: Last Name*: Bunn Suffix: Position/Title: Contracts and Grants Analyst Street1*: 1850 Research Park Drive Street2*: Suite 300 City*: Davis County: State*: CA: California Province: Country*: USA: UNITED STATES ZIP / Postal Code*: 956186153 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu		
6. EMPLOYER IDENTIFICATION NUMBER (EIN) or (TIN)*		946036494
7. TYPE OF APPLICANT*		H: Public/State Controlled Institution of Higher Education
Other (Specify): <input checked="" type="radio"/> Small Business Organization Type <input type="radio"/> Women Owned <input type="radio"/> Socially and Economically Disadvantaged		
8. TYPE OF APPLICATION*		If Revision, mark appropriate box(es).
<input type="radio"/> New <input type="radio"/> Resubmission <input checked="" type="radio"/> Renewal <input type="radio"/> Continuation <input type="radio"/> Revision		<input type="radio"/> A. Increase Award <input type="radio"/> B. Decrease Award <input type="radio"/> C. Increase Duration <input type="radio"/> D. Decrease Duration <input type="radio"/> E. Other (specify) :
Is this application being submitted to other agencies?* <input type="radio"/> Yes <input checked="" type="radio"/> No What other Agencies?		
9. NAME OF FEDERAL AGENCY* National Institutes of Health		10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER TITLE:
11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT* California National Primate Research Center		
12. PROPOSED PROJECT Start Date* Ending Date* 05/01/2015 04/30/2020		13. CONGRESSIONAL DISTRICTS OF APPLICANT CA-003

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: First Name*: Harris Middle Name: A Last Name*: Lewin Suffix:

Position/Title:

Organization Name*: UNIVERSITY OF CALIFORNIA DAVIS

Department:

Division: Office of Research

Street1*: One Shields Ave

Street2:

City*: Davis

County:

State*: CA: California

Province:

Country*: USA: UNITED STATES

ZIP / Postal Code*: 956165270

Phone Number*: 530-754-7764 Fax Number: Email*: lewin@ucdavis.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested* \$61,250,793.00

b. Total Non-Federal Funds* \$0.00

c. Total Federal & Non-Federal Funds* \$61,250,793.00

d. Estimated Program Income* \$59,633,957.00

16. IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ☐ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ☒ PROGRAM IS NOT COVERED BY E.O. 12372; OR

☐ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

☒ I agree*

* The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

18. SFLL or OTHER EXPLANATORY DOCUMENTATION

File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: Alyssa Middle Name: Last Name*: Bunn Suffix:

Position/Title*: Contracts and Grants Analyst

Organization Name*: University of California Davis

Department: Sponsored Programs

Division: Office of Research

Street1*: 1850 Research Park Drive

Street2:

City*: Davis

County:

State*: CA: California

Province:

Country*: USA: UNITED STATES

ZIP / Postal Code*: 956186153

Phone Number*: 530-754-7827 Fax Number: Email*: aabunn@ucdavis.edu

Signature of Authorized Representative*

Alyssa Bunn

Date Signed*

07/15/2014

20. PRE-APPLICATION File Name:**21. COVER LETTER ATTACHMENT** File Name:

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**Component
Summary**

Components	Component Project Title	Organization Name	Contact PD/PI Name or Project Lead Name
Overall	California National Primate Research Center	UNIVERSITY OF CALIFORNIA DAVIS	Lewin, Harris A
Admin-Core-001 (566)	Administrative Overview	Regents of the University of California	Excluded by Requester
Admin-Core-002 (706)	Director's Office	Regents of the University of California	
Admin-Core-003 (988)	Administration and Operations Services	Regents of the University of California	
Admin-Core-004 (516)	Information Technology Services	Regents of the University of California	
Admin-Core-005 (282)	Facilities Improvement	Regents of the University of California	
Animal-Resources-001 (079)	Colony Management and Research Services	Regents of the University of California	
Animal-Resources-002 (350)	National Institute of Aging Colony	Regents of the University of California	
Animal-Resources-003 (983)	Primate Medicine Services	Regents of the University of California	
Animal-Resources-004 (760)	Anatomic and Clinical Pathology Services	Regents of the University of California	
Animal-Resources-005 (705)	Behavior Management Services	Regents of the University of California	
Animal-Resources-006 (199)	Genetics Management Services	Regents of the University of California	
Core-Services-001 (371)	Behavior Research Services Core	Regents of the University of California	
Core-Services-002 (755)	Endocrine Core	Regents of the University of California	
Core-Services-003 (976)	Immunology and Pathogen Detection Resources Core	Regents of the University of California	
Core-Services-004 (462)	Inhalation Exposure Core	Regents of the University of California	
Core-Services-005 (985)	Multimodal Imaging Core	Regents of the University of California	
NPRC-Consortium-001 (365)	NPRC Consortium Activities	Regents of the University of California	
Outreach-001 (218)	Outreach Program	Regents of the University of California	
Pilot-Research-001 (446)	Pilot Research Program	Regents of the University of California	
Scientific-Units-001 (056)	Brain, Mind, and Behavior Research Unit	Regents of the University of California	
Scientific-Units-002 (170)	Infectious Diseases Research Unit	Regents of the University of California	
Scientific-Units-003 (916)	Reproductive Sciences and Regenerative Medicine Research Unit	Regents of the University of California	
Scientific-Units-004 (104)	Respiratory Diseases Research Unit	Regents of the University of California	

**Project/Performance
Site Location(s) Summary**

Applicant Organization	City	State/Province	Country
UNIVERSITY OF CALIFORNIA DAVIS	DAVIS	CA	UNITED STATES

Organization Name	City	State/Province	Country	Component
University of California Davis	Davis	CA	UNITED STATES	Admin-Core-001 (566)
University of California Davis	Davis	CA	UNITED STATES	Admin-Core-002 (706)
University of California Davis	Davis	CA	UNITED STATES	Admin-Core-003 (988)
University of California Davis	Davis	CA	UNITED STATES	Admin-Core-004 (516)
University of California Davis	Davis	CA	UNITED STATES	Admin-Core-005 (282)
University of California Davis	Davis	CA	UNITED STATES	Animal-Resources-001 (079)
University of California Davis	Davis	CA	UNITED STATES	Animal-Resources-002 (350)
University of California Davis	Davis	CA	UNITED STATES	Animal-Resources-003 (983)
University of California Davis	Davis	CA	UNITED STATES	Animal-Resources-004 (760)
University of California Davis	Davis	CA	UNITED STATES	Animal-Resources-005 (705)
University of California Davis	Davis	CA	UNITED STATES	Animal-Resources-006 (199)
University of California Davis	Davis	CA	UNITED STATES	Core-Services-001 (371)
University of California Davis	Davis	CA	UNITED STATES	Core-Services-002 (755)
University of California Davis	Davis	CA	UNITED STATES	Core-Services-003 (976)
University of California Davis	Davis	CA	UNITED STATES	Core-Services-004 (462)
University of California Davis	Davis	CA	UNITED STATES	Core-Services-005 (985)
University of California Davis	Davis	CA	UNITED STATES	NPRC-Consortium-001 (365)
University of California Davis	Davis	CA	UNITED STATES	Outreach-001 (218)
University of California Davis	Davis	CA	UNITED STATES	Overall
University of California Davis	Davis	CA	UNITED STATES	Pilot-Research-001 (446)
University of California Davis	Davis	CA	UNITED STATES	Scientific-Units-001 (056)
University of California Davis	Davis	CA	UNITED STATES	Scientific-Units-002 (170)
University of California Davis	Davis	CA	UNITED STATES	Scientific-Units-003 (916)
University of California Davis	Davis	CA	UNITED STATES	Scientific-Units-004 (104)

**Human Subjects
Clinical Trial
Human Embryonic Stem Cells
Vertebrate Animals
Summary**

Components	Human Subjects	Clinical Trial	HESC Involved	Vertebrate Animals
Overall	N	N	Y	Y
Admin-Core-001 (566)	N	N	N	N
Admin-Core-002 (706)	N	N	N	N
Admin-Core-003 (988)	N	N	N	N
Admin-Core-004 (516)	N	N	N	N
Admin-Core-005 (282)	N	N	N	N
Animal-Resources-001 (079)	N	N	N	Y
Animal-Resources-002 (350)	N	N	N	Y
Animal-Resources-003 (983)	N	N	N	Y
Animal-Resources-004 (760)	N	N	N	Y
Animal-Resources-005 (705)	N	N	N	Y
Animal-Resources-006 (199)	N	N	N	Y
Core-Services-001 (371)	N	N	N	Y
Core-Services-002 (755)	N	N	N	Y
Core-Services-003 (976)	N	N	N	Y
Core-Services-004 (462)	N	N	N	Y
Core-Services-005 (985)	N	N	Y	Y
NPRC-Consortium-001 (365)	N	N	N	N
Outreach-001 (218)	N	N	N	N
Pilot-Research-001 (446)	N	N	N	Y
Scientific-Units-001 (056)	N	N	N	Y
Scientific-Units-002 (170)	N	N	N	Y
Scientific-Units-003 (916)	N	N	Y	Y
Scientific-Units-004 (104)	N	N	N	Y

Composite Application Budget Summary

Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Salary, Wages and Fringe Benefits	3,860,596	3,999,940	4,143,540	4,291,457	4,443,770	20,739,303
Equipment	477,626	477,966	516,186	477,344	478,166	2,427,288
Travel	141,000	145,230	149,582	154,068	158,687	748,567
Participant/Trainee Support Costs	0	0	0	0	0	0
Other Direct Costs (excluding Consortium)	5,034,175	5,172,398	5,276,321	5,462,340	5,612,966	26,558,200
Consortium Costs	0	0	0	0	0	0
Direct Costs	9,513,397	9,795,534	10,085,629	10,385,209	10,693,589	50,473,358
Indirect Costs	2,023,470	2,087,439	2,153,833	2,221,437	2,291,256	10,777,435
Total Direct and Indirect Costs	11,536,867	11,882,973	12,239,462	12,606,646	12,984,845	61,250,793

Total Direct Costs less Consortium F&A

Category	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	9,513,397	9,795,534	10,085,629	10,385,209	10,693,589	50,473,358

Component Budget Summary

Components	Categories	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Admin-Core-001 (566)	Salary, Wages and Fringe Benefits	0	0	0	0	0	0
	Equipment	0	0	0	0	0	0
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	0	0	0	0	0	0
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	0	0	0	0	0	0
	Indirect Costs	0	0	0	0	0	0
TOTALS	Total Direct and Indirect Costs	0	0	0	0	0	0
Admin-Core-002 (706)	Salary, Wages and Fringe Benefits	386,165	399,537	411,427	423,362	438,269	2,058,760
	Equipment	0	0	0	0	0	0
	Travel	37,500	38,625	39,783	40,976	42,205	199,089
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	30,340	31,250	32,189	33,155	34,150	161,084
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	454,005	469,412	483,399	497,493	514,624	2,418,933
	Indirect Costs	103,059	106,557	109,732	112,931	116,820	549,099
TOTALS	Total Direct and Indirect Costs	557,064	575,969	593,131	610,424	631,444	2,968,032

Admin-Core-003 (988)	Salary, Wages and Fringe Benefits	308,618	322,797	336,258	350,123	364,669	1,682,465
	Equipment	0	0	0	0	0	0
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	23,500	24,205	24,932	25,679	26,449	124,765
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	332,118	347,002	361,190	375,802	391,118	1,807,230
	Indirect Costs	75,391	78,769	81,991	85,307	88,784	410,242
TOTALS	Total Direct and Indirect Costs	407,509	425,771	443,181	461,109	479,902	2,217,472
Admin-Core-004 (516)	Salary, Wages and Fringe Benefits	499,947	520,118	544,971	567,197	590,579	2,722,812
	Equipment	0	0	0	0	0	0
	Travel	9,000	9,270	9,548	9,834	10,129	47,781
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	48,480	49,935	51,433	52,976	54,566	257,390
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	557,427	579,323	605,952	630,007	655,274	3,027,983
	Indirect Costs	126,536	131,506	137,551	143,011	148,747	687,351
TOTALS	Total Direct and Indirect Costs	683,963	710,829	743,503	773,018	804,021	3,715,334
Admin-Core-005 (282)	Salary, Wages and Fringe Benefits	0	0	0	0	0	0
	Equipment	477,626	477,966	516,186	477,344	478,166	2,427,288
	Travel	0	0	0	0	0	0

	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	121,800	121,800	81,200	121,800	121,800	568,400
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	599,426	599,766	597,386	599,144	599,966	2,995,688
	Indirect Costs	0	0	0	0	0	0
TOTALS	Total Direct and Indirect Costs	599,426	599,766	597,386	599,144	599,966	2,995,688
Animal-Resources-001 (079)	Salary, Wages and Fringe Benefits	339,858	357,031	373,381	385,404	391,201	1,846,875
	Equipment	0	0	0	0	0	0
	Travel	6,000	6,180	6,365	6,556	6,753	31,854
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	3,716,280	3,827,619	3,944,449	4,061,348	4,182,597	19,732,293
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	4,062,138	4,190,830	4,324,195	4,453,308	4,580,551	21,611,022
	Indirect Costs	922,105	951,318	981,592	1,010,901	1,039,785	4,905,701
TOTALS	Total Direct and Indirect Costs	4,984,243	5,142,148	5,305,787	5,464,209	5,620,336	26,516,723
Animal-Resources-002 (350)	Salary, Wages and Fringe Benefits	6,348	6,453	6,520	6,579	6,642	32,542
	Equipment	0	0	0	0	0	0
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	94,019	96,840	99,745	102,737	105,819	499,160
	Consortium Costs	0	0	0	0	0	0

	Direct Costs	100,367	103,293	106,265	109,316	112,461	531,702
	Indirect Costs	22,783	23,448	24,122	24,815	25,529	120,697
TOTALS	Total Direct and Indirect Costs	123,150	126,741	130,387	134,131	137,990	652,399
Animal-Resources-003 (983)	Salary, Wages and Fringe Benefits	230,731	241,919	246,066	256,210	266,951	1,241,877
	Equipment	0	0	0	0	0	0
	Travel	10,500	10,815	11,139	11,473	11,817	55,744
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	24,000	24,720	25,462	26,226	27,013	127,421
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	265,231	277,454	282,667	293,909	305,781	1,425,042
	Indirect Costs	60,207	62,982	64,165	66,717	69,412	323,483
TOTALS	Total Direct and Indirect Costs	325,438	340,436	346,832	360,626	375,193	1,748,525
Animal-Resources-004 (760)	Salary, Wages and Fringe Benefits	254,042	266,498	273,235	283,647	295,909	1,373,331
	Equipment	0	0	0	0	0	0
	Travel	6,000	6,180	6,365	6,556	6,753	31,854
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	31,500	32,445	33,418	34,421	35,454	167,238
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	291,542	305,123	313,018	324,624	338,116	1,572,423
	Indirect Costs	66,180	69,263	71,056	73,690	76,752	356,941
TOTALS	Total Direct and Indirect Costs	357,722	374,386	384,074	398,314	414,868	1,929,364

Animal-Resources-005 (705)	Salary, Wages and Fringe Benefits	89,842	94,945	99,834	104,870	110,207	499,698
	Equipment	0	0	0	0	0	0
	Travel	1,500	1,545	1,591	1,639	1,688	7,963
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	18,500	19,055	19,627	20,215	20,821	98,218
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	109,842	115,545	121,052	126,724	132,716	605,879
	Indirect Costs	24,934	26,228	27,479	28,766	30,127	137,534
TOTALS	Total Direct and Indirect Costs	134,776	141,773	148,531	155,490	162,843	743,413
Animal-Resources-006 (199)	Salary, Wages and Fringe Benefits	78,192	81,532	84,591	87,749	91,045	423,109
	Equipment	0	0	0	0	0	0
	Travel	3,000	3,090	3,183	3,278	3,376	15,927
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	11,500	11,845	12,200	12,566	12,943	61,054
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	92,692	96,467	99,974	103,593	107,364	500,090
	Indirect Costs	21,041	21,898	22,694	23,516	24,372	113,521
TOTALS	Total Direct and Indirect Costs	113,733	118,365	122,668	127,109	131,736	613,611
Core-Services-001 (371)	Salary, Wages and Fringe Benefits	56,067	58,555	60,883	63,239	65,716	304,460
	Equipment	0	0	0	0	0	0
	Travel	1,500	1,545	1,591	1,639	1,688	7,963

	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	6,000	6,180	6,366	6,557	6,754	31,857
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	63,567	66,280	68,840	71,435	74,158	344,280
	Indirect Costs	14,430	15,046	15,627	16,216	16,834	78,153
TOTALS	Total Direct and Indirect Costs	77,997	81,326	84,467	87,651	90,992	422,433
Core-Services-002 (755)	Salary, Wages and Fringe Benefits	35,283	36,649	38,000	39,387	40,836	190,155
	Equipment	0	0	0	0	0	0
	Travel	1,500	1,545	1,591	1,639	1,688	7,963
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	10,000	10,300	10,609	10,927	11,255	53,091
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	46,783	48,494	50,200	51,953	53,779	251,209
	Indirect Costs	10,620	11,008	11,395	11,793	12,208	57,024
TOTALS	Total Direct and Indirect Costs	57,403	59,502	61,595	63,746	65,987	308,233
Core-Services-003 (976)	Salary, Wages and Fringe Benefits	184,773	192,899	200,514	208,268	216,410	1,002,864
	Equipment	0	0	0	0	0	0
	Travel	3,000	3,090	3,183	3,278	3,376	15,927
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	31,000	31,930	32,888	33,875	34,891	164,584
	Consortium Costs	0	0	0	0	0	0

	Direct Costs	218,773	227,919	236,585	245,421	254,677	1,183,375
	Indirect Costs	49,661	51,738	53,705	55,711	57,812	268,627
TOTALS	Total Direct and Indirect Costs	268,434	279,657	290,290	301,132	312,489	1,452,002
Core-Services-004 (462)	Salary, Wages and Fringe Benefits	154,521	159,189	167,551	173,964	180,698	835,923
	Equipment	0	0	0	0	0	0
	Travel	3,000	3,090	3,183	3,278	3,376	15,927
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	18,500	19,055	19,627	20,216	20,823	98,221
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	176,021	181,334	190,361	197,458	204,897	950,071
	Indirect Costs	39,957	41,163	43,212	44,823	46,512	215,667
TOTALS	Total Direct and Indirect Costs	215,978	222,497	233,573	242,281	251,409	1,165,738
Core-Services-005 (985)	Salary, Wages and Fringe Benefits	204,020	208,554	211,176	216,118	220,006	1,059,874
	Equipment	0	0	0	0	0	0
	Travel	3,000	3,090	3,183	3,278	3,376	15,927
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	16,500	16,995	17,505	18,030	18,571	87,601
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	223,520	228,639	231,864	237,426	241,953	1,163,402
	Indirect Costs	50,739	51,901	52,633	53,896	54,923	264,092
TOTALS	Total Direct and Indirect Costs	274,259	280,540	284,497	291,322	296,876	1,427,494

NPRC-Consortium-001 (365)	Salary, Wages and Fringe Benefits	8,713	8,946	9,496	9,869	10,261	47,285
	Equipment	0	0	0	0	0	0
	Travel	13,500	13,905	14,320	14,751	15,193	71,669
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	480,256	494,664	509,504	524,791	540,535	2,549,750
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	502,469	517,515	533,320	549,411	565,989	2,668,704
	Indirect Costs	114,060	117,476	121,064	124,716	128,480	605,796
TOTALS	Total Direct and Indirect Costs	616,529	634,991	654,384	674,127	694,469	3,274,500
Outreach-001 (218)	Salary, Wages and Fringe Benefits	86,213	88,468	93,974	97,799	101,817	468,271
	Equipment	0	0	0	0	0	0
	Travel	1,500	1,545	1,591	1,639	1,688	7,963
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	11,500	11,845	12,201	12,567	12,944	61,057
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	99,213	101,858	107,766	112,005	116,449	537,291
	Indirect Costs	22,521	23,122	24,463	25,425	26,434	121,965
TOTALS	Total Direct and Indirect Costs	121,734	124,980	132,229	137,430	142,883	659,256
Pilot-Research-001 (446)	Salary, Wages and Fringe Benefits	0	0	0	0	0	0
	Equipment	0	0	0	0	0	0
	Travel	0	0	0	0	0	0
	Participant/Trainee Support Costs	0	0	0	0	0	0

	Other Direct Costs (excluding Consortium)	300,000	300,000	300,000	300,000	300,000	1,500,000
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	300,000	300,000	300,000	300,000	300,000	1,500,000
	Indirect Costs	68,100	68,100	68,100	68,100	68,100	340,500
TOTALS	Total Direct and Indirect Costs	368,100	368,100	368,100	368,100	368,100	1,840,500
Scientific-Units-001 (056)	Salary, Wages and Fringe Benefits	217,382	222,150	224,771	231,974	244,469	1,140,746
	Equipment	0	0	0	0	0	0
	Travel	10,500	10,815	11,139	11,473	11,817	55,744
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	10,500	10,815	11,139	11,473	11,817	55,744
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	238,382	243,780	247,049	254,920	268,103	1,252,234
	Indirect Costs	54,113	55,338	56,081	57,867	60,860	284,259
TOTALS	Total Direct and Indirect Costs	292,495	299,118	303,130	312,787	328,963	1,536,493
Scientific-Units-002 (170)	Salary, Wages and Fringe Benefits	238,934	243,326	250,152	260,140	267,335	1,259,887
	Equipment	0	0	0	0	0	0
	Travel	12,000	12,360	12,731	13,113	13,506	63,710
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	12,000	12,360	12,731	13,113	13,506	63,710
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	262,934	268,046	275,614	286,366	294,347	1,387,307

	Indirect Costs	59,686	60,846	62,564	65,005	66,817	314,918
TOTALS	Total Direct and Indirect Costs	322,620	328,892	338,178	351,371	361,164	1,702,225
Scientific-Units-003 (916)	Salary, Wages and Fringe Benefits	265,187	270,117	280,273	287,980	295,710	1,399,267
	Equipment	0	0	0	0	0	0
	Travel	9,000	9,270	9,548	9,834	10,129	47,781
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	9,000	9,270	9,548	9,834	10,129	47,781
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	283,187	288,657	299,369	307,648	315,968	1,494,829
	Indirect Costs	64,283	65,525	67,956	69,836	71,725	339,325
TOTALS	Total Direct and Indirect Costs	347,470	354,182	367,325	377,484	387,693	1,834,154
Scientific-Units-004 (104)	Salary, Wages and Fringe Benefits	215,760	220,257	230,467	237,578	245,040	1,149,102
	Equipment	0	0	0	0	0	0
	Travel	9,000	9,270	9,548	9,834	10,129	47,781
	Participant/Trainee Support Costs	0	0	0	0	0	0
	Other Direct Costs (excluding Consortium)	9,000	9,270	9,548	9,834	10,129	47,781
	Consortium Costs	0	0	0	0	0	0
	Direct Costs	233,760	238,797	249,563	257,246	265,298	1,244,664
	Indirect Costs	53,064	54,207	56,651	58,395	60,223	282,540
TOTALS	Total Direct and Indirect Costs	286,824	293,004	306,214	315,641	325,521	1,527,204
TOTALS		11,536,867	11,882,973	12,239,462	12,606,646	12,984,845	61,250,793

Categories Budget Summary

Categories	Components	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
R&R Budget - Senior/Key Person Funds Requested	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	265,148	273,276	280,266	287,198	296,855	1,402,743
	Admin-Core-003 (988)	33,716	35,303	36,741	38,186	39,706	183,652
	Admin-Core-004 (516)	99,763	101,416	108,714	112,988	117,489	540,370
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	50,194	50,985	51,498	51,952	52,427	257,056
	Animal-Resources- 002 (350)	6,348	6,453	6,520	6,579	6,642	32,542
	Animal-Resources- 003 (983)	148,159	155,077	157,889	164,136	170,762	796,023
	Animal-Resources- 004 (760)	88,878	93,643	96,049	99,972	104,718	483,260
	Animal-Resources- 005 (705)	40,278	42,583	44,747	46,959	49,304	223,871
	Animal-Resources- 006 (199)	40,564	42,138	43,585	45,121	46,708	218,116
	Core-Services-001 (371)	30,812	32,262	33,577	34,896	36,287	167,834
	Core-Services-002 (755)	16,336	16,826	17,345	17,882	18,437	86,826

	Core-Services-003 (976)	32,992	34,089	35,053	36,014	37,013	175,161
	Core-Services-004 (462)	29,808	30,440	31,664	32,522	33,420	157,854
	Core-Services-005 (985)	44,157	44,555	44,833	45,087	45,349	223,981
	NPRC-Consortium- 001 (365)	5,461	5,607	5,951	6,185	6,431	29,635
	Outreach-001 (218)	22,478	23,079	24,494	25,458	26,470	121,979
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	104,561	106,750	107,918	110,306	113,708	543,243
	Scientific-Units-002 (170)	148,241	150,628	152,243	157,662	160,712	769,486
	Scientific-Units-003 (916)	120,308	121,825	123,932	125,698	127,397	619,160
	Scientific-Units-004 (104)	94,778	96,485	99,983	102,421	104,978	498,645
TOTALS		1,422,980	1,463,420	1,503,002	1,547,222	1,594,813	7,531,437
R&R Budget - Other Personnel Funds Requested	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	121,017	126,261	131,161	136,164	141,414	656,017
	Admin-Core-003 (988)	274,902	287,494	299,517	311,937	324,963	1,498,813
	Admin-Core-004 (516)	400,184	418,702	436,257	454,209	473,090	2,182,442
	Admin-Core-005 (282)	0	0	0	0	0	0

	Animal-Resources-001 (079)	289,664	306,046	321,883	333,452	338,774	1,589,819
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	82,572	86,842	88,177	92,074	96,189	445,854
	Animal-Resources-004 (760)	165,164	172,855	177,186	183,675	191,191	890,071
	Animal-Resources-005 (705)	49,564	52,362	55,087	57,911	60,903	275,827
	Animal-Resources-006 (199)	37,628	39,394	41,006	42,628	44,337	204,993
	Core-Services-001 (371)	25,255	26,293	27,306	28,343	29,429	136,626
	Core-Services-002 (755)	18,947	19,823	20,655	21,505	22,399	103,329
	Core-Services-003 (976)	151,781	158,810	165,461	172,254	179,397	827,703
	Core-Services-004 (462)	124,713	128,749	135,887	141,442	147,278	678,069
	Core-Services-005 (985)	159,863	163,999	166,343	171,031	174,657	835,893
	NPRC-Consortium-001 (365)	3,252	3,339	3,545	3,684	3,830	17,650
	Outreach-001 (218)	63,735	65,389	69,480	72,341	75,347	346,292
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	112,821	115,400	116,853	121,668	130,761	597,503

	Scientific-Units-002 (170)	90,693	92,698	97,909	102,478	106,623	490,401
	Scientific-Units-003 (916)	144,879	148,292	156,341	162,282	168,313	780,107
	Scientific-Units-004 (104)	120,982	123,772	130,484	135,157	140,062	650,457
TOTALS		2,437,616	2,536,520	2,640,538	2,744,235	2,848,957	13,207,866
R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	386,165	399,537	411,427	423,362	438,269	2,058,760
	Admin-Core-003 (988)	308,618	322,797	336,258	350,123	364,669	1,682,465
	Admin-Core-004 (516)	499,947	520,118	544,971	567,197	590,579	2,722,812
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	339,858	357,031	373,381	385,404	391,201	1,846,875
	Animal-Resources- 002 (350)	6,348	6,453	6,520	6,579	6,642	32,542
	Animal-Resources- 003 (983)	230,731	241,919	246,066	256,210	266,951	1,241,877
	Animal-Resources- 004 (760)	254,042	266,498	273,235	283,647	295,909	1,373,331
	Animal-Resources- 005 (705)	89,842	94,945	99,834	104,870	110,207	499,698
	Animal-Resources- 006 (199)	78,192	81,532	84,591	87,749	91,045	423,109

	Core-Services-001 (371)	56,067	58,555	60,883	63,239	65,716	304,460
	Core-Services-002 (755)	35,283	36,649	38,000	39,387	40,836	190,155
	Core-Services-003 (976)	184,773	192,899	200,514	208,268	216,410	1,002,864
	Core-Services-004 (462)	154,521	159,189	167,551	173,964	180,698	835,923
	Core-Services-005 (985)	204,020	208,554	211,176	216,118	220,006	1,059,874
	NPRC-Consortium- 001 (365)	8,713	8,946	9,496	9,869	10,261	47,285
	Outreach-001 (218)	86,213	88,468	93,974	97,799	101,817	468,271
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	217,382	222,150	224,771	231,974	244,469	1,140,746
	Scientific-Units-002 (170)	238,934	243,326	250,152	260,140	267,335	1,259,887
	Scientific-Units-003 (916)	265,187	270,117	280,273	287,980	295,710	1,399,267
	Scientific-Units-004 (104)	215,760	220,257	230,467	237,578	245,040	1,149,102
TOTALS		3,860,596	3,999,940	4,143,540	4,291,457	4,443,770	20,739,303
R&R Budget - Section C. Total Equipment	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0

	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	477,626	477,966	516,186	477,344	478,166	2,427,288
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	0	0	0	0	0	0
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0

	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		477,626	477,966	516,186	477,344	478,166	2,427,288
R&R Budget - Domestic Travel	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	37,500	38,625	39,783	40,976	42,205	199,089
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	9,000	9,270	9,548	9,834	10,129	47,781
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	6,000	6,180	6,365	6,556	6,753	31,854
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	10,500	10,815	11,139	11,473	11,817	55,744
	Animal-Resources- 004 (760)	6,000	6,180	6,365	6,556	6,753	31,854

	Animal-Resources-005 (705)	1,500	1,545	1,591	1,639	1,688	7,963
	Animal-Resources-006 (199)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-001 (371)	1,500	1,545	1,591	1,639	1,688	7,963
	Core-Services-002 (755)	1,500	1,545	1,591	1,639	1,688	7,963
	Core-Services-003 (976)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-004 (462)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-005 (985)	3,000	3,090	3,183	3,278	3,376	15,927
	NPRC-Consortium-001 (365)	13,500	13,905	14,320	14,751	15,193	71,669
	Outreach-001 (218)	1,500	1,545	1,591	1,639	1,688	7,963
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	10,500	10,815	11,139	11,473	11,817	55,744
	Scientific-Units-002 (170)	12,000	12,360	12,731	13,113	13,506	63,710
	Scientific-Units-003 (916)	9,000	9,270	9,548	9,834	10,129	47,781
	Scientific-Units-004 (104)	9,000	9,270	9,548	9,834	10,129	47,781
TOTALS		141,000	145,230	149,582	154,068	158,687	748,567
R&R Budget - Foreign Travel	Admin-Core-001 (566)	0	0	0	0	0	0

	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	0	0	0	0	0	0
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0

	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget - Section D. Total Travel	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	37,500	38,625	39,783	40,976	42,205	199,089
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	9,000	9,270	9,548	9,834	10,129	47,781
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources-001 (079)	6,000	6,180	6,365	6,556	6,753	31,854
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	10,500	10,815	11,139	11,473	11,817	55,744

	Animal-Resources-004 (760)	6,000	6,180	6,365	6,556	6,753	31,854
	Animal-Resources-005 (705)	1,500	1,545	1,591	1,639	1,688	7,963
	Animal-Resources-006 (199)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-001 (371)	1,500	1,545	1,591	1,639	1,688	7,963
	Core-Services-002 (755)	1,500	1,545	1,591	1,639	1,688	7,963
	Core-Services-003 (976)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-004 (462)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-005 (985)	3,000	3,090	3,183	3,278	3,376	15,927
	NPRC-Consortium-001 (365)	13,500	13,905	14,320	14,751	15,193	71,669
	Outreach-001 (218)	1,500	1,545	1,591	1,639	1,688	7,963
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	10,500	10,815	11,139	11,473	11,817	55,744
	Scientific-Units-002 (170)	12,000	12,360	12,731	13,113	13,506	63,710
	Scientific-Units-003 (916)	9,000	9,270	9,548	9,834	10,129	47,781
	Scientific-Units-004 (104)	9,000	9,270	9,548	9,834	10,129	47,781
TOTALS		141,000	145,230	149,582	154,068	158,687	748,567

R&R Budget - Tuition/Fees/Health Insurance	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources-001 (079)	0	0	0	0	0	0
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0

	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget - Stipends	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0

	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0

	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget - Trainee Travel	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	0	0	0	0	0	0
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0

	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget - Subsistence	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0

	Animal-Resources-001 (079)	0	0	0	0	0	0
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0

	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget 1/2 Other Participants/Trainee Support Costs	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	0	0	0	0	0	0
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0

	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget 1½ Section E. Total Participants/Trainee Support Costs	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0

	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	0	0	0	0	0	0
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0

	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget 1/2 Materials and Supplies	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	7,340	7,560	7,787	8,021	8,262	38,970
	Admin-Core-003 (988)	20,500	21,115	21,749	22,401	23,073	108,838
	Admin-Core-004 (516)	46,310	47,699	49,130	50,604	52,122	245,865
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	3,594,605	3,702,294	3,815,365	3,928,391	4,045,652	19,086,307
	Animal-Resources- 002 (350)	94,019	96,840	99,745	102,737	105,819	499,160
	Animal-Resources- 003 (983)	23,000	23,690	24,401	25,133	25,887	122,111
	Animal-Resources- 004 (760)	10,000	10,300	10,609	10,927	11,255	53,091

	Animal-Resources-005 (705)	18,000	18,540	19,097	19,669	20,259	95,565
	Animal-Resources-006 (199)	10,000	10,300	10,609	10,927	11,255	53,091
	Core-Services-001 (371)	5,000	5,150	5,305	5,464	5,628	26,547
	Core-Services-002 (755)	6,000	6,180	6,365	6,556	6,753	31,854
	Core-Services-003 (976)	30,000	30,900	31,827	32,782	33,765	159,274
	Core-Services-004 (462)	17,500	18,025	18,566	19,123	19,697	92,911
	Core-Services-005 (985)	13,000	13,390	13,792	14,205	14,631	69,018
	NPRC-Consortium-001 (365)	25,826	26,601	27,398	28,221	29,068	137,114
	Outreach-001 (218)	2,500	2,575	2,652	2,732	2,814	13,273
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	3,500	3,605	3,713	3,824	3,939	18,581
	Scientific-Units-002 (170)	4,000	4,120	4,244	4,371	4,502	21,237
	Scientific-Units-003 (916)	3,000	3,090	3,183	3,278	3,376	15,927
	Scientific-Units-004 (104)	3,000	3,090	3,183	3,278	3,376	15,927
TOTALS		3,937,100	4,055,064	4,178,720	4,302,644	4,431,133	20,904,661
R&R Budget & ½ Publication Costs	Admin-Core-001 (566)	0	0	0	0	0	0

	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	1,000	1,030	1,061	1,093	1,126	5,310
	Animal-Resources- 004 (760)	1,000	1,030	1,061	1,093	1,126	5,310
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	1,000	1,030	1,061	1,093	1,126	5,310
	Core-Services-001 (371)	1,000	1,030	1,061	1,093	1,126	5,310
	Core-Services-002 (755)	1,000	1,030	1,061	1,093	1,126	5,310
	Core-Services-003 (976)	1,000	1,030	1,061	1,093	1,126	5,310
	Core-Services-004 (462)	1,000	1,030	1,061	1,093	1,126	5,310
	Core-Services-005 (985)	1,000	1,030	1,061	1,093	1,126	5,310

	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	7,000	7,210	7,426	7,649	7,878	37,163
	Scientific-Units-002 (170)	8,000	8,240	8,487	8,742	9,004	42,473
	Scientific-Units-003 (916)	6,000	6,180	6,365	6,556	6,753	31,854
	Scientific-Units-004 (104)	6,000	6,180	6,365	6,556	6,753	31,854
TOTALS		35,000	36,050	37,131	38,247	39,396	185,824
R&R Budget 1½ Consultant Services	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	14,000	14,420	14,853	15,299	15,758	74,330
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources-001 (079)	0	0	0	0	0	0
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0

	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium-001 (365)	454,430	468,063	482,106	496,570	511,467	2,412,636
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		468,430	482,483	496,959	511,869	527,225	2,486,966

R&R Budget 1/2 ADP/Computer Services	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources-001 (079)	0	0	0	0	0	0
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0

	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget ½ Subawards/Consortium/Contractual Costs	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0

	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0

	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget $\frac{1}{2}$ Equipment or Facility Rental User Fees	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	0	0	0	0	0	0
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	0	0	0	0	0	0
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0

	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		0	0	0	0	0	0
R&R Budget 1½ Alterations and Renovations	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0

	Admin-Core-005 (282)	121,800	121,800	81,200	121,800	121,800	568,400
	Animal-Resources-001 (079)	0	0	0	0	0	0
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0
	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	0	0	0	0	0	0
	Pilot-Research-001 (446)	0	0	0	0	0	0

	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		121,800	121,800	81,200	121,800	121,800	568,400
R&R Budget 1/2 Other Direct Cost	Admin-Core-001 (566)	0	0	0	0	0	0
1	Admin-Core-002 (706)	4,000	4,120	4,244	4,371	4,502	21,237
	Admin-Core-003 (988)	3,000	3,090	3,183	3,278	3,376	15,927
	Admin-Core-004 (516)	250	258	266	274	283	1,331
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources-001 (079)	1,500	1,545	1,591	1,639	1,688	7,963
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	500	515	530	546	562	2,653
	Animal-Resources-005 (705)	500	515	530	546	562	2,653

	Animal-Resources-006 (199)	500	515	530	546	562	2,653
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	3,000	3,090	3,183	3,278	3,376	15,927
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	2,500	2,575	2,652	2,732	2,814	13,273
	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	3,000	3,090	3,183	3,278	3,376	15,927
	Pilot-Research-001 (446)	300,000	300,000	300,000	300,000	300,000	1,500,000
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		318,750	319,313	319,892	320,488	321,101	1,599,544
R&R Budget 1 1/2 Other Direct Cost 2	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	5,000	5,150	5,305	5,464	5,628	26,547

	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	1,920	1,978	2,037	2,098	2,161	10,194
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	116,000	119,480	123,064	126,756	130,558	615,858
	Animal-Resources- 002 (350)	0	0	0	0	0	0
	Animal-Resources- 003 (983)	0	0	0	0	0	0
	Animal-Resources- 004 (760)	20,000	20,600	21,218	21,855	22,511	106,184
	Animal-Resources- 005 (705)	0	0	0	0	0	0
	Animal-Resources- 006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium- 001 (365)	0	0	0	0	0	0

	Outreach-001 (218)	4,000	4,120	4,244	4,371	4,502	21,237
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		146,920	151,328	155,868	160,544	165,360	780,020
R&R Budget 1/2 Other Direct Cost 3	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	0	0	0	0	0	0
	Admin-Core-003 (988)	0	0	0	0	0	0
	Admin-Core-004 (516)	0	0	0	0	0	0
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources-001 (079)	4,175	4,300	4,429	4,562	4,699	22,165
	Animal-Resources-002 (350)	0	0	0	0	0	0
	Animal-Resources-003 (983)	0	0	0	0	0	0
	Animal-Resources-004 (760)	0	0	0	0	0	0

	Animal-Resources-005 (705)	0	0	0	0	0	0
	Animal-Resources-006 (199)	0	0	0	0	0	0
	Core-Services-001 (371)	0	0	0	0	0	0
	Core-Services-002 (755)	0	0	0	0	0	0
	Core-Services-003 (976)	0	0	0	0	0	0
	Core-Services-004 (462)	0	0	0	0	0	0
	Core-Services-005 (985)	0	0	0	0	0	0
	NPRC-Consortium-001 (365)	0	0	0	0	0	0
	Outreach-001 (218)	2,000	2,060	2,122	2,186	2,252	10,620
	Pilot-Research-001 (446)	0	0	0	0	0	0
	Scientific-Units-001 (056)	0	0	0	0	0	0
	Scientific-Units-002 (170)	0	0	0	0	0	0
	Scientific-Units-003 (916)	0	0	0	0	0	0
	Scientific-Units-004 (104)	0	0	0	0	0	0
TOTALS		6,175	6,360	6,551	6,748	6,951	32,785
R&R Budget 1½ Section F. Total Other Direct Cost	Admin-Core-001 (566)	0	0	0	0	0	0

	Admin-Core-002 (706)	30,340	31,250	32,189	33,155	34,150	161,084
	Admin-Core-003 (988)	23,500	24,205	24,932	25,679	26,449	124,765
	Admin-Core-004 (516)	48,480	49,935	51,433	52,976	54,566	257,390
	Admin-Core-005 (282)	121,800	121,800	81,200	121,800	121,800	568,400
	Animal-Resources- 001 (079)	3,716,280	3,827,619	3,944,449	4,061,348	4,182,597	19,732,293
	Animal-Resources- 002 (350)	94,019	96,840	99,745	102,737	105,819	499,160
	Animal-Resources- 003 (983)	24,000	24,720	25,462	26,226	27,013	127,421
	Animal-Resources- 004 (760)	31,500	32,445	33,418	34,421	35,454	167,238
	Animal-Resources- 005 (705)	18,500	19,055	19,627	20,215	20,821	98,218
	Animal-Resources- 006 (199)	11,500	11,845	12,200	12,566	12,943	61,054
	Core-Services-001 (371)	6,000	6,180	6,366	6,557	6,754	31,857
	Core-Services-002 (755)	10,000	10,300	10,609	10,927	11,255	53,091
	Core-Services-003 (976)	31,000	31,930	32,888	33,875	34,891	164,584
	Core-Services-004 (462)	18,500	19,055	19,627	20,216	20,823	98,221
	Core-Services-005 (985)	16,500	16,995	17,505	18,030	18,571	87,601

	NPRC-Consortium-001 (365)	480,256	494,664	509,504	524,791	540,535	2,549,750
	Outreach-001 (218)	11,500	11,845	12,201	12,567	12,944	61,057
	Pilot-Research-001 (446)	300,000	300,000	300,000	300,000	300,000	1,500,000
	Scientific-Units-001 (056)	10,500	10,815	11,139	11,473	11,817	55,744
	Scientific-Units-002 (170)	12,000	12,360	12,731	13,113	13,506	63,710
	Scientific-Units-003 (916)	9,000	9,270	9,548	9,834	10,129	47,781
	Scientific-Units-004 (104)	9,000	9,270	9,548	9,834	10,129	47,781
TOTALS		5,034,175	5,172,398	5,276,321	5,462,340	5,612,966	26,558,200
R&R Budget 1/2 Section G. Total Direct Cost (A thru F)	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	454,005	469,412	483,399	497,493	514,624	2,418,933
	Admin-Core-003 (988)	332,118	347,002	361,190	375,802	391,118	1,807,230
	Admin-Core-004 (516)	557,427	579,323	605,952	630,007	655,274	3,027,983
	Admin-Core-005 (282)	599,426	599,766	597,386	599,144	599,966	2,995,688
	Animal-Resources-001 (079)	4,062,138	4,190,830	4,324,195	4,453,308	4,580,551	21,611,022
	Animal-Resources-002 (350)	100,367	103,293	106,265	109,316	112,461	531,702
	Animal-Resources-003 (983)	265,231	277,454	282,667	293,909	305,781	1,425,042

	Animal-Resources-004 (760)	291,542	305,123	313,018	324,624	338,116	1,572,423
	Animal-Resources-005 (705)	109,842	115,545	121,052	126,724	132,716	605,879
	Animal-Resources-006 (199)	92,692	96,467	99,974	103,593	107,364	500,090
	Core-Services-001 (371)	63,567	66,280	68,840	71,435	74,158	344,280
	Core-Services-002 (755)	46,783	48,494	50,200	51,953	53,779	251,209
	Core-Services-003 (976)	218,773	227,919	236,585	245,421	254,677	1,183,375
	Core-Services-004 (462)	176,021	181,334	190,361	197,458	204,897	950,071
	Core-Services-005 (985)	223,520	228,639	231,864	237,426	241,953	1,163,402
	NPRC-Consortium-001 (365)	502,469	517,515	533,320	549,411	565,989	2,668,704
	Outreach-001 (218)	99,213	101,858	107,766	112,005	116,449	537,291
	Pilot-Research-001 (446)	300,000	300,000	300,000	300,000	300,000	1,500,000
	Scientific-Units-001 (056)	238,382	243,780	247,049	254,920	268,103	1,252,234
	Scientific-Units-002 (170)	262,934	268,046	275,614	286,366	294,347	1,387,307
	Scientific-Units-003 (916)	283,187	288,657	299,369	307,648	315,968	1,494,829
	Scientific-Units-004 (104)	233,760	238,797	249,563	257,246	265,298	1,244,664
TOTALS		9,513,397	9,795,534	10,085,629	10,385,209	10,693,589	50,473,358

R&R Budget 1/2 Section H. Indirect Costs	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	103,059	106,557	109,732	112,931	116,820	549,099
	Admin-Core-003 (988)	75,391	78,769	81,991	85,307	88,784	410,242
	Admin-Core-004 (516)	126,536	131,506	137,551	143,011	148,747	687,351
	Admin-Core-005 (282)	0	0	0	0	0	0
	Animal-Resources- 001 (079)	922,105	951,318	981,592	1,010,901	1,039,785	4,905,701
	Animal-Resources- 002 (350)	22,783	23,448	24,122	24,815	25,529	120,697
	Animal-Resources- 003 (983)	60,207	62,982	64,165	66,717	69,412	323,483
	Animal-Resources- 004 (760)	66,180	69,263	71,056	73,690	76,752	356,941
	Animal-Resources- 005 (705)	24,934	26,228	27,479	28,766	30,127	137,534
	Animal-Resources- 006 (199)	21,041	21,898	22,694	23,516	24,372	113,521
	Core-Services-001 (371)	14,430	15,046	15,627	16,216	16,834	78,153
	Core-Services-002 (755)	10,620	11,008	11,395	11,793	12,208	57,024
	Core-Services-003 (976)	49,661	51,738	53,705	55,711	57,812	268,627
	Core-Services-004 (462)	39,957	41,163	43,212	44,823	46,512	215,667

	Core-Services-005 (985)	50,739	51,901	52,633	53,896	54,923	264,092
	NPRC-Consortium-001 (365)	114,060	117,476	121,064	124,716	128,480	605,796
	Outreach-001 (218)	22,521	23,122	24,463	25,425	26,434	121,965
	Pilot-Research-001 (446)	68,100	68,100	68,100	68,100	68,100	340,500
	Scientific-Units-001 (056)	54,113	55,338	56,081	57,867	60,860	284,259
	Scientific-Units-002 (170)	59,686	60,846	62,564	65,005	66,817	314,918
	Scientific-Units-003 (916)	64,283	65,525	67,956	69,836	71,725	339,325
	Scientific-Units-004 (104)	53,064	54,207	56,651	58,395	60,223	282,540
TOTALS		2,023,470	2,087,439	2,153,833	2,221,437	2,291,256	10,777,435
R&R Budget ½ Section I. Total Direct and Indirect Costs (G +H)	Admin-Core-001 (566)	0	0	0	0	0	0
	Admin-Core-002 (706)	557,064	575,969	593,131	610,424	631,444	2,968,032
	Admin-Core-003 (988)	407,509	425,771	443,181	461,109	479,902	2,217,472
	Admin-Core-004 (516)	683,963	710,829	743,503	773,018	804,021	3,715,334
	Admin-Core-005 (282)	599,426	599,766	597,386	599,144	599,966	2,995,688
	Animal-Resources-001 (079)	4,984,243	5,142,148	5,305,787	5,464,209	5,620,336	26,516,723
	Animal-Resources-002 (350)	123,150	126,741	130,387	134,131	137,990	652,399

	Animal-Resources-003 (983)	325,438	340,436	346,832	360,626	375,193	1,748,525
	Animal-Resources-004 (760)	357,722	374,386	384,074	398,314	414,868	1,929,364
	Animal-Resources-005 (705)	134,776	141,773	148,531	155,490	162,843	743,413
	Animal-Resources-006 (199)	113,733	118,365	122,668	127,109	131,736	613,611
	Core-Services-001 (371)	77,997	81,326	84,467	87,651	90,992	422,433
	Core-Services-002 (755)	57,403	59,502	61,595	63,746	65,987	308,233
	Core-Services-003 (976)	268,434	279,657	290,290	301,132	312,489	1,452,002
	Core-Services-004 (462)	215,978	222,497	233,573	242,281	251,409	1,165,738
	Core-Services-005 (985)	274,259	280,540	284,497	291,322	296,876	1,427,494
	NPRC-Consortium-001 (365)	616,529	634,991	654,384	674,127	694,469	3,274,500
	Outreach-001 (218)	121,734	124,980	132,229	137,430	142,883	659,256
	Pilot-Research-001 (446)	368,100	368,100	368,100	368,100	368,100	1,840,500
	Scientific-Units-001 (056)	292,495	299,118	303,130	312,787	328,963	1,536,493
	Scientific-Units-002 (170)	322,620	328,892	338,178	351,371	361,164	1,702,225
	Scientific-Units-003 (916)	347,470	354,182	367,325	377,484	387,693	1,834,154

	Scientific-Units-004 (104)	286,824	293,004	306,214	315,641	325,521	1,527,204
TOTALS		11,536,867	11,882,973	12,239,462	12,606,646	12,984,845	61,250,793

**Senior/Key Personnel
Summary**

Name	Organization	Role on Project	Components
Lewin, Harris A	University of California Davis	PD/PI(Contact)	Overall
Excluded by Requester	University of California Davis	Other: Core Scientist	Scientific-Units-001 (056)
	University of California Davis	Other: Scientific Unit Leader/Core Scientist	Scientific-Units-001 (056)
	University of California Davis	Other: Interim Director	Admin-Core-001 (566)
	University of California Davis	Other: Interim Director	Admin-Core-002 (706)
	University of California Davis	Other: Interim Director	NPRC-Consortium-001 (365)
	University of California Davis	Other: Core Scientist	Scientific-Units-002 (170)
	University of California Davis	Other: Other Significant Contributor	Animal-Resources-004 (760)
	University of California Davis	Other: Core Scientist	Core-Services-001 (371)
	University of California Davis	Other: Core Scientist	Scientific-Units-001 (056)
	University of California Davis	Other: Core Scientist	Core-Services-005 (985)
	University of California Davis	Other: Core Scientist	Scientific-Units-003 (916)
	University of California Davis	Other: Primate Medicine Senior Manager	Animal-Resources-003 (983)
	University of California Davis	Other: Senior Veterinarian	Animal-Resources-003 (983)
	University of California Davis	Other: Senior Veterinarian	Animal-Resources-003 (983)
	University of California Davis	Other: Core Scientist	Scientific-Units-002 (170)
	University of California Davis	Other: Senior Veterinarian	Animal-Resources-003 (983)
	University of California Davis	Other: Assistant Director for IT Services	Admin-Core-004 (516)
	University of California Davis	Other: Core Leader/Core Scientist	Core-Services-003 (976)
	University of California Davis	Other: Core Scientist	Scientific-Units-002 (170)
	University of California Davis	Other: Core Scientist	Scientific-Units-003 (916)
	University of California Davis	Other: Core Scientist	Core-Services-005 (985)
	University of California Davis	Other: Core Scientist	Scientific-Units-004 (104)
	University of California Davis	Other: Associate Veterinary Pathologist	Animal-Resources-004 (760)
	University of California Davis	Other: Postdoc Pathologist	Animal-Resources-004 (760)

Excluded by Requester	University of California Davis	Other: Core Leader/Core Scientist	Core-Services-002 (755)
	University of California Davis	Other: Core Scientist	Scientific-Units-003 (916)
	University of California Davis	Other: Senior Veterinarian	Animal-Resources-003 (983)
Lewin, Harris A	University of California Davis	Other: Vice Chancellor for Research	Admin-Core-002 (706)
Excluded by Requester	University of California Davis	Other: Scientific Unit Leader/Core Scientist	Scientific-Units-002 (170)
	University of California Davis	Other: Core Scientist	Scientific-Units-001 (056)
	University of California Davis	Other: Core Leader/Core Scientist	Animal-Resources-005 (705)
	University of California Davis	Other: Core Leader/Core Scientist	Core-Services-001 (371)
	University of California Davis	Other: Core Scientist	Scientific-Units-001 (056)
	University of California Davis	Other: Core Scientist	Scientific-Units-002 (170)
	University of California Davis	Other: Associate Director for Research	Admin-Core-002 (706)
	University of California Davis	Other: Associate Director for Research	Pilot-Research-001 (446)
	University of California Davis	Other: Scientific Unit Leader/Core Scientist	Scientific-Units-004 (104)
	University of California Davis	Other: Assoc Director for Admin and Operations	Admin-Core-002 (706)
	University of California Davis	Other: Assoc Director for Admin and Operations	Admin-Core-003 (988)
	University of California Davis	Other: Assoc Director for Admin and Operations	Admin-Core-005 (282)
	University of California Davis	Other: Assoc Director for Admin and Operations	Outreach-001 (218)
	University of California Davis	Other: Core Scientist	Core-Services-004 (462)
	University of California Davis	Other: Core Scientist	Scientific-Units-004 (104)
	University of California Davis	Other: Pathology Senior Manager	Animal-Resources-004 (760)
	University of California Davis	Other: Associate Director for Primate Services	Admin-Core-002 (706)
	University of California Davis	Other: Assoc Director for Primate Services	Animal-Resources-001 (079)
	University of California Davis	Other: Assoc Director for Primate Services	Animal-Resources-002 (350)

Excluded by Requester	University of California Davis	Other: Assoc Director for Primate Services	Animal-Resources-003 (983)
	University of California Davis	Other: Assoc Director for Primate Services	Animal-Resources-004 (760)
	University of California Davis	Other: Assoc Director for Primate Services	Core-Services-003 (976)
	University of California Davis	Other: Associate Veterinarian	Animal-Resources-003 (983)
	University of California Davis	Other: Senior Veterinarian	Animal-Resources-003 (983)
	University of California Davis	Other: Core Leader/Core Scientist	Core-Services-004 (462)
	University of California Davis	Other: Core Scientist	Scientific-Units-004 (104)
	University of California Davis	Other: Core Leader	Animal-Resources-006 (199)
	University of California Davis	Other: Core Scientist	NPRC-Consortium-001 (365)
	University of California Davis	Other: Core Scientist	Scientific-Units-002 (170)
	University of California Davis	Other: Core Leader/Core Scientist	Core-Services-005 (985)
	University of California Davis	Other: Scientific Unit Leader/Core Scientist	Scientific-Units-003 (916)
	University of California Davis	Other: Senior Veterinary Pathologist	Animal-Resources-004 (760)
	University of California Davis	Other: Core Scientist	Animal-Resources-001 (079)
	University of California Davis	Other: Core Scientist	Scientific-Units-003 (916)

Biosketches Excluded by Requester- pages 78-187

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: — 1 — 2 — 3 — 4 — 5 — 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input checked="" type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number A3433-01	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename OV_Abstract.pdf
8. Project Narrative*	OV_Narrative.pdf
9. Bibliography & References Cited	OV_BibliographyandReferencesCited.pdf
10. Facilities & Other Resources	OV_FacilitiesandOtherResources.pdf
11. Equipment	OV_Equipment.pdf

OVERVIEW

ABSTRACT

The California National Primate Research Center (CNPRC), located at the University of California, Davis, requests funds to renew the base operating grant #P51-OD011107 for the next five year period (May 1, 2015 through April 30, 2020). The CNPRC renewal reflects a strategic emphasis on multidisciplinary research teams that focus on the development and use of nonhuman primate models of human health and disease. Currently in the 53rd year of operation, the CNPRC serves a range of NIH-supported investigators nationwide. From inception through the current year, the CNPRC has been highly responsive to the research community by providing high quality animals, facilities, tools, and services driven by the intellectual infrastructure of the Core Scientists that guide and conduct basic and translational research with nonhuman primates. The goals for the next funding period are reflected in the following Specific Aims: (1) Conduct state-of-the-art research and scientifically contribute to the understanding and treatment of human disease with nonhuman primate models across the age spectrum, (2) Provide exceptional nonhuman primate expertise and services to investigators at the local, regional, and national levels to advance NIH-supported research excellence, (3) Mentor and train the next generation of translational investigators with nonhuman primate expertise, and (4) Ensure the highest standards of responsible conduct of research and animal care. Plans for the next funding period build upon expertise, productivity, and innovation; strong ties with the host institution and national programs; and maximizing resources for NIH-funded research. Support is requested for Administrative Services (Director's Office, Administration and Operations Services, Information Technology Services, Facilities Improvement), Primate Services (Colony Management and Research Services, National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, Genetics Management Services), Service Cores (Behavior Research, Endocrine, Immunology and Pathogen Detection, Inhalation Exposure, Multimodal Imaging), Scientific Research Units (Brain, Mind, and Behavior, Infectious Diseases, Reproductive Sciences and Regenerative Medicine, Respiratory Diseases), and for Outreach, the Pilot Research Program, and NPRC Consortium activities. Through targeted opportunities and University of California initiatives, the CNPRC will actively promote the recruitment of faculty to the program, and continue to build infrastructure, expertise, and essential services to meet the growing needs of investigators and trainees.

OVERVIEW

NARRATIVE

The CNPRC is an established national resource that has as a primary mission to conduct nonhuman primate research at the highest quality level, and to provide services and resources to the greater research community. The overriding objective of the program is to advance human and nonhuman primate health and healthy aging.

OVERVIEW

FACILITIES AND OTHER RESOURCES

The overall facility consists of 175,409 sq. ft., which includes research laboratories, an inhalation exposure facility, indoor animal housing, a Quarantine Facility, animal support areas, and administrative space. The field corrals and corn cribs (outdoor housing) encompasses [REDACTED] Construction was also completed for the Respiratory Disease Center building, which has increased office, laboratory, and inhalation exposure space by 19,000 sq. ft. Included on the Primate Center grounds is the Center for Comparative Medicine that provides laboratory and office space for Core Scientists in the Infectious Diseases Research Unit.

Specific Animal Location

Laboratories: See individual sections of the application.

Clinical: Primate Medicine provides centralized clinical care and veterinary oversight to ensure compliance with the highest quality standards of research conduct and animal care. The Primate Medicine team is responsible for the clinical care of ~5,000 nonhuman primates which encompasses a range of health care needs across the lifespan, from neonatal to geriatric stages, and from preventive medicine to intensive care. Clinical care and related procedures are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see Primate Services).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. The Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and Information Technology Services provides desktop support and other related services. See Information Technology Services section for details.

Office: See individual sections of the application.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. See individual sections of the application.

OVERVIEW

EQUIPMENT

See individual sections of the application.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
Prefix:	First Name*: Harris	Middle Name A	Last Name*: Lewin	Suffix:
Position/Title*:				
Organization Name*:	University of California Davis			
Department:				
Division:	Office of Research			
Street1*:	One Shields Ave			
Street2:				
City*:	Davis			
County:				
State*:	CA: California			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	956165270			
Phone Number*: 530-754-7764		Fax Number:		E-Mail*: lewin@ucdavis.edu
Credential, e.g., agency login:	eRA Commons User Name			
Project Role*: PD/PI		Other Project Role Category:		
Degree Type: PhD		Degree Year: 1984		
Attach Biographical Sketch*:		File Name		
Attach Current & Pending Support:		Lewin-bio.pdf		

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☒ Yes ☐ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	10,685,000.00	Sales, Services, Per Diem
2	11,272,675.00	Sales, Services, Per Diem
3	11,892,672.00	Sales, Services, Per Diem
4	12,546,769.00	Sales, Services, Per Diem
5	13,236,841.00	Sales, Services, Per Diem

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?*

☐ No ☒ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

0043

0062

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	OV_SpecificAims.pdf
3. Research Strategy*	OV_ResearchStrategy.pdf
4. Progress Report Publication List	OV_ProgressReportPubs.pdf
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	OV_VertebrateAnimals.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	OV_LETTERS.pdf
13. Resource Sharing Plan(s)	OV_ResourceSharingPlan.pdf
Appendix (if applicable)	
14. Appendix	TableofEmployeesandEffort.pdf ListofAffiliateandVisitingScientists.pdf OverallSourcesofSupport.pdf

OVERVIEW

SPECIFIC AIMS

The California National Primate Research Center (CNPRC) presents a strategic vision for the future in this renewal application of the base operating grant #P51-OD011107. The CNPRC renewal reflects an emphasis on multidisciplinary research teams that focus on the development and use of nonhuman primate models of human health and disease. Currently in the 53rd year of operation, the CNPRC remains a central component and driving force in the National Primate Research Centers (NPRCs) program, serving a spectrum of NIH-supported investigators nationwide as evident by a strong grant portfolio of approximately \$150 million during the current funding period. From inception through the current year, the CNPRC has been highly responsive to the research community in meeting NIH strategic priorities by providing high quality animals, facilities, tools, and services driven by the intellectual infrastructure of the Core Scientists that guide and conduct basic and translational research with nonhuman primates. The goals for the next funding period are reflected in the following Specific Aims that address accessible state-of-the-art research opportunities for investigators and trainees, and promote the study of human health and healthy aging in nonhuman primates.

Specific Aim 1. Conduct state-of-the-art research and scientifically contribute to the understanding and treatment of human disease with nonhuman primate models across the age spectrum.

Plan. The overriding objective is to advance the CNPRC resource through scientific achievements driven by Core Scientists in translational teams that focus on Brain, Mind, and Behavior; Infectious Diseases; Reproductive Sciences and Regenerative Medicine; and Respiratory Diseases. Key strategic priorities include studies that address the remediation of abnormal function at the level of the brain and behavior; the role of development and aging on immunity, infection, and organ structure and function; and the conduct of innovative investigational new drug (IND)-enabling investigations to support new regenerative medicine and gene therapy clinical trials in all age groups. Research activities will contribute to the understanding of the underpinnings of chronic disease from the earliest developmental stages through maturation and aging, and using new biomarkers and novel *in vivo* imaging tools.

Specific Aim 2. Provide exceptional nonhuman primate expertise and services to investigators at the local, regional, and national levels to advance NIH-supported research excellence.

Plan. The primary goal is to facilitate research and ensure a supportive environment for the investigation of behavioral, neurologic, infectious, reproductive, developmental, and organ-specific inherited and acquired disorders, such as those related to the lung, through specialized facilities, expertise, and resources specific to nonhuman primates. Established CNPRC Cores (Behavior, Endocrine, Immunology and Pathogen Detection, Inhalation Exposure, Multimodal Imaging) and specialized repositories of nonhuman primate cells, tissues, and data will provide unique opportunities for collaborative research, training, pilot projects, and new NIH grants.

Specific Aim 3. Mentor and train the next generation of translational investigators with nonhuman primate expertise.

Plan. A central mission is to mentor and train new investigators at all career stages in order to achieve expertise in primatology, the design and study of nonhuman primate models of human health and disease, team science, and the conduct of multidisciplinary translational investigations.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

Plan. The CNPRC will continue to deliver high quality veterinary care and research support integrated with specialized expertise in nonhuman primate behavior, genetics, infectious diseases, and reproduction for colony management, psychological well-being, and genetic heterogeneity to meet current and future research needs.

The overarching vision for the next funding period builds upon expertise, productivity, and innovation; strong ties with institutional and national programs; and maximizing resources for NIH funded research. Core Scientists will promote interdisciplinary areas of common interest, such as lifespan health, translation of research findings to clinical trials, and build upon a strong track record of successful partnerships locally, regionally, and nationally. Through targeted opportunities and University of California initiatives, the CNPRC will actively promote the recruitment of faculty to the program, and continue to build infrastructure, expertise, and essential services to meet the growing needs of investigators and trainees.

OVERVIEW

RESEARCH STRATEGY

INTRODUCTION

The California National Primate Research Center (CNPRC), located at the University of California, Davis (UC Davis), unifies key personnel, infrastructure, and services across research domains for a common goal: ***the advancement of nonhuman primate models for the study and treatment of human disease***. The CNPRC brings together a strong team of Core Scientists, veterinarians, technicians, and administrative staff to capitalize on the depth and breadth of translational research with nonhuman primate models that cuts across the human lifespan. The CNPRC is an established national resource that has as a primary mission to conduct nonhuman primate research at the highest quality level, and to provide services and resources to the greater research community. This established infrastructure includes experienced Core Scientists with joint appointments in academic departments in UC Davis schools and colleges (e.g., Schools of Medicine and Veterinary Medicine, Colleges of Engineering and Letters and Science) and integrates and leverages several key institutional Centers and programs (Figure 1). Four broad Scientific Research Units (Brain, Mind, and Behavior; Infectious Diseases; Reproductive Sciences and Regenerative Medicine; Respiratory Diseases) include 20 Core Scientists that maintain active NIH-supported research, service, and training programs, and are collectively a resource for investigators and trainees nationwide. Working with nonhuman primates requires specialized knowledge and expertise, and Core Scientists provide the intellectual infrastructure for a range of collaborative opportunities, multidisciplinary partnerships, and novel services to support and facilitate research with nonhuman primates. During the current funding period, Core Scientists collaborated with approximately 350 Affiliate Scientists and other investigators from institutions across the U.S. (128 from UC Davis), published over 400 manuscripts, and mentored 300 trainees (undergraduate to junior faculty). Extramural grants during the current funding period for all Units and facilities combined totaled approximately \$150 million.

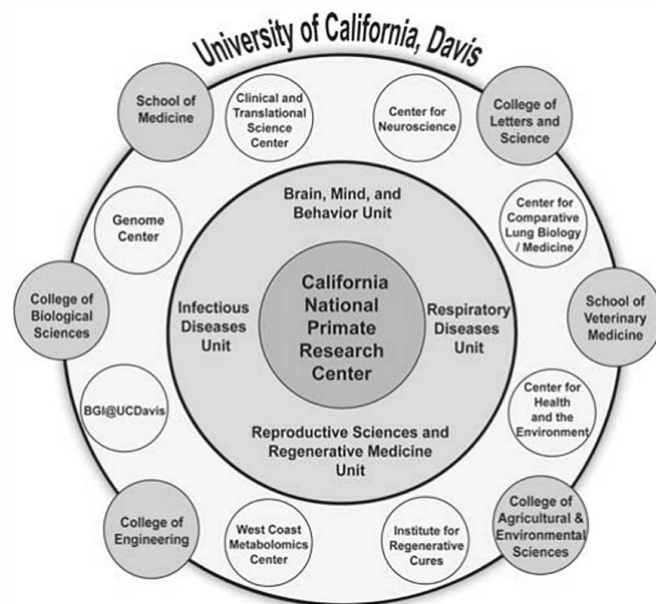


Figure 1. UC Davis provides a rich academic home for the California National Primate Research Center.

Response to Summary Statement

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE

Background and Mission

The CNPRC is one of seven National Primate Research Centers (NPRCs) supported by the NIH, Office of the Director (NIH/OD), and is currently in the 53rd year of operation. The CNPRC is an Organized Research Unit placed administratively under the UC Davis Office of the Vice Chancellor for Research (see Organizational Chart, below). Administrative placement within the Office of the Vice Chancellor for Research is advantageous because the CNPRC conducts multidisciplinary research, and the Core Scientists represent many UC Davis schools and colleges. The CNPRC's central mission, as defined in the broad objectives stated in the Program Guidelines for NPRCs (7th Edition), is *to provide support for scientists who use nonhuman primates in their research, to increase understanding of nonhuman primate biology, and to improve human health and quality of life through support of exceptional nonhuman primate research programs.*

Nonhuman Primates: Models of Human Health and Disease. Nonhuman primates are essential to understand biological functions, study complex human diseases, and address safety of new diagnostics and therapies proposed for human use. They share many important features with humans because of their close phylogenetic relationship; similarities in reproduction, development, physiology, immunology, anatomy, genetics, cognition, and social complexity aid in overcoming

Excluded by Requester dblocks to clinical translation [redacted] 2014].

similarities also include organ ontogeny and maturation, placental structure, length of gestation, growth characteristics, and the development of the immune system. For example, there is a strong history of use of simian immunodeficiency virus (SIV) infection in rhesus monkeys as a model of HIV/AIDS; this model has provided a significant understanding of pathogenic mechanisms, disease prevention, and promoted the development of new interventional strategies [redacted] 2013]. The testing of new antiretroviral drugs has been instrumental in

Excluded by Requester dramatically reducing the morbidity and mortality of HIV-

Excluded by Requester individuals [redacted] 2012]. Monkeys and

share many reproductive features including a menstrual cycle of a similar length and the 'rescue' of the corpus luteum by chorionic gonadotropin, which is a comparable feature of the conceptive cycle in both species. Monkeys have also been widely used as preclinical models for human bone marrow transplantation and stem cell gene therapy, and have shown substantial advantages when compared to other species. Long-term engraftment is challenging to assess in a short-lived mouse model, and differences between mouse and human host cell receptors have led to findings that have not predicted outcomes in the human clinical setting [redacted] 2010]. Studies

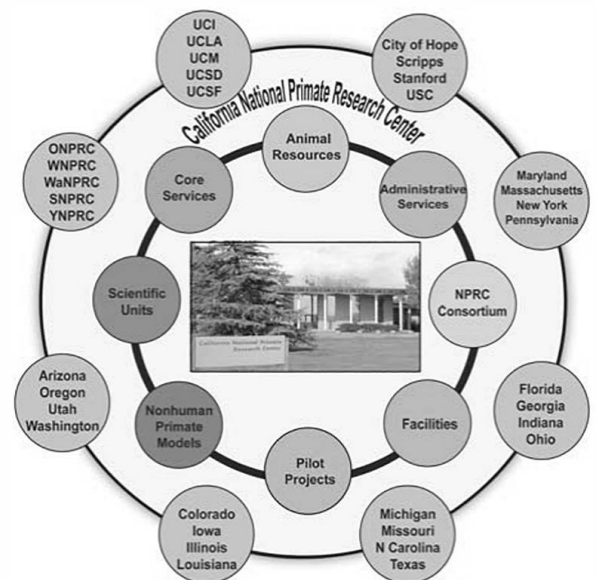


Figure 2. The CNPRC Scientific Research Units and Core Services are utilized by investigators on the UC and other California campuses and by researchers at institutions across the U.S. Collaborative interactions are also in place with other NPRCs, both with individual Core Scientists and through NPRC Consortium projects.

have also indicated that the histology and time course for allograft rejection in monkeys parallels humans because of similarities in major histocompatibility complex (MHC) genes and immune ontogeny [2001; Excluded by Requester 2009]. While rodents are very useful for early discovery, recent investigations have noted that mice show different responses to inflammatory pathways when compared to humans [2013] and raise concerns regarding reproducibility [2013]. Nonhuman primates represent a crucial step in validating research findings and filling a critical gap between murine models and humans. Thus, there is a pressing need for nonhuman primates that parallel the human condition, and within a supportive infrastructure with the necessary expertise to facilitate access and use.

Importance of the CNPRC as a National Resource. The CNPRC has successfully supported a broad program of research, providing essential resources to investigators nationwide (Figure 2). Fostered by the intellectual infrastructure of the Core Scientists, this robust program has produced an outstanding record of scientific achievements demonstrated by the CNPRC grant portfolio of approximately \$150 million, unique services (e.g., assays, tools, imaging, training), and research opportunities for scientists at the regional, national, and international levels. Examples include:

- **Affiliate Scientists** (University of Arizona) and (Mt. Sinai School of Medicine) with (Maryland) and Core Scientist (Brain, Mind, and Behavior Research Unit) have assessed cognitive function in aging rhesus macaques through 4 NIH-funded R01s and a program project grant. Analyses of complex behaviors across the lifespan of animals have elucidated brain regions that are impacted by the normal aging process. Data from rats, monkeys, and humans converge, all indicating that recognition memory and vision perception are impaired with advanced age, and that these cognitive processes are also disrupted in animals with lesions of the perirhinal cortex, indicating that the functional integrity of this structure is disrupted in old age [et al., 2012]. These studies also support the importance of the **National Institute on Aging (NIA) Colony** located at the CNPRC, and the integrated infrastructure and services that ensure the research goals of off-site investigators can be achieved.

- also collaborates with Core Scientist **Reproductive Sciences and Regenerative Medicine Research Unit** through an NIH program project grant supported since 1999 (P01-AG016765). Studies recently tested the hypothesis that the number and morphology of mitochondria in dorsolateral prefrontal cortex presynaptic boutons are altered with aging and menopause in rhesus monkeys. It was shown that these metrics correlated with delayed response accuracy, a well-characterized measure of dorsolateral prefrontal cortex-dependent working memory. Published outcomes have suggested that hormone replacement therapy, highly relevant to women's healthy aging, may benefit cognitive aging in part by promoting mitochondrial and synaptic health in the dorsolateral prefrontal cortex [201]. long-standing program has benefited substantially from the expertise in reproductive endocrinology groundbreaking research on the menopausal transition at the CNPRC; the physiology of the menopausal transition is only shared by higher primate species. After decades of focusing only on ovarian function, a new understanding of the endocrine foundations has been uncovered through studies in nonhuman primates at the CNPRC [2012]. has also benefited from the many services available at the CNPRC to facilitate his ongoing research including those provided in **Primate Services** (e.g., animal selection, special husbandry and enrichment needs, veterinary and pathology support) and through Core Science Services such as those provided in the **Endocrine Core**.

- The National Heart, Lung, and Blood Institute (NHLBI) Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases was established at the CNPRC in 2001, and is a unique resource that has served a crucial role in the gene therapy field by addressing essential questions in gene delivery and providing NHLBI-funded investigators with opportunities to assess new vector constructs in nonhuman primates that advance the field [2012]. This program aids investigators in addressing crucial gaps, and to accelerate new NIH grant submissions and investigational new drug (IND) applications. For example, (University of Florida) has achieved the overall goal of utilizing adeno-associated virus (AAV) expression of human acid alpha-glucosidase in Pompe patients; the utility of AAV was established in nonhuman primates, resulting in use in 3-14 year-old Pompe patients who have developed ventilator dependence [2013]. Similarly, in collaboration with (City of), the safety and gene transfer efficiency of a lentiviral vector were evaluated, demonstrating a lack of toxicity and no adverse effects in fetal and juvenile monkeys which was critical in gaining approval for an IND

application and conducting the first-in-human trial of an expressed siRNA in a lentiviral vector [Excluded by Requester] et al., 2010].

- A vital component of research efforts of Affiliate Scientist [Excluded by Requester] (Oregon Health and Sciences University) is to evaluate human cytomegalovirus (CMV) as a vaccine vector for HIV and other clinically relevant pathogens for which no vaccines currently exist [Excluded by Requester] 2013]. These studies utilize the fetal rhesus monkey CMV (RhCMV) pathogenesis model jointly optimized by Core Scientists [Excluded by Requester] (Infectious Diseases Research Unit) and [Excluded by Requester] (Reproductive Sciences and Regenerative Medicine Research Unit) [Excluded by Requester] et al., 2006; [Excluded by Requester] et al., 2002] [Excluded by Requester] and colleagues have published multiple studies demonstrating that engineered RhCMV genomes expressing SIV antigens elicits 50% protective efficacy against repeated challenge with pathogenic SIV. In an effort to translate findings in the monkey model to human clinical trials, [Excluded by Requester] are working together to test modified RhCMV vectors for safety through two NIH grants (R01-AI095113, P01-AI094417) and a [Private Source] Award. The results of these studies inform [Excluded by Requester] decisions on the vectors to advance to preclinical/clinical testing. One example that highlights the unique capability and importance of this model is the observation that a modified RhCMV variant, demonstrated to be extremely attenuated for growth in adult monkeys, retained pathogenicity in fetal monkeys.

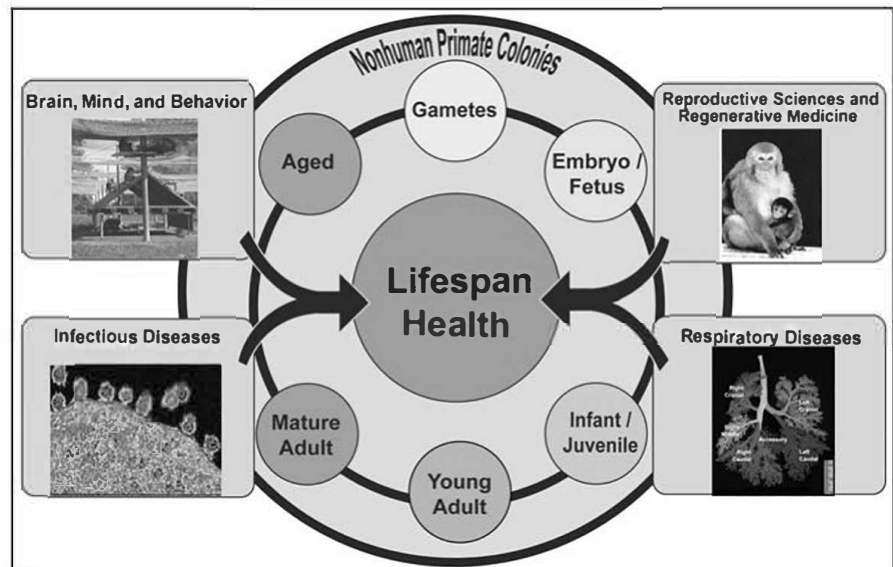
- The gastric pathogen, *Helicobacter pylori*, which is prevalent in many developing countries, was shown by [Excluded by Requester] Scientist [Excluded by Requester] (Infectious Diseases Research Unit) for the first time to induce expression of microbial peptides (defensins) in the gastric mucosa of rhesus monkeys, but only in those bacterial strains with the cag-pathogenicity island [Excluded by Requester] et al., 2009]. [Excluded by Requester] has utilized the rhesus model to examine the interplay between expression of host glycans that serve as receptors for *H. pylori* on the one hand, and expression of bacterial outer membrane proteins that serve as adhesins on the other. *H. pylori* commonly infects socially housed nonhuman primates, thus an ELISA was developed in [Excluded by Requester] laboratory with antigen from endemic rhesus *H. pylori* strains. His laboratory has also begun to characterize the gastric microbiota using NextGen sequencing methods. As a result of these seminal studies, [Excluded by Requester] is collaborating with other investigators interested in this model including [Excluded by Requester] (University of Maryland) and [Excluded by Requester] (UC San Diego), who have [Pending Support].

- In collaboration with investigators from Genentech Inc., Respiratory Diseases Research Unit Core Scientists [Excluded by Requester] reported microarray gene expression data obtained from the adult house dust mite-induced rhesus asthma model developed at the CNPRC [Excluded by Requester] et al., 2001], and compared these data to those obtained from human Th2-high asthma [Excluded by Requester] et al., 2011]. A comparison of lung gene expression profiles from human Th2-high asthma, the house dust mite-induced rhesus asthma model, and a common mouse asthma model indicated that genes associated with Th2 inflammation are shared by all three species. However, pathophysiologic aspects of human asthma (e.g., subepithelial fibrosis, angiogenesis, neural biology, immune host defense biology) were best represented in the gene expression profile of the rhesus monkey model. This study has confirmed that the CNPRC rhesus model of allergic asthma is the animal model that most closely recapitulates the human disease phenotype.

[Excluded by Requester] Private Source [Excluded by Requester] Core Scientists [Excluded by Requester] with [Excluded by Requester] Scientist [Excluded by Requester] developed a model of an emphysema phenotype of chronic obstructive pulmonary disease (COPD). Rhesus monkeys were treated with a vascular endothelial growth factor (VEGF) receptor 2 antagonist (Sugen), intratracheal polyinosinic-polycytidylic acid (poly I:C), and cyclic exposures of dilute tobacco smoke over 6 months. Outcomes included increased inflammatory (neutrophils, eosinophils) and immune responses (CD8+ T-cells) by serial bronchoalveolar lavage, histopathology of mucous cell metaplasia in the conducting airways, inflammatory/immune cells in distal airways and blood vessels, and loss of interalveolar septa (30% loss of alveoli), most notably in the proximal acinus.

Lifespan Health. The examples above provide insights into a wealth of scientific expertise and research opportunities at the CNPRC that clearly foster collaborative NIH research and multidisciplinary partnerships and teams. A common theme throughout all of the CNPRC Scientific Research Units is *Lifespan Health*. All stages of development, maturation, and aging are well represented in the nonhuman primate colonies maintained at the CNPRC (see below), and extensively studied in NIH-funded research and training programs (Figure 3).

Figure 3. The Scientific Research Units at the CNPRC include programs that address all nonhuman primate age groups. Individual Unit descriptions present details related to research activities, contributions, and collaborative partnerships that focus on bottlenecks and translational roadblocks to improving human health, while concurrently furthering studies on nonhuman primate development, health, aging, and disease.



Many current human health challenges, and those in the foreseeable future, include chronic diseases and their manifestations. The development of disease can begin at a very early age and establish a path that remains throughout life [Excluded by Requester 2014]. Thus, a research focus by teams of investigators is warranted on prevention, early treatment, and to address early life experiences, subsequent manifestations, and lifelong consequences. In order to pursue such studies, a model that closely mirrors humans across the lifespan with similar complexities in terms of immunology, endocrinology, ontogeny, reproduction, development, and neurobehavior is needed. While significant insights into specific molecular pathways and genetic/epigenetic changes can be obtained in non-primate species, the nonhuman primate model offers a critically needed bridge and fills the gap to bring the systems together for true translational applications. Thus, the unique and accomplished group of CNPRC Core Scientists provides a rich synergistic environment for the development, validation, and study of nonhuman primate models of human disease, and innovative approaches to overcome translational roadblocks to new diagnostics and therapies. This also presents fertile ground for trainees to work in a supportive environment that has the spectrum of research opportunities available at the CNPRC, and with mentors that specialize in the research domains reflected across the Scientific Research Units.

Core Scientists in the **Brain, Mind, and Behavior Research Unit** study neuroanatomical organization, biobehavioral organization, neuroimmune interactions and the etiology of autism, social bonds and social development, the human-animal interface, and social networks. This team of investigators specializes in research on sociality, temperament, and development with a lifespan approach that utilizes measures from early stages to aged animals, including new primate models of human psychiatric diseases. The Unit Core Scientists lead vibrant research programs that contribute to the training of students and visiting scientists. Major focus areas include neurodevelopmental disorders, particularly those with social deficits such as autism. The effects of social development on lifespan health has been a central theme since inception of the Unit by [Excluded by Requester] whose early work on attachment in monkeys and its effects on later behavior was central to the field. The BioBehavioral Assessment (BBA) Program is a resource unique to the NPRC system. This program is based on more than three decades of psychobiological research documenting the existence of stable, individual differences in patterns of adaptation to the environment throughout the lifespan, which have been shown to be associated with genetics, brain function, neuroendocrine organization, patterns of neural innervation of lymphoid tissue, and immune function. These and related activities are also provided by Unit Core and Affiliate Scientists through the **Behavior Research Services Core** and the management of the CNPRC colonies in **Primate Services** through **Behavior Management Services**.

Core Scientists in the **Infectious Diseases Research Unit** conduct preclinical/translational studies on a wide range of viral and bacterial pathogens (e.g., SIV, CMV, *H. pylori*), vaccine and drug interventions, and mechanisms of host-microbe interactions. Lifespan-related research is conducted through studies that focus on the impact of age on infection, pathogenesis, and vaccine efficacy. Research is also contributing to the management and health of nonhuman primates through infectious disease diagnostics, provided through a long-standing program that is a component of the **Immunology and Pathogen Detection Resources Core**. Investigations aim to examine the consequences of age on immune responses. For example, in the rhesus monkey model of influenza virus, two novel proprietary adjuvants have been shown to enhance immune

responses to FluZone®, the commercial influenza vaccine; importantly, these enhanced responses improved vaccine mediated control of viral replication in both aged and juvenile animals. The potential impact of early feeding practices on the development of the immune system has also been demonstrated in studies with breast- and bottle-fed infants. In particular, breast-fed infants were shown to develop robust populations of memory T cells, as well as Th17 cells within the memory pool. These findings may partly explain the variable susceptibility to conditions with an immune basis, and variable protection against some infectious diseases.

Core Scientists in the **Reproductive Sciences and Regenerative Medicine Research Unit** conduct studies on gamete biology and reproductive toxicology, study fetal models of congenital and acquired diseases, and have unique strengths in gene- and cell-based therapy/regenerative medicine with a particular focus on the fetus and infant. The Unit has a long-standing commitment to the development and application of novel *in vivo* imaging technologies and tools including ultrasound, optical imaging, and positron emission tomography/computed tomography (PET/CT) as described in the **Multimodal Imaging Core**. Collaborative studies in the Unit have focused on healthy aging, the menopausal transition, and the impact of environmental agents on reproduction. For example, Bisphenol A (BPA) exposure at levels similar to those measured in humans has been shown to disrupt development and potentially impact the function of reproductive and other organ systems which may not emerge for a generation. Studies in the Unit have also addressed ontogeny of organ systems such as the kidney and myeloid:lymphoid and hematopoietic systems. Goals of these studies include applying findings to new regenerative approaches and transplant protocols with correlative *in vivo* imaging to monitor cell trafficking and fate. Core Scientists provide their extensive reproductive and developmental expertise to the **reproductive management** of the CNPRC colonies (see **Primate Services: Colony Management and Research Services**) and through a range of services in the **Endocrine Core**, **Multimodal Imaging Core**, and the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases. Studies have revolutionized the ability to monitor long-term gene expression and transplant efficiency of human cells in the rhesus host, providing new ways to compare and contrast outcomes when different cell sources and routes of administration are used.

Core Scientists in the **Respiratory Diseases Research Unit** integrate the fields of inhalation toxicology, mucosal immunology, and neurophysiology in a comprehensive fashion to address critical scientific problems in pulmonary medicine. Each Unit Core Scientist contributes a unique area of expertise in pulmonary research from toxicology and neurophysiology to immunology and airway remodeling. A major emphasis of the Unit is pediatric models of lung disease with an overall goal of understanding how early life environments impact health outcomes with maturity. The rhesus model of allergic asthma reported by Unit Core and Affiliate Scientists in 2001 was the first nonhuman primate model to utilize the common human allergen, house dust mite. The CNPRC rhesus model of allergic asthma exhibits all parameters of human asthma, including airways hyperresponsiveness, eosinophilia, and airway remodeling. Unit Core Scientists have also advanced stereologic techniques in the **Multimodal Imaging Core** including accurate measures of alveolar number in aged rhesus macaques, and showed that alveolar number significantly declines with advancing age and particularly in post-menopausal females. These findings correspond with gender-dependent differences in susceptibility to chronic obstructive pulmonary disease (COPD) in human subjects. Recent construction of the Respiratory Diseases Center on-site will provide expanded inhalation exposure capabilities and opportunities for investigation of human respiratory disease in the **Inhalation Exposure Core**.

All of the CNPRC Core Scientists provide unique scientific and technical expertise that contributes to a synergistic environment benefiting Affiliate Scientists nationwide. From a colony perspective, the Brain, Mind, and Behavior Research Unit also provides scientific direction for the Primate Well-Being Plan. The Infectious Diseases Research Unit provided the genesis for the Specific Pathogen Free (SPF) program, and more recently, essential insights on the immunology of colony animals and endemic microbial populations. The Reproductive Sciences and Regenerative Medicine Research Unit developed the reproductive and developmental monitoring program (ultrasound-based and endocrine), and the Respiratory Diseases Research Unit provides critical information for understanding the respiratory physiology of animals, particularly in the outdoor field corrals. This depth of multidisciplinary scientific knowledge and expertise presents a framework for important cutting-edge NIH-funded research with nonhuman primates, bolstered by a robust spectrum of support and services for colony management that effectively meet investigator needs. Tightly linked with the services provided by Core Scientists and Core Science Services is a strong foundation of **Administrative Services** (Director's Office, Administration and Operations Services, Information Technology Services, Facilities Improvement), and **Primate Services**

(Colony Management and Research Services, National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, Genetics Management Services), all of which contribute to the rich infrastructure available to investigators nationwide.

The CNPRC vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no suggestions for improvement, attesting to the high quality standards for animal research at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. The CNPRC leadership, Core Scientists, and staff work together as an integrated team with the IACUC and the overall UC Davis Animal Care Program infrastructure to ensure that investigators nationwide can gain ready access to the unique resources and capabilities available. This is accomplished by:

- State-of-the-art husbandry for ~5,000 nonhuman primates in a variety of housing conditions.
- Specific management programs for different animal colonies based on age and viral status.
- High quality veterinary care and veterinary research support to meet colony and investigator needs.
- Outstanding anatomic and clinical pathology services for management of the colony, and to provide investigators with pathology support for research projects.
- A team of highly trained research technicians with expertise working with nonhuman primates to support colony management needs and provide individualized research support to investigators.
- Expertise in nonhuman primate behavior to assist in colony management, and ensure the psychological well-being of the colonies.
- Maintaining an extensive pedigree database on colony animals to provide information to investigators on the genetic background of individual animals.
- Management of outdoor field corrals for animal production that provide multigenerational, complex social communities, and a unique resource to study the interaction of environment, behavior, genetics, immunology, reproduction, and health across the lifespan.

The CNPRC is working with the six other NPRCs through the **NPRC Consortium** to continually improve and maintain the high quality of the research primate, and ensure best practices for colony management and care.

Specific Animal Location

The CNPRC is located on 300 acres with approximately 100 acres used for research, administration, and indoor and outdoor animal housing, and is approximately 10 miles west of the main campus (Figure 4). The overall facility includes research laboratories, a state-of-the-art inhalation exposure facility, indoor animal housing, modular buildings, animal housing, a quarantine housing facility, and administrative and laboratory support space (See **Facilities Improvement**). Construction was recently completed for the Respiratory Diseases Center building, which has increased office, laboratory, and inhalation exposure space. Included on the

Specific Animal Location

Specific Animal Location

CNPRC grounds is the **Center for Comparative Medicine (CCM)** that provides laboratory and office space for Infectious Diseases Research Unit Core Scientists

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The research mission of the Center for Comparative Medicine is to investigate the pathogenesis of

human disease, using experimental animal models and naturally occurring animal diseases. The CCM embraces the concept of “One Health” through interdisciplinary comparative medical research, teaching, and model development. Schools of Medicine and Veterinary Medicine faculty work side-by-side to facilitate innovative approaches aimed at understanding the pathogenesis of complex human diseases; the mission of the CCM synergizes with the broad mission of the CNPRC (see letter). The **UC Davis Translational Human Stem Cell Shared Research Facility**, which is dedicated to human stem cell research and training as a component of the UC Davis **Stem Cell Program**, is also located on-site (see below).

UC Davis is a major research university with a particular strength in biomedical research, and is ranked 15th in research funding among U.S. public universities and 22nd for public and private universities. Extramural funding in FY 2012-2013 was \$754 million. The university annually trains the largest number of biological science PhD's in the nation, and is home to one of the nation's fastest rising School of Medicine and top ranked School of Veterinary Medicine, with outstanding Colleges of Agricultural and Environmental Sciences, Biological Sciences, Engineering, Law, and Letters and Science. With an emphasis on disciplines relevant to translational research, UC Davis is also the most academically comprehensive campus in the UC system. This contributes to an intellectually rich environment with highly collaborative interactions between faculty representing different schools and colleges. For example, faculty from the Schools of Medicine and Veterinary Medicine and Colleges of Engineering and Letters and Science are Core Scientists at the CNPRC.

A nationally competitive program in functional genomics is located in the **Genome and Biomedical Sciences Facility** which is a \$95 million facility that houses several School of Medicine and Colleges of Biological Sciences and Engineering faculty including CNPRC Core Scientists [Excluded by Requester]. The Genome Center's technology cores and expertise are focused on high throughput genotyping, physical gene mapping, gene expression/array analysis, proteomics, metabolomics, and population genetics. The **West Coast Metabolomics Center**, funded by the NIH in 2012, is one of six regional resource cores designed to expand the availability of metabolomics services to investigators in many diverse fields, while simultaneously advancing the state-of-the art in metabolomics research. CNPRC Core Scientists [Excluded by Requester] (Reproductive Sciences and Regenerative Medicine Unit) have active roles in this program.

In February 2012, UC Davis also signed a master agreement with China-based Beijing Genomics Institute (BGI), the world's largest genomics organization, cementing a partnership to change the landscape of genomic sciences in California and the western U.S. by establishing a joint facility: **BGI@UCDavis**. This alliance fosters critical breakthroughs in the areas of human, animal, and environmental health, and offers new and exciting opportunities for nonhuman primate research at the CNPRC. The UC Davis **Host-Microbe Systems Biology**

[Excluded by Requester] ed by Core Scientist [Excluded by Requester] and Affiliate Scientist [Excluded by Requester] provides microbiome expression analyses for nonhuman primate studies and meets the current investigative need [Excluded by Requester] measuring changes in microbiome diversity with far-reaching implications for health. Other complementary bioinformatics capabilities are leveraged to enhance research at the CNPRC. Developments in “-omics” methods offer important new opportunities to significantly enhance infectious disease research in nonhuman primates and thereby enhance translation of the outcomes of this preclinical research into clinical settings. Core and Affiliate Scientists in the Infectious Diseases Research Unit use genomics and transcriptomics technologies with an emphasis on studying microbial flora (microbiomics, viromics) and host responses (pathways and networks of innate and adaptive immunity, stress responses, and regulatory and metabolic responses). The genetics/genomics efforts in the **NPRC Consortium** (see Approach, below) are very timely for the CNPRC as there is a major effort underway in institutional commitment that is escalating at a rapid pace including sequencing, faculty recruitment, and efforts to expand the infrastructure. *This will be a fruitful area for recruitment and research that will be further developed in the next funding period.*

The **UC Davis Health System**, comprised of the School of Medicine and Medical Center, is nationally recognized and excels at translating scientific discoveries and new technologies into improved patient care and community-wide health. The UC Davis Health System mission is to educate and train medical professionals; provide superior care to a large geographically dispersed population; contribute to the nation's basic, translational, and clinical research enterprises; and to further serve the public through outreach and health education programs. Within the School of Medicine is the UC Davis **Clinical and Translational Science Center** (CTSC), one of the initial 12 NIH CTSA sites, under the leadership of [Excluded by Requester] Senior Associate Dean for Research (see letter). The CTSC is physically housed in a 16,000 sq. ft. facility on the Sacramento campus, and draws talent and leadership from departments and divisions across the campuses as well as community and institutional partners in the region. The CNPRC has strong ties with the CTSC

through Core Scientist Excluded by Requester who serves as the director of the Pilot Translational and Clinical Studies and Translational Technologies, Methodologies, and Resources Programs, and provides a new model for evolving the CNPRC Pilot Research Program to ensure leveraging of funds and resources in the next funding period. Key CTSC initiatives implemented that have direct links with the CNPRC include the *Facilities, Cores, and Resources website* which is a searchable database and highlights research opportunities and Cores at the CNPRC. The School of Medicine strategic plan also emphasizes Regenerative Medicine, with over \$30 million in matching funds, which have been provided for the Translational Shared Research Facility located on-site at the CNPRC and the **Institute for Regenerative Cures** on the Medical Center campus. The Stem Cell Program combines unique capabilities for stem cell research with training in diseases that might be prevented, reversed, or ameliorated by stem cell therapy (see letter from Director Excluded by Requester). The program links basic "discovery" efforts with translational investigations in nonhuman primates. The **Good Manufacturing Practices** (GMP) facility in the Institute for Regenerative Cures, housed in the same building as the CTSC, enables researchers to readily move new stem/progenitor cell therapies into patients once they have been rigorously tested in nonhuman primates. The CNPRC Reproductive Sciences and Regenerative Medicine Research Unit is an integral component of these efforts, and conducts preclinical studies in nonhuman primates through research supported by the NIH and the State of California Stem Cell Agency, the California Institute for Regenerative Medicine (CIRM) (e.g., Huntington's disease, tissue engineered trachea; see Unit).

The **Medical Investigation of Neurodevelopmental Disorders (MIND) Institute**, is a unique collaboration between parent advocacy groups and UC Davis, conducts multidisciplinary research, and provides clinical programs focused on neurodevelopmental disorders. The MIND Institute was founded in 1998 as a unique interdisciplinary research center where families, community leaders, researchers, clinicians, and volunteers work together toward a common goal: researching causes, treatments, and eventual preventions and cures for neurodevelopmental disorders. The institute has major research efforts in autism, fragile X syndrome, chromosome 22q11.2 deletion syndrome, attention-deficit/hyperactivity disorder, and Down syndrome. The MIND Institute was recently named an **Intellectual and Developmental Disabilities Research Center**, through a prestigious NIH grant, a distinction held by only a handful of neurodevelopmental centers nationwide. Intellectual and Developmental Disabilities Research Centers conduct comprehensive interdisciplinary research that promotes the discovery and translation of basic science investigations into clinical applications (see letter from Director Excluded by Requester). The designation will provide the MIND Institute with new tools to further strengthen its neurodevelopmental research across the schools, programs, and departments of the entire university by knitting together the work of basic science researchers and clinicians to advance the development of new therapies. Core Scientist Excluded by Requester (Brain, Mind, and Behavior Research Unit) is the MIND Institute Director of Research, and conducts multidisciplinary studies directed at determining the neuroanatomical, behavioral, and electrophysiological organization and functions of brain systems that are involved in learning, memory, emotion, and social behavior in the human brain and nonhuman primate models. Excluded by Requester also conducts research on neurobiological correlates of autism in nonhuman primates and has recently initiated studies with Core Scientists Excluded by Requester that focus on the trafficking of antibodies during pregnancy, capitalizing on the unique strengths in fetal development and *in vivo* imaging at the CNPRC.

Related to these efforts are studies by Affiliate Scientists in the **Center for Neuroscience**, an interdisciplinary, independent research unit managed through the College of Biological Sciences that was established in 1991. Schizophrenia, autism, depression, Parkinson's disease, Alzheimer's disease, and the after-effects of stroke are studied. Teams of internationally recognized scientists work in areas ranging from cellular and molecular neurobiology, through systems and developmental neuroscience, to studies of human perception, attention, memory, language, and the nature of consciousness. Center for Neuroscience investigators benefit greatly from the UC Davis CNPRC by access to high quality animals and extensive veterinary expertise. Affiliate Scientist Excluded by Requester is studying the role of immune molecules in schizophrenia in a mouse model, nonhuman primate model, and in human patients in collaboration with Core Scientists Excluded by Requester

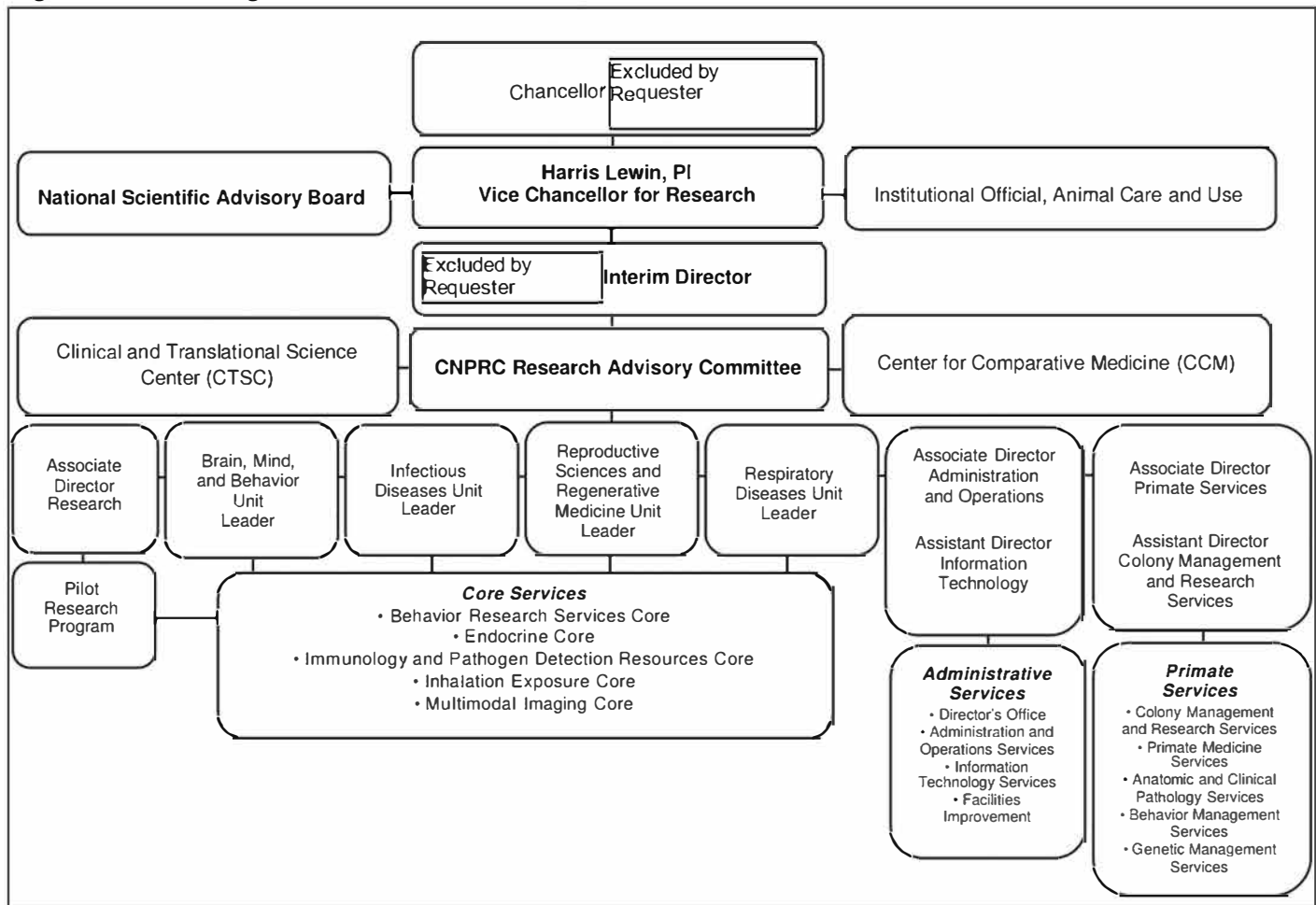
The **Center for Health and the Environment** is a program in the John Muir Institute of the Environment (directed by Core Scientists Excluded by Requester) that focuses on the effect of environmental agents, including chemicals, on the health of humans, animals, and other organisms. A central mission is to coordinate, facilitate, and perform multidisciplinary research related to environmental exposures and the causes and prevention of adverse health effects. Related to this program is an extensive network of investigators and clinicians working in pulmonary biology and medicine that are linked with the Respiratory Diseases Research Unit. The 23 faculty in the **Center for Comparative Lung Biology and Medicine** have home departments in

the Schools of Medicine and Veterinary Medicine, and work to resolve respiratory disease problems associated with air pollution, asthma, cystic fibrosis, lung cancer, emphysema, chronic bronchitis, and idiopathic pulmonary fibrosis using a multidisciplinary approach. This program integrates basic cellular biology with animal models, including nonhuman primates, and clinical applications of new therapies. The program hosts a NIH-supported T32 Training Program in Comparative Lung Biology and Medicine (see below), a weekly Pulmonary Seminar, and an annual "Lung Research Day" that is held every spring.

Organization and Administration

The CNPRC is an Organized Research Unit placed administratively under the Office of the Vice Chancellor for Research (Figure 5).

Figure 5. CNPRC Organizational Chart



The Primate Center Interim Director [Excluded by Requester] PhD) is responsible through the Principal Investigator (PI) for the P51 base grant, the Vice Chancellor for Research (Harris Lewin, PhD), to both the University of California and the NIH for administrative functions of the CNPRC. The Associate Director for Administration and Operations [Excluded by Requester] is responsible for all fiscal and administrative activities including budget, personnel, grants/contracts administration, business office, facilities management and equipment, central storehouse, purchasing, security, and administrative support to the Scientific Research Units. The Associate Director for Research [Excluded by Requester] PhD) oversees the Pilot Research Program and Cores Services. The Associate Director for Primate Services [Excluded by Requester] DVM, DACLAM) provides primary management of the nonhuman primate colonies. Primate Services includes Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. The Assistant Director for Information Technology [Excluded by Requester] PhD) provides information and computing support for the daily operation of CNPRC.

Research Unit Leaders provide administrative and scientific oversight for each of the four Scientific Research Units. [Excluded by Requester] (Professor and Vice Chair, Department of Psychology, College of Letters and Science)

is Unit Leader for the Brain, Mind, and Behavior Research Unit, Excluded by Requester (Professor, Department of Pathology and Laboratory Medicine, School of Medicine) is Unit Leader for the Infectious Diseases Research Unit, Excluded by Requester (Professor and Vice Chair for Research, Department of Pediatrics, and Department of Cell Biology and Human Anatomy, School of Medicine) is Unit Leader for the Reproductive Sciences and Regenerative Medicine Research Unit, and Excluded by Requester (Professor, Anatomy, Physiology, and Cell Biology, of Veterinary Medicine) is Unit Leader for the Respiratory Diseases Research Unit (Tables 1).

Table 1. CNPRC Core Scientists

Core Scientist	Department	School or College	Unit and Service
Excluded by Requester	Psychiatry and Behavioral Sciences	Medicine	• Brain, Mind, and Behavior
	Psychology	Letters and Science	• Brain, Mind, and Behavior
	Pathology and Laboratory Medicine	Medicine	• Director's Office • Infectious Diseases
	Psychology	Letters and Science	• Brain, Mind, and Behavior • Behavior Research Services Core
	Biomedical Engineering	Engineering	• Reproductive Sciences and Regenerative Medicine • Multimodal Imaging Core
	Medical Microbiology and Immunology	Medicine	• Infectious Diseases
	Medical Microbiology and Immunology	Medicine	• Infectious Diseases and Reproductive Sciences and Regenerative Medicine • Immunology and Pathogen Detection Resources Core
	Anatomy, Physiology, and Cell Biology	Veterinary Medicine	• Respiratory Diseases • Multimodal Imaging Core
	Population Health and Reproduction	Veterinary Medicine	• Reproductive Sciences and Regenerative Medicine • Endocrine Core
	Pathology and Laboratory Medicine	Medicine	• Infectious Diseases
	Psychology	Letters and Science	• Brain, Mind, and Behavior
	Population Health and Reproduction	Veterinary Medicine	• Brain, Mind, and Behavior • Behavior Management Services • Behavior Research Services Core
	Pathology, Microbiology, and Immunology	Veterinary Medicine	• Infectious Diseases Unit
	Anatomy, Physiology, and Cell Biology	Veterinary Medicine	• Respiratory Diseases • Associate Director for Research
	Anatomy, Physiology, and Cell Biology; Pediatrics	Veterinary Medicine and Medicine	• Respiratory Diseases • Inhalation Exposure Core
	Anatomy, Physiology, and Cell Biology	Veterinary Medicine	• Respiratory Diseases • Inhalation Exposure Core
	Anthropology	Letters and Science	• Genetics Management Services
	Infectious Diseases	Medicine	• Infectious Diseases
	Pediatrics and Cell Biology and Human Anatomy	Medicine	• Reproductive Sciences and Regenerative Medicine • Multimodal Imaging Core • Colony Management
	Obstetrics and Gynecology	Medicine	• Reproductive Sciences and Regenerative Medicine • Colony Management

*Core Scientists also faculty in the Center for Comparative Medicine

Core Scientists are appointed by the CNPRC Director in strict conformance with the host institutions' academic and personnel policies and are approved by the NIH. Appointments of Core Scientists are made on the basis of whether demonstrated experience and expertise is appropriate to their proposed scientific and/or research service responsibilities within the CNPRC. Joint appointments of Core Scientists in academic departments ensure mutually beneficial relationships between the CNPRC and the host institution. Core Scientists have teaching appointments at UC Davis, and their primary research activities are conducted at the CNPRC. Tables 1 and 2 shows the academic diversity of the Core Scientists and services provided. All Core Scientists meet the minimum % Effort of the required commitment to the monkey model and the CNPRC through these activities.

Core Scientists provide the scientific expertise, services, and infrastructure necessary to facilitate the research needs of Affiliate Scientists, who are defined as PIs that have their own source of research support and use Primate Center resources. There were approximately 350 Affiliate Scientists representing institutions across the U.S. and Canada participating in the program during the current funding period.

As highlighted above, Core Scientists also have a large number of **intra- and inter-unit collaborations** through publications and grants (Figure 6). In the social network analysis shown for the Core Scientists the size of the nodes represents the number of collaborations for each Core Scientist within and across Units.

Figure 6. Interactions within and across Scientific Research Units. Core Scientists are represented in colors according to their Unit (Green=Brain, Mind, and Behavior; Red=Infectious Diseases, Blue=Reproductive Sciences and Regenerative Medicine; Purple=Respiratory Diseases). The collaborative network indicates a clustering coefficient of 0.45 (ranging from 0-1) that reflects high connectivity and a centralization index of 0.30 (ranging from 0-1) that indicates that this network does not exhibit high centralization and thus would not be vulnerable to fragmentation of collaborative relationships should any individuals no longer be a part of the network (et al., 2012).

Excluded by Requester

Changes in Personnel (2010 to 2014)

2010

- Excluded by Requester was appointed Assistant Director for Information Technology.

2011

- Excluded by Requester Personal Info as a Core Scientist in the Respiratory Diseases Unit.
- Excluded by Requester changed from Core to Affiliate Scientist in the Infectious Diseases Unit.
- Vice Chancellor Excluded by Requester was replaced by Vice Chancellor Harris A. Lewin as the PI of the P51 base grant.
- Excluded by Requester Personal Info as Associate Director for Research and remains a Core Scientist in the Brain, Mind, and Behavior Unit.

2012

- Excluded by Requester Personal Info his position as Associate Director for Primate Services.
- Excluded by Requester was appointed Core Scientist with a joint appointment in the Infectious Diseases and Reproductive Sciences and Regenerative Medicine Units.
- Excluded by Requester was appointed Core Scientist in the Infectious Diseases Unit.
- Excluded by Requester replaced Excluded by Requester as Unit Leader of the Infectious Diseases Unit.

2013

- Excluded by Requester Personal Info as a Core Scientist in the Brain, Mind, and Behavior Unit.
- Excluded by Requester was appointed Associate Director for Research.
- Excluded by Requester Assistant Director for Administration Personal Info

2014

- Excluded by Requester was appointed Associate Director for Primate Services.

- [Redacted] as Director of the CNPRC.
- [Redacted] was named Interim Director during the recruitment of a new director.
- [Redacted] was named Interim Associate Director of Administration and Operations

Core Science Services

Core Science Services provide resources for data, consultative expertise, biologic and genetic material, and specialized services, facilities, and equipment that are crucial to facilitate nonhuman primate-related research (Table 2). The Cores also train undergraduate, graduate, postdoctoral students, as well as fellows and visiting scientists (see individual Cores for further information).

Table 2. CNPRC Service Cores

Core	Core Faculty	Services
Behavior Research Services Core	Excluded by Requester	Developmental, cognitive, emotional, motor, sensory, and social dimension assessments; positive reinforcement training
Endocrine Core		Steroid and protein hormone immunoassays
Immunology and Pathogen Detection Resources Core		Immune-based assays, flow cytometry, pathogen detection, viral stocks, species-specific reagents
Inhalation Exposure Core		Exposures to oxidant gases, reactive gases, aerosols, mixed gases, allergens, and microbes; pulmonary function testing
Multimodal Imaging Core		Microscopy, stereology, digital imaging, qualitative and quantitative applications; <i>in vivo</i> imaging (ultrasound, optical, microPET, PET/CT)

*Affiliate Scientist

Each of the Service Cores contributes to stellar science, meets investigator needs, and implement unique assays and technologies that address scientific questions specific to nonhuman primates. For example, many of the Endocrine Core assays employ reagents that are unique to the CNPRC. Monkey chorionic gonadotropin (mCG) and the urinary estrogen and progesterone metabolite assays are prime examples. Since purified mCG is not available, the validation of such assays requires the collection and characterization of hundreds of well-documented samples in order to establish normative ranges. Other examples are provided in the Multimodal Imaging Core where new stereological techniques were developed to count alveoli in the lung without the bias of lung inflation. New PET/CT imaging paradigms are also now possible in the Multimodal Imaging Core with new instrumentation obtained during the current funding period through an NIH S10 High-End Instrumentation [Redacted] PI). Overall, the CNPRC has enjoyed considerable success in several S10 grant applications, [Redacted] throughout the submission. Through the Inhalation Exposure Core, the long-term health outcomes of perinatal environmental tobacco smoke exposure has been explored and shown to result in deleterious effects on immunity, lung structure, cardiopulmonary physiology, and neural physiology in young rhesus monkeys. New biomarkers and tools in all Cores have promoted a myriad of new NIH grant submissions that address NIH strategic priorities that are made possible by the expertise and services of the Core faculty.

Support for investigators at UC Davis and other institutions is provided by Core Scientists, Core Science Services, Administrative Services, and Primate Services, all in compliance with the 7th edition of the NPRC Program Guidelines. Primate Services operates a centralized program that addresses all aspects of animal husbandry and care, and includes research support, assistance with budget preparation, and animal care staff training. The goal is to maintain a cost-effective program of support to ensure an adequate supply of healthy, well-characterized nonhuman primates for the biomedical research community, and a staff of well-trained animal handlers. Administrative Services provides assistance for all grant-related and administrative activities, Human Resources, Facilities Operations, and ensures compliance with University and federal regulations. The position of CNPRC Safety and Compliance Officer has been elevated to directly report to the Director to emphasize the central importance of safety across all aspects of the CNPRC mission.

Training and Outreach

Core Scientists lecture in undergraduate, professional, graduate academic, and graduate clinical courses, and train undergraduate and graduate students, and postdoctoral fellows within Primate Center facilities. Core Scientists are actively engaged in UC Davis graduate groups, both through teaching and mentoring but also by

participating in leadership positions, including as graduate group and designated emphasis chairs, academic advisors, and thesis committee members. Graduate education at UC Davis is designed to be multidisciplinary, with graduate education organized to transcend departmental and school/college boundaries through two mechanisms: graduate groups and designated emphasis programs. UC Davis graduate programs are matrix organizations governed by a structure under the UC Davis Office of Graduate Studies. The 90 graduate groups do not belong to any one department; rather, they are centered around broad topical areas of study and draw upon faculty from any department, college, or school to participate based on their commitment and expertise. Graduate students in PhD programs may also participate in a "Designated Emphasis" such as a Designated Emphasis in Biotechnology. This provides cross-disciplinary training in biotechnology research, and integrates biological science, engineering, and computational disciplines, which supplements a student's PhD curriculum. Similarly, students who successfully complete the Stem Cell Training Program are awarded a PhD in their discipline with a Designated Emphasis in Stem Cell Biology, a prestigious acknowledgement of exceptional achievement in stem cell training and research.

Approximately 150 graduate and postdoctoral trainees participate in the CNPRC program annually. Graduate students represent many of the graduate groups because of Core Scientist research diversity that is integrated through the focus on primatology and translational research (e.g., Animal Behavior, Biomedical Engineering, Cell and Developmental Biology, Comparative Pathology, Epidemiology, Genetics, Immunology, Microbiology, Pharmacology and Toxicology, Physiology, Psychology). Core Scientists participate in many training programs that bring graduate students and postdoctoral trainees to the CNPRC (Table 3).

Table 3. Examples of Trainee and Core Scientist Participation in UC Davis Training Grants (2010 to 2014)

Training Grant	School	CNPRC Trainee (Mentor)
CTSC T32 Predoctoral Clinical Research Training Program	Medicine	Excluded by Requester
NIH Animal Models of Infectious Diseases Training Program	Medicine	
NIH Interdisciplinary Training for Autism Researchers	Medicine	
CIRM Stem Cell Training Program	Medicine	
NIH Training in Comparative Lung Biology and Medicine Program	Medicine and Veterinary Medicine	
NIH T32 Year-Long Exposure to Advanced Research (YEAR) Program	Veterinary Medicine	
NIH T35 Students Trained in Advanced Research (STAR) Program	Veterinary Medicine	
NIH Building Interdisciplinary Research Careers in Women's Health	Medicine	
NIH Bay Area Affective Science Training Grant	UC Davis, UCSF, UC Berkeley, Stanford	

Other training and mentoring activities that build capacity for translational nonhuman primate researchers include the following:

- The CNPRC provides opportunities for students from non-UC Davis graduate programs, both national and international, to conduct significant parts of their thesis research while in residence at the CNPRC. For example, a visiting trainee from Germany studied oocyte cryopreservation under the mentorship of Dr. Excluded by Requester (Reproductive Sciences and Regenerative Medicine Research Unit).

- Under the supervision of many CNPRC Core and Affiliate Scientists, UC Davis students participate in research within the CNPRC facilities to fulfill undergraduate research credits through 199 standing courses, internships in the Biology Undergraduate Scholars Program, and graduate research rotation requirements in 299 standing courses. These students participate in bench and related research in individual laboratories or in field corral observations with faculty studying behavior. For example, during the current funding period, Brain, Mind, and Behavior Core and Affiliate Scientists trained 147 undergraduates, 26 graduate students, 6 visiting students, and 10 postdoctoral fellows. For several years there has been a formal, funded summer internship program with students from Brigham Young University. Brain, Mind, and Behavior Core Scientists also hosted 6 Master's students from universities in France who conducted research in the Unit as a component of their Master's theses.
- Excluded by Requester professor in the Department of Anthropology at UC Davis, teaches a biennial course in Anthropology (*Field Methods in Primate Behavior*) at the CNPRC. This course has a laboratory component that involves small groups of undergraduates conducting behavioral studies at the CNPRC's field corrals. Students present their studies at the end of the quarter in a mini-symposium that is held in the CNPRC Seminar Hall. The CNPRC also hosts biannually a class from American River College, Anthropology 301.
- Core Scientists in all of the Scientific Research Units participate in seminar series where specialty training is provided. For example, the Respiratory Diseases Unit participates in a Friday morning seminar series hosted by the Center for Comparative Lung Biology and Medicine that is supported by the Schools of Medicine and Veterinary Medicine. The Center for Comparative Medicine hosts a weekly seminar series held at the CNPRC that actively recruits graduate students and postdoctoral fellows to speak annually and attend regularly. The Stem Cell Training Program has a Stem Cell/Regenerative Medicine Seminar Series and weekly journal club supported by the training program and the School of Medicine that includes videoconferencing with trainees at UC Merced and other California stem cell training program sites.
- The NHLBI Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases is currently in the 13th year of NIH support (matching funds provided by the CNPRC, CTSC, and Office of Research). The intent of these annual interdisciplinary scientific symposia is to provide a novel and informal scientific setting for the dissemination and exchange of new ideas and research findings by bringing together trainees and investigators who do not typically interact at other meetings. Trainees are supported through a competitive process and have the opportunity to present their research in a brief oral presentation followed by a poster session, and directly interact with leading scientists in the gene therapy and regenerative medicine fields.
- The CNPRC's residency programs in Primate Medicine and Pathology are affiliated with the Laboratory Animal Medicine and Pathology Programs, School of Veterinary Medicine, and include training in laboratory animal medicine, zoological medicine, and laboratory animal pathology. Since 2010, 10 veterinarians successfully completed the resident training program in Primate Medicine and 4 completed the resident training program in Primate Pathology. Residents from UC Berkeley and UC San Francisco also participate in the program. In addition, weekly rounds in Primate Medicine and Pathology engage Core Scientists and trainees providing stimulating case discussions.
- Since May 2010, the CNPRC Training Coordinator has provided training in the in-house American Association for Laboratory Animal Science (AALAS) certification preparation class to 85 staff members, 45 of which have taken the AALAS test and were subsequently certified. To date, 95% of the CNPRC animal care staff participated in the in-house class, and 63% are AALAS certified.

Educational Outreach. The CNPRC Education Outreach Program's mission is to introduce K to 12th grade students and educators to nonhuman primates, topics in health sciences, translational research, and careers in science. Students are presented with a two-hour program at their school site, which includes an introductory lecture, followed by a rotation through several displays, educational tools, and experiments (Figure 7).

Figure 7. A. Hands-on activities are used to engage young students in the K to 6 grades. Presentations are given throughout the calendar year at the school site. Teachers are engaged in the training process along with parents. **B.** Members of the CNPRC also represented the NPPRC Program in Washington, DC at the USA Science and Engineering Festival in 2012 and 2014. Individual discussions with students and their parents provide opportunities to communicate the importance of nonhuman primate research and future careers in science.

A. Classroom setting **B. Science and Engineering Festival 2012**
Excluded by Requester

Since inception, the program has presented in both English and Spanish to over 10,000 K-6 students, teachers, and parents at more than 90 public and private schools over Northern California, home school groups, nonprofit organizations, Spanish Immersion classes, and developmentally and physically challenged children as well as high-risk schools.

Presentations are also given in cooperation with UC Davis outreach programs. These include GEAR UP, which mentors high-risk and minority students from the Sacramento community; the Early Academic Outreach Program which was created to help more students meet the requirements to attend college; and the School of Veterinary Medicine Summer Enrichment Program, which helps disadvantaged applicants improve their chances of getting into veterinary school.

Oversight Committees

National Scientific Advisory Board. The National Scientific Advisory Board is composed of 14 nationally eminent scientists with experience using nonhuman primates for research, veterinarians, and administrative members who cover the range of CNPRC expertise and technical subjects (Table 4). As a group, the National Scientific Advisory Board specifically addresses and reviews overall structure and function over a two-day period annually and provides a written report to PI Lewin and Director. Under the direction of the PI, the Director's Office is responsible for implementing recommendations.

Excluded by Requester

Table 4. National Scientific Advisory Board Members

Members	Title	Institution
Excluded by Requester	Professor	Department of Medicine, UC San Francisco
	Senior Director	Animal Resources, The Scripps Research Institute
	Professor	Department of Microbiology and Medicine Genetics, University of Pittsburgh
	Professor	Laboratory of Diagnostic Radiology Research, NIH
	Former Associate Director	Yerkes NPPRC, Emory University (Retired)
	Distinguished Professor	Department of Pathobiology and Diagnostic Investigation, Michigan State University
	Director	Department of Pathology and Comparative Medicine, Wake Forest University
	Professor	Division of Experimental Medicine, UC San Francisco
	Consultant	Private Consultant
	Professor	Center for Environmental Medicine, Asthma and Lung Biology, University of North Carolina
	Professor	Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh
	Associate Professor	Department of Neurobiology and Anatomy, University of Rochester
	Professor	Barshop Institute for Longevity and Aging Studies, University of Texas
	Professor	Department of Pediatrics, Indiana University

The CNPRC also has a standing **Research Advisory Committee** that provides advice to the CNPRC Director regarding prioritization of projects and resources, overall CNPRC function, and research needs. The Research

Advisory Committee includes the four Research Unit Leaders, the Associate and Assistant Directors, and the Senior Veterinary Managers for Primate Medicine Services and Anatomic and Clinical Pathology Services. The Research Advisory Committee has a pre-proposal mechanism in place for the review of all proposed projects to be conducted at the CNPRC including all grant and contract submissions that propose to use CNPRC resources. The CNPRC has other standing committees that are responsible for the overall function and mission of the CNPRC, and address critical areas related to management and regulatory compliance (Table 5).

Table 5. CNPRC Standing Committees

CNPRC Committee	Frequency and Function
Research Advisory Committee	<ul style="list-style-type: none"> • Biweekly • Address research needs and overall CNPRC function • Review proposed research projects; ~60 pre-proposals for submitted grants and contracts reviewed annually; all projects discussed and evaluated in terms of scientific merit, resources available, animal availability, meeting the NPRC mission, applicability, and NIH priority
Senior Management Committee	<ul style="list-style-type: none"> • Weekly • CNPRC programmatic, administrative, facility, and management topics many of which are brought in a more formal manner to the Research Advisory Committee for discussion and consensus building
Colony Management Advisory Committee	<ul style="list-style-type: none"> • Monthly • Issues impacting colony management (e.g., SPF colony, reproductive colony, behavioral management and environmental enrichment, colony genetics)
Morbidity and Mortality Committee	<ul style="list-style-type: none"> • Quarterly • Review spontaneous deaths in outdoor field corrals • Recommendations to the Director
Environmental Enrichment Committee	<ul style="list-style-type: none"> • Quarterly • Review ongoing practices, areas of focus or concern, new concepts and suggestions, and efficacy of current practices
Injury and Illness Prevention Program Safety Committee	<ul style="list-style-type: none"> • Quarterly • Reviews any safety concerns, disseminates safety information including injury and illness prevention programs, emergency action plans, infection and exposure control practices, hazardous material procedures, biosafety guidelines, and medical waste procedures
Infection Control Committee	<ul style="list-style-type: none"> • Quarterly • Reviews ongoing practices including health surveillance for employees and visitors, vaccination policies, BSL3 policies and practices, and personal protective equipment (PPE) requirements

NPRC Consortium Activities

The NPRC Consortium exists to strengthen communications, leverage system-wide resources, and facilitate sharing of information and best practices across NPRCs and their host institutions. The CNPRC is an active participant in these NPRC director-driven activities (Table 6).

Table 6. NPRC Consortium Working Groups

Working Group	CNPRC Representative
Behavioral Management	Core Scientist and Lead, Behavior Management Services
Breeding and Colony Management	Assistant Director, Colony Management and Research Services
Clinical and Surgical Techniques	Primate Medicine Senior Veterinary Manager
Consortium Project Management	Assistant Director, Information Technology
Data Access Guidelines	Associate Director, Administration and Operations
Genetics and Genomics	Core Scientist and Lead, Genetics Management Services
Integrity and Compliance	Associate Director, Administration and Operations
Occupational Health and Safety	Core Scientist and Lead, Immunology and Pathogen Detection Resources Core
Outreach	Public Information Officer
Pathology	Anatomic and Clinical Pathology Senior Veterinary Manager
Training	Primate Medicine Senior Veterinary Manager

For example, the CNPRC has taken a leadership role in coordinating two high priority initiatives, the first the *Virology Testing Quality Improvement Initiative* that is led by staff in the Immunology and Pathogen Detection Resources Core, and is focused on assessing whether resource laboratories are within acceptable limits for virology testing. Results from this Initiative are being incorporated into a white paper on virus testing standards commissioned by the Division of Comparative Medicine and the SPF Directors. Similarly, the *Multi-Center Measles Vaccination Safety and Efficacy Study* is currently testing an alternative measles vaccine candidate. NPRC breeding colonies are at risk for a measles epizootic since vaccination programs for measles have lapsed with the discontinuation of domestic monovalent measles vaccines. This project has been ongoing since 2011, and the CNPRC provided the leadership and expertise in designing the study.

In addition to the formal Consortium activities, CNPRC staff members regularly consult with their counterparts at the other NPRCs via telephone conferences and listserv to problem solve. The Associate Directors for Administration, Public Information Officers, Information Technology Managers, Veterinarians, Safety Officers, Enrichment Program Managers, and Security Managers are examples of groups from each of the NPRC's that regularly teleconference. Face-to-face meetings by members of these groups are periodically held in conjunction with the semi-annual NPRC Director's meeting and occasionally during the weekly Director's conference calls as part of the evaluation process for the Consortium Working Groups. The semi-annual face-to-face meetings are two-day agenda-rich meetings that interface with representatives from the Office of Research Infrastructure Programs (ORIP) and discuss common issues critical to all of the NPRCs (e.g., Genetics/Genomics white paper, NPRC/Center for AIDS Research collaborations, development of a NPRC website of capabilities and phenotypes, strategic planning). The weekly NPRC Director's conference call allows for timely follow-up on issues discussed at the semi-annual meetings as well as collaborative projects among the NPRCs.

Animal Colonies

The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different

Figure 8. Rhesus monkeys are housed in three paradigms: indoor paired housing, corn cribs (left), and half-acre field cages (right).



conditions: indoor housing, group housing in corn cribs (which accommodates approximately 12-20 individuals), and half-acre outdoor field corrals each of which can house up to approximately 150 animals (Figure 8). The advantage of half-acre field corrals is that they provide a cost-effective system to enable sufficient numbers of healthy animals for research with known life histories and demographic profiles. The long-term production colony is housed in the field corrals with a current population of 2,800. These animals provide infants,

juveniles, adults, and aged animals. This housing paradigm also provides a very valuable opportunity for the investigation of social behavior. As the population of the field corrals has grown, the CNPRC has split these cages in an effort to decrease the density, and to populate new production corrals. Input from Behavior Management Services and Genetics Management Services aids in implementing these events. The live birth rate remains constant (approximately 80%), resulting in an average of 600 live births annually.

The indoor colony is housed in caging with partitions to allow daily socialization of compatible pairs. The indoor population also includes animals housed in nurseries, weanling groups, and the aged colony including a subset of 42 animals supported by the National Institute on Aging. These animals are managed as one colony and participate in a semi-annual geriatric veterinary work-ups and routine evaluations. The indoor time-mate colony also provides investigators with pregnancies of known gestational age that are monitored closely during pregnancy. The time-mate colony population is approximately 300 animals (males and females). Pregnancies are detected by ultrasound in early gestation using established protocols and are assigned to IACUC-approved projects on a rotational basis. Computerized reproductive histories are maintained for all breeding animals in the WebVitals program, which is maintained by the CNPRC **Information Technology Services** team.

Long-Tailed Macaques and Titi Monkeys. The CNPRC supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) is generally housed in family groups, and utilized by Core and Affiliate Scientists in the Brain, Mind, and Behavior Unit (see Unit description).

SPF Colonies. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of four viruses including *Cercopithecine herpesvirus-1* (Herpes B-virus). The SPF Level 1 colony includes ~1,500 animals ranging in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and RhCMV. The SPF Level 2 colony currently totals 234 animals and is supported by a non-P51 NIH grant; animals are available for AIDS-related investigators.

Providing Animals for Research. The high level of production from the rhesus colony is needed to meet the age range requirements for investigators. Using harvest strategies from all areas of the colony, the CNPRC has been able to meet these requests. During the current funding period the greatest demand has been for newborns, females of prime reproductive age, and aged rhesus females. The CNPRC currently maintains approximately 5 project nurseries to support research in areas such as infectious disease, immunology, nutrition, and regenerative medicine/gene therapy.

Operating Budget and Facility Improvements

There are five primary sources of funding that support the CNPRC operations (Table 7).

Table 7. Sources of Support for CNPRC Operations

Source	Application
P51 Base Grant	• Supports CNPRC infrastructure, primarily breeding colonies
Program Income	• Generated from grants, contracts, and other sources • Established rates in compliance with NIH and UC Davis policy • Animal sales in compliance with NPRC Program Guidelines
B- and C-Indirect Cost Rate	• B-rate specific to NPRC Programs; reported as Program Income • Provided to offset expenses that cannot be directly recharged to grants • B-rate for federal grants and contracts and C-rate for non-federal • 21% of indirect costs retained by campus, remainder returned to the CNPRC
Non-University Differential (NUD)	• UC policy requires non-university clients to pay all costs through the NUD (51%) of which 29.5% is returned to the CNPRC • NUD is waived for other NPRCs supported by a P51 base grant
UC Davis Support	• Office of the Vice Chancellor for Research ~\$134,000/year • Campus-wide indirect cost return program ~\$350,000/year

Facility Improvements. During the current funding period, the vast majority of funds have been used to support colony management. The current funding period shows significant success in obtaining NIH C06 and G20 grants for construction and renovations totaling \$21,167,901 that substantially improved and expanded CNPRC capacity. In addition, successful collaboration with the UC Davis campus provided \$9,537,888 in support of the renovation and expansion of the CNPRC infrastructure. Overall, through application of P51 base grant Facilities Improvement funds, supplements, campus investment, grant support, program income, and non-federal funding sources, funds were provided to support colony management and improve the CNPRC infrastructure. The CNPRC has managed approximately \$37 million in facility improvements during the current funding period.

INNOVATION

Major Accomplishments and Contributions to the NPRC Mission and Goals

Overall, the CNPRC has shown an outstanding record of scientific achievements supported by the collaborations of Core and Affiliate Scientists and other investigators. Some examples are presented of highly innovative programs that have had a major impact on the development of unique monkey models, and mechanisms to facilitate their use. Other examples are provided in the Research Units and Service Cores.

- The BBA Program, which is based on more than three decades of psychobiological research, documents the existence of stable, individual differences in patterns of adaptation to the environment throughout the lifespan. More than 3,800 animals have been assessed through the program, which involves quantification of

individual differences in biobehavioral organization. The data from this program has been used in 38 grant proposals from PIs from Brigham Young University, Cincinnati Children's Hospital, Columbia University, Harvard University, Michigan State University, Stanford University, UC Davis, UCLA, and Wright State University. The focus of these grants covered a broad range in **scientific questions over the lifespan**. While the BBA Program assesses animals in the infancy period, data are used to identify temperament patterns that are linked to behavioral and health outcomes at later ages. Funded projects have examined asthma in juveniles, social motivation in young adults, and preterm labor in adult females.

- The NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases is a unique resource that has served a crucial role in the gene therapy community by addressing essential questions in gene delivery and providing investigators with opportunities to test new vector constructs and approaches that advance the field. Any investigator funded by the NHLBI is eligible to submit a Letter of Intent and apply through a competitive process to conduct studies with monkeys. The potential ramifications of gene transfer in humans at any age underscores the importance of rigorous assessments of gene transfer efficiency and safety. Since inception in 2001, the Center for Fetal Gene Transfer has conducted over 44 projects for investigators across the U.S. (e.g., Childrens Hospital Los Angeles, City of Hope, George Washington University, Harvard University, St. Jude Children's Research Hospital, Stanford University, UCLA, UCSF, University of Florida, University of North Carolina, University of Pennsylvania, Washington University at St. Louis). The established infrastructure can rapidly test new paradigms, move new hypotheses and emerging gene transfer vectors into a preclinical setting, and provide critical preliminary data for new NIH grants (R01s, P01s) and IND submissions (e.g., Pompe Disease, ADA-SCID, Duchenne muscular dystrophy, hematopoietic disorders, HIV/AIDS). Each aspect of the clinical development plan for these studies was facilitated by interactions with the program, and showed substantial support for the research community in addressing regulatory barriers. The leap from preclinical discovery to human subject research is challenging, and the Center for Fetal Gene Transfer is a crucial component in this process. Many novel **therapies tailored to the age of the patient** have been studied, with a focus on the fetus and infant.
- Recent investigations using design-based stereology to assess normal **lung growth over the lifespan** have shown that alveolarization in humans and nonhuman primates begins during prenatal development, but continues in a rapid growth phase during the first two years of postnatal life and assumes a slower growth rate until full somatic growth. Alveoli in rhesus monkeys showed a constant alveolar size after two years of age indicating that lung volume during somatic growth primarily increases through the addition of new alveoli and not expansion of existing alveoli. Studies in aging macaques indicated a significant decline in alveoli from age 9 to 33 years, with a greater decline in females. By 30 years of age, females had 30% fewer alveoli than males. Ovariectomy of adult female macaques resulted in a similar 30% loss of alveoli after 1 year that was prevented by estrogen/progesterone implants.
- Investigations in rhesus monkeys aim to examine the **consequences of the lifespan on immune responses**. The human immune system is in a state of flux from birth onward due to developmentally regulated events and the host's responses to a wide range of beneficial and pathogenic infectious agents. There is considerable evidence suggesting that repeated exposure to antigens, particularly latent/persistent infections, may shape the immune system such that deleterious long-term effects, including inflammation and immune senescence, become manifest later in life. The potential association between chronic infections and age-related morbidity remains tentative and requires more investigation. A rhesus monkey model was used to investigate if, and to what extent, the immunological environment differs between juvenile and adult monkeys infected with multiple persistent viruses, including RhCMV. Additionally, immune responses and immune cell subpopulations from a cohort of juveniles that were from the SPF Level 2 colony were analyzed and compared to non-SPF age-matched animals. Neutralizing antibodies to RhCMV and oral shedding of RhCMV were compared between juvenile and adult animals and were analyzed for potential correlations with immune markers. Multivariate statistical analysis revealed significant differences between age and SPF cohorts in the percentages and absolute numbers of peripheral lymphocyte subsets, concentration of cytokines secreted by peripheral blood mononuclear cells in response to mitogen and RhCMV antigen, and the percentage of animals and magnitude of shedding RhCMV. These results suggest that monkeys exhibit progressive age-related immune modifications similar to humans, and that such alterations may be shaped by persistent stimulation through chronic pathogens such as RhCMV that can elicit long-term immune changes for many years beyond primary infection.

Two **Pilot Research Programs**, the P51-supported program and an ARRA supplement to the base grant for a Postdoctoral Pilot Research Program, were administered by the CNPRC during the current funding period. The Pilot Research Program capitalizes on the expertise of CNPRC Core Scientists who can facilitate new areas of study by investigators that are interested in incorporating nonhuman primates in their research programs but do not have the expertise, resources, or funds available to obtain preliminary data for new grant submissions. Through this program, investigators new to nonhuman primate research and interested in pursuing nonhuman primate models for translational studies are identified. Rigorous criteria for review are used and peer-review committees with members outside of the CNPRC are selected to rank proposals that indicate the highest potential for success for future extramural submissions. During the current funding period, 77 Letters of Intent were received, 37 proposals were solicited from the submitted letters, and 15 proposals were funded. Of these proposals two have been leveraged to new extramural funding (Table 8). A pilot project was also co-supported by the UC Davis CTSC and the CNPRC that was leveraged into a CIRM Disease Team Award (includes a clinical trial; see Reproductive Sciences and Regenerative Medicine Unit).

Table 8. Subset of Pilot Project Recipients with New Grant Funding (May 1, 2010 to April 30, 2014)

Investigator	Project Title	P51 Pilot Funds	Funding Outcomes
Excluded by Requester	Immune Modulation of the Fetus by Intra-amniotic IL-1	\$20,000	<ul style="list-style-type: none"> Private Source (\$600,000) R01 (\$2,023,732)
	The Role of Oxytocin Biology in Primate Social Impairments	\$20,000	<ul style="list-style-type: none"> Private Source (\$250,000) R21 (\$457,486)
	Biosafety Testing of Intracranial MSC Delivery	*	<ul style="list-style-type: none"> Private Source (\$17.8 million)

*Pilot project funded through the Clinical and Translational Science Center (CTSC); CNPRC provided two animals for the project. CIRM=California Institute for Regenerative Medicine

An important example that highlights integration of the CNPRC with the UC Davis campus is the outcome of the **Research Investments in Science and Engineering (RISE) Program**, which was implemented to facilitate the formation and enhancement of interdisciplinary teams to carry out joint research activities in areas of strategic importance to California, the nation, and globally. Successful proposals were considered those with the greatest potential for future high impact discoveries and innovation, judged by their scientific merit, potential impact on society, and sustainability. Following a rigorous review process of 119 proposals, the UC Davis Office of Research committed \$10.9 million to 13 highly innovative interdisciplinary RISE themes over a 3-year period that include 81 faculty representing 38 academic departments and campus units. Of the 13 selected, three of the projects/teams are led by CNPRC Core and Affiliate Scientists. Each address highly innovative research and represents significant areas of growth over the next funding period.

• **UC Davis Center of Excellence in Translational Molecular Imaging** is led by Core Scientist [Excluded by Requester] and theme faculty [Excluded by Requester] (Reproductive Sciences and Regenerative Medicine Unit) with collaborators [Excluded by Requester] (Departments of Biomedical Engineering and Internal Medicine), [Excluded by Requester] (Department of Radiology), [Excluded by Requester] (Comprehensive Cancer Center), and [Excluded by Requester] (PI, UC Davis CTSC). The goal is to build the infrastructure and expertise necessary to translate novel molecular imaging agents and devices for clinical research studies and perform first-in-human molecular imaging studies at UC Davis. Dynamic PET/CT imaging using the new imaging system acquired through an NIH S10 High-End Instrumentation Grant (first such unit installed in the U.S. and at a Primate Center) is a major component of these studies, and has as a primary goal the translation to human imaging protocols using new fluorine-18 compounds developed by [Excluded by Requester]. These new compounds will be produced in the UC Davis GMP facility and ensure the necessary data is obtained to conduct an FDA-approved clinical trial in cancer patients. These studies represent a strong example of campus investment but also the unique capabilities for translational *in vivo* imaging at the CNPRC that will be further developed during the next funding period (see below). The new **Radiochemistry Research and Training Facility** (directed by [Excluded by Requester]) is related to these efforts and will vastly improve logistics for bench-to-bedside radiopharmaceutical conveyance. The facility is located within the building that houses the Institute for Regenerative Cures, GMP facility, and the UC Davis CTSC. This new facility was developed cooperatively by the UC Davis Health System, PETNET Solutions Inc., and the Northern California PET Imaging Center. The unique partnership with PETNET functions as a pipeline for commercialization of the concepts and compounds that researchers develop, which will be tested pre-clinically in nonhuman primates, while the CTSC will expedite translation of

successful diagnostic and therapeutic radiopharmaceutical agents. These activities form the basis for a range of new tools under development that will be available in the **Multimodal Imaging Core**, and capitalizes on the highly innovative expertise in place at the CNPRC for IND-enabling studies. Since funding of the RISE proposal, several NIH grants have been submitted that propose a wealth of new PET/CT imaging paradigms, and that focus in novel ways on fetal/maternal interactions, trafficking of cells and microbes, and the monitoring of stem/progenitor cell fate post-transplantation.

• **Protecting the Fragile Intestine: Integrating Microbiota and Mucosal Health** is led by Core Scientist

Excluded by Requester [redacted] (Infectious Diseases Unit) and theme [redacted] facility Excluded by Requester [redacted] (Food Science and Technology), Excluded by Requester [redacted] (Department of Pediatrics), Excluded by Requester [redacted] Department of Viticulture and Enology), Excluded by Requester [redacted] Director, Comprehensive Cancer Center), Excluded by Requester [redacted] Infectious Diseases), and Excluded by Requester [redacted] Internal Medicine). The human gastrointestinal tract harbors >80% of the immune cells and also hosts 10 times more commensal bacteria than the total number of cells in the body. The immune cells are essential for protection against pathogens yet uncontrolled immune activation can cause chronic inflammatory diseases. Unresolved inflammation contributes to tissue injury, changes in the gut microbiota, and inflammatory diseases. Despite the intense interest in developing therapeutic strategies to repair gut damage and renew intestinal epithelial barriers, effective treatment regimens are lacking. The goal of this RISE proposal is to apply novel approaches for repairing and protecting the fragile intestine in critical clinical populations: premature infants, HIV-infected adults with incomplete immune recovery, cancer patients on chemotherapy, and adults with inflammatory bowel disease. A novel combination of milk derived oligosaccharides and uniquely human *Bifidobacterium* species under study have anti-inflammatory effects on immune cells. The program combines previous findings and collective expertise in human milk glycobiology and bioactive molecules, gut mucosal immunology in humans and nonhuman primates, commensal bacteria, neonatology, infectious diseases, cancer, clinical research, genomics, and single cell analysis, with a dynamic and innovative platform for multidisciplinary training and mentoring of students. Since funding of the RISE proposal several new NIH grants have been submitted by CNPRC Core and Affiliate Scientists that address the microbiome from a variety of anatomical perspectives. In addition, idiopathic chronic diarrhea is a leading cause of mortality for rhesus monkeys under four years of age. Because no significant new treatment options have been developed since oral rehydration solution production in 1995, the CNPRC has been studying new clinical approaches by investigating lysozyme from transgenic goat's milk, raw bovine colostrum, serum derived bovine immunoglobulin, inulin, fecal transplantation, and a Paleolithic diet to address this problem Excluded by Requester [redacted] et al., 2014]. These and related studies focused on the microbiome represent another area of research growth during the next funding period.

• **I-CAN SZ (Interdisciplinary, Collaborative, Analysis of Neuroimmune-based Schizophrenia)** is led by

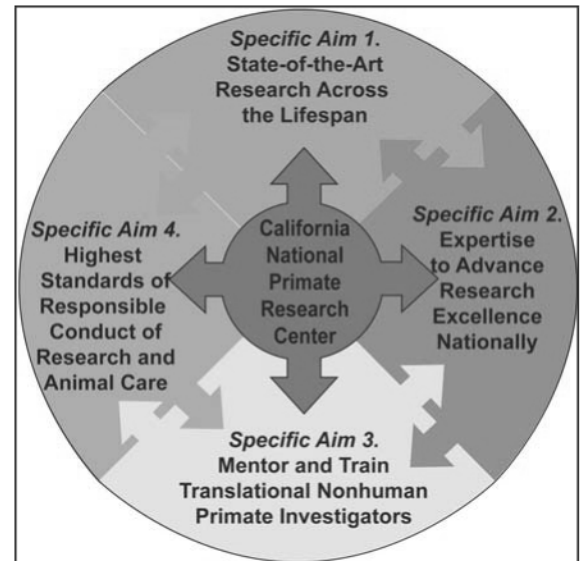
Affiliate Scientist Excluded by Requester [redacted] Center for Neuroscience, and includes Core Scientists Excluded by Requester [redacted]

Excluded by Requester [redacted] and Affiliate Scientist Excluded by Requester [redacted] Schizophrenia (SZ) is a disabling brain disorder affects 1% of the population worldwide. The social and economic costs of SZ are enormous and current treatments do little to reduce the devastating social and occupational disability associated with the disorder. Although SZ is usually diagnosed in young adults, it is believed to result from changes in how brain connections are formed during early development. SZ is heritable but the genes that cause this disorder in most people remain unknown. A wide range of environmental exposures also contributes to SZ and many of those factors alter immune function. This initiative brings together eight research groups to test the idea that maternal infection during pregnancy contributes to the development of SZ by altering immune molecules in the brains of offspring, which leads to changes in the way cells in the brain make connections. This is the first study to characterize changes in immune responses, brain inflammation, brain anatomy, and behaviors simultaneously in high-risk individuals during their first-break for SZ as well as two non-human model systems. This initiative also provides a unique environment for training in innovative, multidisciplinary approaches to bench-to-bedside research. Most important, this project has the potential to improve the lives of individuals with SZ through the discovery of novel diagnostic tools and new therapies for treating the currently untreatable negative symptoms of this disease. This RISE program highlights ongoing efforts focused on brain disorders, and utilizing the unique tools and resources available at UC Davis and the CNPRC including translational *in vivo* imaging. As noted above, new grant submissions are focused on antibody-induced psychiatric illness and establishing the mechanisms through which anti-brain antibodies might influence brain development and function.

APPROACH

Chronic diseases are increasingly dominating the nation's health care needs. While significant progress has been made over the last decade to reduce mortality from many common disease manifestations, the U.S. faces an expanding health care demand due to chronic conditions that require long-term management. It is becoming increasingly clear that many of these conditions are directly related to the normal aging process, although metabolic and immunological underpinnings of many of these conditions can be initiated very early in life. While the concept of a commonality of pathways leading to multiple diseases may offer opportunities for prevention, such mechanisms are highly complex and require a multidisciplinary team science approach. The CNPRC has significant strengths and an array of scientific achievements that, when coupled with key UC Davis initiatives, can build and enhance research excellence and opportunities. Key resources and core facilities in genomics, metabolomics, and bioinformatics linked with the unique nonhuman primate models in place at the CNPRC provides a strong foundation for the future.

The goals for the next funding period are reflected in the Specific Aims that focus on providing readily accessible state-of-the-art research opportunities to investigators and trainees for studies that promote human health and healthy aging. The overarching vision builds upon expertise, productivity, and innovation; strong ties with the host institution and national programs; and maximizes resources for NIH funded research. Core and Affiliate Scientists will work together to expand areas of common research interest, translate research findings to clinical trials, and continue a strong track record of building partnerships locally, regionally, and nationally. Through targeted opportunities, and key UC Davis initiatives the CNPRC will actively promote the recruitment of faculty to the program, and continue to build infrastructure, expertise, and essential services to meet the growing needs of investigators and trainees.



Specific Aim 1. Conduct state-of-the-art research and scientifically contribute to the understanding and treatment of human disease with nonhuman primate models across the age spectrum.

Plan. The overriding objective is to advance the CNPRC resource through scientific achievements driven by the Core and Affiliate Scientists in translational teams. Nonhuman primates provide an essential translational bridge between rodents and humans, and are necessary to ensure clinical translation. CNPRC Core Scientists possess critical intellectual and practical expertise, and serve as an essential conduit through which investigators that work with rodents can transition to nonhuman primates, and address novel concepts and/or therapies in a model system that closely simulates humans.

The **Brain, Mind, and Behavior Research Unit** will continue to support research excellence including the study of lifespan health with a focus on neurodevelopment, individual differences, and social network theory. The BBA Program will further enhance the value of the field corral resource for concepts related to personalized medicine. The natural variation in large field corral populations has been used to study the effects of temperament on asthma, SIV infection, and idiopathic chronic diarrhea. A goal for the next funding period is to include a measure of inflammation enhanced by collaboration with Core and Affiliate Scientists that study infectious diseases. New technological advances have included reversible neural lesions, advances in non-invasive eye-tracking technology, and a robotic device to assess impaired hand function. New areas in neuroscience will be explored in collaboration with Core Scientists in the Infectious Diseases and Reproductive Sciences and Regenerative Medicine Unit, such as whether congenital RhCMV infection significantly increases the risk for development of autism spectrum disorder. Excluded by Requester also investigating the effectiveness and behavioral consequences of transiently inactivating structures such as the amygdala or hippocampus using designer receptors exclusively activated by designer drugs. In collaboration with Core and Affiliate Scientists, monkey models of spinal cord injury and Alzheimer's disease will continue to be studied and expanded to new areas of research to increase neuronal survival and to improve memory and executive functioning.

Areas of research excellence in the **Infectious Diseases Research Unit** include infectious disease models, immunology and vaccines, and therapies for infectious pathogens. A major area of study will continue to focus

on the long-term effects of persistent pathogens on the immune system. There has been increased recognition from human natural history studies that persistent infections can have a detrimental effect on immune function, particularly in the context of an aging immune system. The SPF Levels 1 and 2 rhesus colonies represent an invaluable resource to investigate the long-term effects of indigenous viral flora on development and maturation of the immune system as well as to evaluate susceptibility to various pathogens. All Scientific Research Units have ongoing research interests related to the immune system and the role in development and chronic diseases. Several key areas of research link Core Scientists such as the use of the fetal RhCMV pathogenesis model to study novel vaccines and *in vivo* imaging paradigms. As members of the NIH-supported Collaboratory of Antiviral Researchers for Eradication (CARE), Core Scientists Excluded by Requester and Affiliate Scientists Excluded by Requester have begun to test novel pharmacologic approaches for inducing (re)activating virus from latent cell reservoirs. Core Scientists Excluded by Requester have demonstrated the feasibility of stereologic sampling principles for the quantitation of bacterial burden and granulomas in experimentally infected animals. New CT imaging capabilities can also be considered in the future to assess the impact of anti-*M. tuberculosis* drugs and vaccines during the in life-phase of preclinical trials.

Reproductive health is a high priority research area in the **Reproductive Sciences and Regenerative Medicine Research Unit** where nonhuman primates will continue to play an essential role. Reproductive health is tightly linked with the focus on lifespan health and the impact of early environmental exposures on the development and evolution of reproductive functions particularly during lifetime transitions (e.g., puberty, menopause). Environmental exposure models will be expanded to interface with other disciplines such as the role the oocyte plays in the epigenetics of transgenerational effects. Long-standing expertise in fetal development and fetal/maternal interactions (e.g., cell and DNA trafficking) and immune ontogeny will be crucial in the study of models focused on the developmental origins of disease. In addition, progress in the regenerative medicine and gene therapy fields, which have been hampered by the need for predictive primate models, will build on existing strengths in xenogeneic primates and using novel *in vivo* imaging methods to explore crucial gaps and roadblocks, including new tools for the *in vitro* design (cells, natural scaffolds) and *in vivo* testing (transplant, *in vivo* imaging) of regenerative strategies tailored to the age of the patient. Innovative chimeric AAV vectors developed for cell targeting will be essential to explore in the monkey model, and to validate organ and tissue targeting while exploring safety and the potential for inflammation with PET/CT. *In vivo* imaging will continue to focus on new and sensitive tools that will enable all Core and Affiliate Scientists to implement studies in monkeys to assess a myriad of novel hypotheses including the changes that occur with chronic inflammation associated with advancing age, and the use of new imaging agents and diagnostic tools.

A major research emphasis for the **Respiratory Diseases Research Unit** will continue in the understanding of how early life exposures impact future health outcomes. Collaborations between Core Scientists in the Respiratory Diseases and Infectious Diseases Units previously explored the impact of *H. pylori* on development of lung mucosal immunity, and are now focused on the microbiome of the distal lung. In conjunction with recent success with a pediatric influenza model, collaborations between influenza and vaccine investigators in the Infectious Diseases Unit (Core Scientists Excluded by Requester) are strategically positioned for new funding mechanisms that target respiratory infections in highly susceptible age groups (e.g., young and old). The new Respiratory Diseases Center building provides state-of-the art exposure chambers that will allow investigators to explore new questions relative to environmental air pollution, secondhand tobacco smoke, and infectious diseases, and the mechanistic changes that can result in a chronic disease state.

The CNPRC will continue to foster an environment that emphasizes scientific expertise that is critical to carry out the mission of the NPRC program. Internal and external research collaborations will be promoted by all Core Scientists who will actively participate in further developing the resource and will also ensure best practices for colony management (see below). Over the next funding period, Core Scientists will continue to foster relationships with key campus and national programs, and actively promote translational research through collaborative extramural funding opportunities and pilot project programs. Notably, the commitment by the campus to recruit 10 new FTE positions with faculty that have nonhuman primate-based research programs and whose home departments will be within multiple Schools and Colleges across the campus is a powerful demonstration of the UC Davis leadership to a prominent role for the CNPRC.

Opportunities. The value of nonhuman primate models derives from their genetic diversity, behavioral complexity, and anatomy, immunology, and physiology. The scientific resources that have been developed

in genetics and genomics provide a means to better define individual rhesus monkeys over a lifespan, and to identify novel models of human disease. The **NPRC Consortium** has initiated an “Extreme Phenotype” survey, and plans are underway for a white paper on a program using targeted and state-of-the-art genomics to discover genotype-phenotype relationships related to human disease. The proposal primary goals are to identify common genetic variations across the NPRCs, develop an online searchable database as a resource to the research community, and establish a genome sequencing service that will generate whole genome or whole exome sequences for specific animals with significant phenotypes. As an active member of the NPRC Consortium, the CNPRC will participate in these efforts.

The CNPRC will foster relationships with key campus programs central to the mission (e.g., CTSC, CCM, MIND Institute, Stem Cell Program, Genome Center, West Coast Metabolomics Center, BGI@UCDavis, Center for Health and the Environment, Center for Comparative Lung Biology and Medicine, Center for Neuroscience) and capitalize on areas of growth that will add strength to the CNPRC and provide new research opportunities for investigators regionally and nationally. Examples include the following:

Human Genomics Initiative. As noted above, genetics/genomics efforts in the **NPRC Consortium** are very timely as there is a comparable major effort underway at UC Davis. Precision genomics and personalized medicine will improve human health care, and the School of Medicine *Human Genomics Initiative* is poised to capitalize on infrastructure already in place to address the national priority of human genomics to manage chronic illnesses. This program will link closely with the CNPRC, CTSC, Stem Cell Program, MIND Institute, Genome Center, West Coast Metabolomics Center, BGI@UCDavis, and the Center for Molecular and Genomic Imaging, to name a few. As noted, a white paper has been generated through the NPRC Consortium that provides the rationale to enhance nonhuman primate resources through the application of genomics in order to develop new models of human disease through DNA sequencing and related efforts. There currently exists in the NIH-supported rhesus monkey colonies tens of thousands of naturally occurring genetic variants and many disease phenotypes that are directly relevant to human diseases. The CNPRC is poised to rapidly advance these concepts based on the depth and breadth of resources and expertise at UC Davis. It is important to note that one of the focus areas in the West Coast Metabolomics Center is integrating metabolomics data with genomics information. With the direct involvement of Core Scientists in this program, developmental projects are currently underway to explore integrating metabolomics and *in vivo* imaging using the monkey model, and to encourage new pilot project applications from investigators to utilize the unique capabilities in the West Coast Metabolomics Center and the CNPRC.

Translational Life Sciences Collaborations. Several Core Scientists have initiated studies that use genomics and transcriptomics technologies to analyze interactions of the microbial flora and host responses. Further expansion and coordination of -omics research at the CNPRC will be important for implementing a “systems biology” approach, for example to the understanding of the complexities of infectious diseases, particularly chronic infections. New collaborative efforts are underway between UC Davis and the Lawrence Livermore National Laboratory, which is a resource with many relevant technologies for biomedical research (e.g., high performance computing capabilities, accelerated mass spectrometry, microbial detection array toolkit). A multidisciplinary effort to develop a systems biology algorithm for selected bacterial and viral pathogens could define the architecture (networks) and dynamics of systems-wide host/pathogen molecular interactions during infection, and using integrated datasets generated from a combination of -omics technologies. Synergies with microbiomics will be important for defining the systems biology of host-pathogen interactions, for testing and validating therapeutic targets and predictive biomarkers, and defining new therapeutic targets for development of countermeasures against infection and disease progression.

Big Data Initiative. Through genomics and related efforts, there will be a dramatic rise in the quantity of data collected by investigators, and particularly with the development of electronic medical records across the NPRCs program (see **Information Technology Services** and **NPRC Consortium**). Although on a smaller scale, these new initiatives in information technology parallel the human setting with the use of large databases for unique research opportunities. “Big Data” refers to the massive volumes of datasets that are complex and too large to process and manage using traditional database and software tools. UC Davis recently posted a report on Big Data Implementation, which proposes to address the opportunities related to Big Data from a research, education, and infrastructure perspective. The major outcome of the report was a proposed *Data Science Institute* that will bring together mathematicians, computer scientists, statisticians, and research

domain scientists to work in new research and Big Data challenges in a collaborative setting. The ultimate goal is to develop an environment that will support collaborations among scientists that will tackle the challenges of Big Data and an infrastructure for domain scientists to interact with these experts. There are also major initiatives in the NIH Common Fund including the addition of biomedical training to currently active institutional training grants that would benefit investigators and trainees at UC Davis and the CNPRC.

NIH Strategic Priorities. Coupled with the above opportunities and array of capabilities are key NIH funding priorities where nonhuman primate models, and hence the CNPRC, will play a crucial role. Examples include:

- *NHLBI Shaping the Future of Research* has multiple goals including developing an understanding of mechanisms that maintain health throughout the lifespan; determine the role of systemic pathologic processes such as inflammation, immunity, and infection in the development and evolution of disease; and developing *in vivo* imaging methods and probes for investigating the biology of disease processes.
- *NIA Living Long and Well in the 21st Century* includes research goals on improving the understanding of healthy aging and disease, and the challenges to determining how cellular changes associated with aging contribute to decreased function including the role stem/progenitor cells and their microenvironment play.
- *NIAID Strategic Plans* include areas of emphasis such as host-pathogen interactions; new targets for therapeutics and vaccines; -omics approaches and bioinformatics which are key to analyzing and understanding large data sets generated by high-throughput technologies; and immune-mediated diseases.
- *NICHD Scientific Vision for the Next Decade* highlights research areas such as epigenetic changes due to environment and other influences; changes in microbial flora during reproductive transitions and health effects of these changes; causes of developmental disorders such as autism; and new cellular and molecular therapies to induce plasticity and enhance function resulting from injury and disease.
- *NIEHS Strategic Plan for Environmental Health Research* includes the study of environmental exposures including chemical pollutants, the microbiome, infectious agents, nutritional sources, and stress, and the need for new metrics of exposures that focus on key pathways involved in disease pathogenesis across the lifespan and by identifying critical windows of susceptibility.
- The *Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative* is aimed at revolutionizing understanding of the human brain and will include a spectrum of research opportunities for collaborative teams.

A unifying theme for all of these initiatives centers on proactive development of treatments and modalities that improve human health. Small animal models are critical for discovery yet nonhuman primates remain the preeminent model for preclinical evaluation of concepts and strategies that can be directly translated into human clinical trials. However, it should be stressed that human medicine and veterinary medicine represent species-specific variations of one medicine. An implication of similar disease mechanisms and pathways observed in multiple species is that the same process will be observed in humans. Accordingly, UC Davis is uniquely positioned to use the precepts of comparative medicine to advance human medicine, given the strength and breadth of research in multiple species. Because of the strong integration of the CNPRC with the broader UC Davis research programs, the CNPRC is strategically aligned to meet these areas of emphasis and NIH priorities. This is particularly salient in light of the 10 new FTE positions for faculty whose research programs encompass nonhuman primates and will become new CNPRC Core Scientists.

Industry Relations. While the primary focus for growth of the CNPRC will remain on securing NIH-based funding, there will be a strong emphasis on diversifying the CNPRC portfolio. The distinguishing advantage of the CNPRC for attracting industry support derives from the both the nonhuman primate resource and the entrepreneurial nidus built on the intellectual critical mass of nonhuman primate expertise. For example, the **Multimodal Imaging Core** has strong connections with the pharmaceutical, biotechnology, and medical imaging industry. Genentech has been a long-time collaborator in PET imaging studies of nonhuman primates, where the Core radiolabels novel compounds and uses PET imaging to assess the pharmacokinetics of the drug. Most recently this has involved studies to examine a new tau PET tracer being developed for applications in dementia. The Core has also developed a strong working relationship with GE Healthcare around the new PET/CT platform, leveraging their expertise to develop novel protocols, for example, for fetal CT imaging (see Multimodal Imaging Core). Negotiations are currently underway with two new potential industry collaborators, ImaginAb, who are developing new antibody-based cancer biomarkers and therapeutics, and Imanova, a company based in the UK that provides imaging services to many of the large pharmaceutical companies. Imanova is looking to establish a site capable of PET imaging in nonhuman primates, as this is a capability

they do not have in house in London. The business contract has been successfully negotiated and first studies are currently being planned. [redacted] also presented the capabilities of the Multimodal Imaging Core at the International BIO convention in San Diego (2014), which is attended by all the key biotechnology companies; there was great interest in the CNPRC imaging program, with several companies requesting information.

Excluded by Requester

[redacted] (Interim Director, **Infectious Diseases Research Unit**) developed the rhesus CMV model of human cytomegalovirus (HCMV) persistence and pathogenesis at the CNPRC. A central aspect of [redacted] research effort is the incorporation of RhCMV natural history in rhesus macaques into the design and testing of vaccine strategies. A unique feature of his research is that only in the RhCMV model of HCMV can vaccine strategies be tested that recapitulate the many challenges facing clinical HCMV vaccine trials today, including repeated mucosal exposure to antigenically variant challenge viruses. This is not possible in small animal models of HCMV, and because of this, pharmaceutical companies such as Novartis have worked with Dr. [redacted] to test potential HCMV vaccine strategies in the rhesus model.

Excluded by Requester

Challenges. The recruitment of Core Scientists with joint appointments in academic departments has been challenging. However, as noted by the Letter of Support from the Provost, "...the deans of the life sciences colleges (Medicine, Veterinary Medicine, Biological Sciences, Engineering, Letters and Sciences) in collaboration with the Provost have worked with the Primate Center leadership to identify thematic areas of scientific interest. These areas form the basis for at least 10 joint faculty recruitments of Core Scientists in the CNPRC. The necessary infrastructure including space and equipment will be provided to these recruitments as part of the commitment to the CNPRC and the Deans". This unprecedented level of support to the CNPRC represents a blueprint for growth of the CNPRC mission by closely integrating the CNPRC into the broader research, academic, and service missions of the entire campus. Moreover, additional recruitments, such as those being conducted by the CCM, closely align with the strategic mission of the CNPRC, effectively increasing the research base using nonhuman primate resources.

Specific Aim 2. Provide exceptional nonhuman primate expertise and services to investigators at the regional and national levels to advance NIH-supported research excellence.

Plan. The primary goal is to facilitate research and ensure a supportive environment for the investigation of human disease through specialized facilities, expertise, and resources specific to nonhuman primates. The established CNPRC Cores (Behavior Research Services, Endocrine, Immunology and Pathogen Detection Resources, Inhalation Exposure, Multimodal Imaging) are all dedicated to providing a spectrum of services and research opportunities to investigators nationwide. Each of the Core descriptions that follow outlines these capabilities and new technology development driven by research needs and research opportunities. All of the Scientific Research Units also have specialized repositories of nonhuman primate cells, tissues, and data that will provide important opportunities for collaborative research, training, pilot projects, and new NIH grants.

Opportunities. As noted above in Specific Aim 1, there are campus opportunities that will expand the current Core services and infrastructure. The RISE proposals highlight opportunities to study the microbiome and the development of advanced imaging tools that link with campus efforts in translational imaging. It is imperative that the CNPRC continue to develop infrastructure and services to keep pace and remain flexible with evolving NIH priorities and national research needs. Additional imaging modalities will be needed on-site (e.g., MRI) to maintain and grow the highly innovative and unique program focused on translational *in vivo* imaging. Because noninvasive imaging is used routinely in diagnosing and treating human disease, these capabilities will facilitate the translational goals of the CNPRC and reduce the need for terminal procedures. A Primate Services goal identified for the next funding period is to continue to refine clinical and research procedures in collaboration with CNPRC Core Scientists and Service Cores. While many procedures can be refined with small changes, new techniques that have been established in the Multimodal Imaging Core will provide new ways to incorporate imaging in research projects and across an animal's lifespan. Primate Medicine will continue to gain substantially from these advances.

Similarly, in order to further expand imaging capabilities for regenerative medicine, the Multimodal Imaging Core is collaborating with translational and clinical faculty in the UC Davis Center for Vision Science to develop capabilities for translational vision research specific to regenerative medicine in nonhuman primates. In order to translate the gene- and cell-based therapies that need to be developed for blinding eye diseases (e.g., glaucoma, diabetic retinopathy), nonhuman primates and dedicated state-of-the-art imaging are needed (e.g.,

optical coherence tomography, scanning laser ophthalmoscopy, adaptive optics technologies). This instrumentation is currently a roadblock to conducting translational studies in nonhuman primates that can capitalize on the extensive expertise in vision science and regenerative medicine. Current plans include a grant submission

Pending Support

Pending Support

Challenges. The current funding climate has a direct impact on the research activity for investigators nationwide. While the CNPRC has maintained a strong grant portfolio, diversification is warranted. The Core Scientists have shown continued success in funding of NIH grants including a high level of success with instrumentation and facility grants that further develops the resource. Despite the challenges ahead, ongoing outreach efforts continue to develop collaborations in new areas of investigations that have high potential for dedicated funding. One such area includes neurodevelopmental and neurodegenerative diseases where the Brain, Mind, and Behavior Research Unit has a well documented record of success. The UC Davis campus has broad expertise in nationally renowned programs in the MIND Institute, the Center for Neuroscience, and the Alzheimer's Disease Center. Accordingly, a strategic vision for the CNPRC is to leverage the collective expertise of nonhuman primate investigators with clinicians to test new concepts, diagnostics, and therapies prior to translation to humans. As noted above, the Multimodal Imaging Core has developed relationships with the private sector, and the Core sees such relationships as beneficial in maintaining a viable financial model as grant funding can fluctuate from year to year. Studies with the private sector can support new methodologies and techniques that are then made available to all Core users, thus expanding the range of services available benefiting all Core and Affiliate Scientists.

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

Plan. A central mission is to mentor and train the next generation of researchers at all career stages (undergraduate, graduate, postdoctoral, junior faculty) in the development of expertise in primatology, the design and study of nonhuman primate models of human health and disease, team science, and the conduct of multidisciplinary translational investigations. The CNPRC provides the "complete primate experience" for trainees at all levels based on the resources and research programs of the Core Scientists and their integration with campus educational and training programs. For example, a unique resource for training is the 24 half-acre field corrals containing large, stable social groups of rhesus monkeys. These groups are well characterized by Behavior Management Services and the BBA Program, and are utilized in individual research projects of Core and Affiliate Scientists. Future directions of this program will continue the multi-level multidisciplinary study of socioecological effects on health and well-being as a translational model for humans.

The CNPRC's residency programs in Primate Medicine and Pathology, which are affiliated with the Laboratory Animal Medicine and Pathology Programs in the School of Veterinary Medicine, will continue to train in laboratory animal medicine with a focus on nonhuman primates. Graduates of this program are in leadership positions at other NPRCs including Wisconsin and Tulane. Thus, the CNPRC will continue to train veterinary clinicians and pathologists with expertise in the nonhuman primate model.

Trainees have a primary role in all of the RISE team projects described above, and these represent an example of the many training opportunities at the CNPRC and UC Davis. For example, undergraduate and graduate students and postdoctoral fellows affiliated with the RISE *Center of Excellence in Translational Molecular Imaging* will be educated and integrated into the CTSC Research Education, Training, and Career Development Program. This program has a comprehensive approach to translational research training that provides scholars with a rich array of career development opportunities through program curricula, mentored research training, and partnerships with other programs, departments, and institutions. Through collaborations and infrastructure, excellence in scholarship across the continuum of training is fostered. Core curriculum includes didactic courses on clinical research, responsible conduct of research, and grant writing, as well as group experiences that include journal clubs, seminars, research presentations, and CTSC workshops. Trainees also receive training specific to nonhuman primates during their tenure in the program.

Opportunities. The CNPRC has a staff of well-trained and dedicated scientists, administrators, veterinarians, veterinary pathologists, and research and husbandry technicians whose continued professional development is important to nurture. Mentoring and training of students, fellows, junior investigators, and related research

personnel is essential in order to ensure a pipeline of investigators and staff committed to supporting the CNPRC colonies, and providing services to the research community. The link with CTSC educational and training programs will ensure the success of academic programs while promoting national core competencies. Additionally, UC Davis was one of the first institutions to receive an NIH Director's Broadening Experience in Scientific Training (BEST) award, which supports innovative approaches to increase student and trainee exposure to multiple research and research-related career options. To further enhance the pipeline of trainees the CNPRC Pilot Research Program will take a new direction patterned on the highly successful CTSC program where all funded pilot projects require the inclusion of trainees in the research team.

Challenges. A recent PNAS publication [Excluded by Requester et al., 2014] highlights several key points related to the research enterprise and impact on trainees. UC Davis has several training programs that are led by Core Scientists and initiatives involving trainees such as the RISE programs. In addition, the CNPRC has a long history of providing research opportunities for trainees that ensures successful and alternative career paths (see Unit descriptions). While current NIH funding presents challenges, opportunities are available to participate in CNPRC research programs as, for example, a senior scientist or project manager. The recent funding of the BEST program highlights the campus focus in supporting alternative career pathways and the necessary tools and training needed for success.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

Plan. The CNPRC will continue to deliver high quality veterinary care and research support integrated with specialized expertise provided by the Core Scientists and Service Cores. The CNPRC Director is committed to a multidisciplinary approach to research and to the provision of outstanding animal care, facilities operations, and scientific expertise to ensure the goals of investigators nationwide can be achieved. The Director provides vigorous oversight to ensure the highest research standards and animal care. This oversight is enhanced through campus compliance activities, the UC Davis IACUC, participation in the campus Animal Research Communication Coordination Committee, and on-site standing committees such as the Research Advisory Committee, Colony Management Advisory Committee, and Morbidity and Mortality Committee. The IACUC, a faculty-based committee, inspects all animal facilities, evaluates all aspects of the institutional animal care program, establishes policy and procedure for the UC Davis campus, and coordinates training, compliance, and occupational health programs. The most recent AAALAC report on the UC Davis Animal Care Program with Full Accreditation and no suggestions for improvement attest to the high quality standards at UC Davis and the CNPRC. Similar to other programs, the CNPRC has experienced a significant increase in the number of Freedom of Information Act requests from animal rights organizations, and is working closely with campus administration, the UC Office of the President, and at the level of the NIH, USDA, and other regulatory bodies regarding these activities. The UC Davis campus continues a history of AAALAC accreditation recognizing a long-standing commitment to the responsible conduct of research and high quality animal care. A cornerstone in sustainability of such care is the training of staff in daily husbandry, management, and safe practices.

Opportunities. The rhesus monkey production colony offers research subjects that span the entire life history ranging from newborns, infants, and juveniles to adults and geriatric stages. The colony addresses an important national need, and all of these age groups are utilized in current research programs and projects. The advantage of a large, well-managed and characterized colony is an unparalleled economy of scale, i.e., to cost effectively provide sufficient numbers of healthy animals for lifespan research with well documented life histories and demographic profiles. Using harvest strategies from all areas of the CNPRC colonies, including the field corrals, corn cribs, and indoor housing, the CNPRC has been able to meet the needs of investigators. A comparable approach is anticipated for the next funding period; should there be a major increase in demand that exceeds supply, priority will be given to NIH-funded studies. The CNPRC will ensure investigators are provided healthy, well-characterized animals to support lifespan health research objectives, and new tools, technologies, and methodologies to advance this research.

A number of the **NPRC Consortium** Working Groups have shared best practices, regulatory questions and concerns, training methods and resources, as well as new ideas for collaborations including developing evidence-based performance standards. Formation of the NPRC Consortium and the Working Group activities has changed many aspects of NPRC operations and communications, and these activities have facilitated and institutionalized collaborations across many NPRC domains that benefit the entire NPRC program. This forum also provides important channels to disseminate NPRC expertise as well as outreach to the greater nonhuman

primate research community and the lay public. One of the greatest strengths of the Working Groups is the identification and sharing of best practices. CNPRC Core Scientists and veterinarians translate their nonhuman primate experiences into enhancement of animal care and research standards, and share this expertise with regulatory agencies and other governing bodies. Working together in a creative and productive manner ensures that validated data are used to refine policies, standard operating procedures, guidelines, and future planning.

Challenges. Much of the infrastructure at the CNPRC is more than 40 years old. To maintain compliance standards and a reputation as a state-of-the-art facility, the CNPRC will continue to work with NIH/OD, the UC Davis campus, and private sources to identify funding opportunities to modernize existing space, and add new laboratory, research, and animal space to meet growing needs. As part of the plans for the recruitment of a new director, the UC Davis leadership has initiated a review of the space and renovation needs at the CNPRC to ensure that the infrastructure meet the needs of the planned faculty expansion and the strong research program in place. In addition, as previous concerns regarding faculty recruitment and positions have been addressed, the CNPRC looks with confidence to the future.

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OVERVIEW

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC report (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no suggestions for improvement, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC.

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal Location] animal space. [Specific Animal Location] outdoor animal housing area includes [Specific Animal Location] field corrals [Specific Animal Location] corn cribs [Specific Animal Location] The [Specific Animal Location] indoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, and geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), simian retroviruses including Type D simian retrovirus (SRV), Simian Immunodeficiency Virus (SIV), and simian T-cell leukemia virus (STLV). The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) is generally socially housed in family groups.

CNPRC policies provide maximum occupational health and safety, including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and performed according to the standard operating procedures (SOPs) for the colony and for defined procedures, and related facility and laboratory training documents required for employment

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities to humans. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester] Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals

housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Housing and Environmental Monitoring. Animal rooms are maintained within the recommended guidelines established by the current edition of the *ILAR Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. Typical nonhuman primate rooms provide 10-15 air changes per hour and are negatively pressurized relative to anterooms/corridors and the outside. Lighting is provided by fluorescent lights, which are controlled by timers (12 hours on/12 hours off). Room temperature is maintained between 68°F and 80°F, depending on the species and age of the animals in the room, and are checked and recorded daily. Emergency generator power is provided for all animal rooms. Indoor animal housing is monitored on a daily basis for temperature, light, and humidity. Power failures, major temperature fluctuation, and other environmental disturbances are either alarmed directly to Campus Physical Plant Services or monitored by CNPRC personnel on a daily basis. The Colony Operations Supervisor and the Maintenance Shop Supervisor carry pagers 24 hours/day and are alerted to environmental monitoring alarms and rooms that are out of temperature and humidity range.

Caging Systems. Indoor cages are stainless steel construction and either wall or rolling rack mounted. Cages incorporate a squeeze mechanism to bring the animal to the front of the cage for manipulation. Cage sizes are determined by the USDA and NIH policies. Cage designs incorporate sliding partitions to allow socialization or pair housing.

Environmental Enrichment. The Environmental Enrichment program is part of the Colony Management and Research Services component of Primate Services, is integrated with Behavior Management Services, and includes all animals, with emphasis placed on indoor-housed animals on research projects. Indoor cages are outfitted with a variety of enrichment options including manipulation mirrors (allowing the animal to view adjacent animals), and cage toys. Perches are present in all indoor cages. Low caloric items, such as forage, are provided on forage boards located on each cage. Animals also receive fruit or vegetables twice weekly. Non-food enrichment is also emphasized. One example of such enrichment is the placement of televisions, which provide visual stimulus to colony animals. Socialization can provide substantial benefit to the animals and is generally accomplished within the limitations of research protocols and daily management practices. Cages have been retrofitted or purchased with sliding partitions to allow pairing. The current strategy is to pair animals during the day and separate them at night to facilitate the assessment of physical signs each morning. Animals are paired early in the morning when animal care staff members begin daily activities; animals are then separated at night when there are limited personnel available to monitor for potential aggressive interactions. The ability to observe each animal's individual daily physical signs is essential to many research programs and overall clinical care. Behavior Management Services staff members view every animal in the colony during morning health rounds and ensure they receive daily enrichment items targeting their specific behavior aberration. All indoor animals are also assessed monthly to identify any abnormal behaviors; these animals receive a detailed behavioral assessment monthly to monitor their status and progress.

Surveillance. The majority of animals at the CNPRC are from the production colony of Specific Animal Location outdoor field corrals. Animals brought into the CNPRC from off-site facilities complete a 90-day quarantine at the CNPRC Quarantine Facility. During this time, animals undergo a complete physical examination with complete blood counts, blood and fecal parasitology, and rectal culture. Five tuberculin tests are completed, and animals are screened for simian retroviruses SRV, SIV, STLV. Animals of foreign origin are

treated for malaria and intestinal parasites. Animals with positive tuberculosis tests and SRV assays, or demonstrating signs of clinical illness, are humanely euthanized and a complete necropsy performed.

Feeding. The animals are fed commercial monkey chow twice daily. Monkey chow is pre-analyzed for content. The analysis of each lot of feed is reviewed by the CNPRC Quality Assurance Coordinator and a Senior Veterinarian. Animals are supplemented with fruit or vegetables twice weekly. Water is provided by automatic lixits, which are checked daily for proper operation. Portable caging with detachable waterlines is checked daily. The CNPRC potable water supply is obtained from wells operated by UC Davis, which are monitored by the Office of Environmental Health and Safety quarterly. The water is tested for chloroforms, a variety of chemical markers including heavy metals and a variety of toxic minerals, pesticides, and chemical contaminants. Additionally, the CNPRC tests for general mineral, organic, and inorganic contamination annually.

Sanitation. Indoor cages are hosed daily with a quaternary ammonium detergent/disinfectant and are sanitized every 2 weeks in a mechanical cage-washer. A microbiological monitoring program is in place to ensure efficacy of sanitation practices. Each animal area is monitored twice per year. Microbiological monitoring results are reviewed and signed off by each area supervisor, a Senior Veterinarian, and the Assistant Director for Colony Management and Research Services. Monitoring of caging pH during cage washing is included in the cage sanitation surveillance program. In addition, water lines in both the indoor and outdoor colony are monitored with microbiological testing on a rotational basis in conjunction with cage change activities.

Record Keeping. Record keeping includes a written individual animal record and entry of specific information into a computerized WebVitals database (see Information Technology Services). Maintenance of the animal colony database, including information on project history, reproductive history, clinical data, viral status, as well as genealogical data is included. Also included are the current location of the animals, weight history, date of last tuberculosis test, and the date of the last serum banking. These data are available to aid in project design and animal selection by investigators. This database has also been critical for several retrospective studies involving prenatal mortality, transmission of retroviral agents in colony management, effects of housing changes on health, and risk factors for spontaneous diseases such as endometriosis. Management of this informational database represents a valuable resource to the entire biomedical research community. Historical animal-related data are maintained on a yearly basis to reflect the production statistics of the colonies including: conception rates, live birth rates, pregnancy loss, and infant mortality.

Animal Health Program. A health check is performed each morning by the colony management staff. Each animal has a location and animal identification barcode that is scanned, and an animal technician records physical signs listed on a menu using a portable barcode reader. After completion of the health check, the information is downloaded onto the main computer, and a morning health report is generated directly to the veterinary staff. Veterinarians or Animal Health Technicians perform a visual examination of each animal on health report. Results of the health check and assessment by the veterinary clinician are then recorded in the animal's record. For animals on study, a report is generated to the investigator on a daily basis by electronic mail. Animals in the outdoor colony are also checked twice each day, once in the morning and afternoon. Identification of animals in the field corrals is performed by individual dye mark. Technicians check each cage closely for animals potentially requiring medical attention. The afternoon health check was added to the outdoor colony in 2012, and increased health surveillance is particularly important during the birth season.

Centralized Research Support. The various services represented in Primate Services work synergistically to provide high quality, technical research support to investigators utilizing the CNPRC, as needed, whether located locally or at a distant site. Staff veterinarians also provide extensive clinical support to animals on long-term research protocols (see Primate Medicine Services).

Staff Training. The program emphasizes occupational safety, as well as increasing demands for technical expertise in the care and research support of nonhuman primates. Training is viewed not only as the initial step at hire, but also as an ongoing process through in-house classes and support to attend relevant

training programs, meetings, and conferences. A spectrum of training opportunities is available specific to the CNPRC and to meet campus-wide training requirements. These include: UC Davis Primate Handling and Husbandry Training; Injury / Illness Prevention Plan; Infection Control Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management; Campus Back Safety Class; Campus Radiation Safety Class; Pesticide and Antimicrobial Safety; Training in Good Laboratory Practices; Supervisor Training with Job Skills Worksheet; and position specific training for all levels of husbandry, animal care, and technical skills. The training program also includes a series of "*Attention to Detail*" documents that provide very detailed information for each of the training and skill areas the staff is expected to meet including information to enhance understanding and the need to adhere to defined guidelines for critical procedures. The Safety and Compliance Officer reports to the CNPRC Director.

Standard Operating Procedures (SOPs). Primate Services has an extensive collection of 185 SOPs that provide detail on all operational procedures including: husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by all staff and undergo full review and revision every three years. SOPs are available in an electronic format online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC, and SOPs by number can be noted in IACUC protocol submissions.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with PHS Policy on Humane Care and Use of Laboratory Animals, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

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OVERVIEW

LETTERS OF SUPPORT

Letters of support from the individuals named below are provided on the pages that follow.

1. [Excluded by Requester] PhD, Professor of Psychiatry and Behavioral Sciences, Director, UC Davis MIND Institute
2. [Excluded by Requester] MD, PhD, Professor of Medicine, Senior Associate Dean for Research, Director, Clinical and Translational Science Center (CTSC), UC Davis
3. [Excluded by Requester] MD, Professor of Psychiatry and Psychology, Director, Center for Neurosciences, UC Davis
4. [Excluded by Requester] MD, Director, UC Davis Comprehensive Cancer Center
5. [Excluded by Requester] PhD, Dean, College of Agricultural and Environmental Sciences, UC Davis
6. [Excluded by Requester] MD, Vice Chancellor for Human Health Sciences, Dean of the School of Medicine, UC Davis
7. [Excluded by Requester] Provost and Executive Vice Chancellor, UC Davis
8. [Excluded by Requester] DVM, PhD, Dean, School of Veterinary Medicine, UC Davis
9. [Excluded by Requester] PhD, Distinguished Professor, Dean, College of Engineering, UC Davis
10. [Excluded by Requester] PhD, Distinguished Professor of Psychology and Neurology, Dean of Social Sciences, UC Davis
11. [Excluded by Requester] PhD, Associate Professor of Anatomy, Physiology and Cell Biology, School of Medicine, Associate Director, Center for Comparative Medicine, UC Davis

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July 8, 2014

Office of Research Infrastructure Programs

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Dear Colleagues:

I am very pleased to provide this letter of support for the important base grant renewal application for the California National Primate Research Center (CNPRC). Since assuming the position as Director of the Medical Investigations of Neurodevelopmental Disorders (MIND) Institute at UC Davis in 2011, I have been quite impressed by the critically important contributions of the CNPRC to the national research enterprise as well as to the scientific program at the University. The MIND Institute Research Director, [REDACTED] is a CNPRC Core Scientist, and several other MIND Institute faculty members collaborate with [REDACTED] and other CNPRC Core Scientists to explore immunological mechanisms underlying autism spectrum disorders and related neurodevelopmental disorders. These studies have already resulted in findings of translational importance as well as several high impact publications and we look forward to continuing the interactions with the CNPRC during the next funding period. This is a very important research area for the MIND Institute and we are very fortunate to have an outstanding group of collaborators at the CNPRC that can help to further advance these important studies.

It is clear that the CNPRC serves as a driving force in the use of highly relevant nonhuman primate models to explore critically important human disease conditions. In fulfilling these functions, the CNPRC continues to meet NIH strategic priorities by providing high-quality animals, facilities, tools, and services driven by the intellectual infrastructure of the Core Scientists who guide and conduct basic and translational research with nonhuman primates. We are very pleased that the CNPRC puts a strategic emphasis on multidisciplinary research teams focused on developing and using nonhuman primate models of human health and disease. This is particularly evident as shown in its strong grant portfolio, which has approximately \$150 million of funding during the current funding period. The goals for the next CNPRC funding period are to address accessible state-of-the-art research opportunities for investigators and trainees that promote the study of lifespan health in the nonhuman primate model. This overarching vision is closely aligned with the goals of the MIND Institute, which build upon expertise, productivity, and innovation; strong ties with institutional and national programs; and serve to maximize resources for NIH funded research. We are very supportive of the CNPRC application and believe that targeted opportunities and University of California initiatives will facilitate faculty recruitment to the CNPRC. This will clearly strengthen the already impressive infrastructure, expertise, and extensive services in place to meet the growing needs of investigators and trainees locally and nationally.

During its long and fruitful history, the CNPRC has always adhered to the central goal of advancing nonhuman primate models for studying and treating human disease. This broad and encompassing vision has provided many opportunities for successful collaborations with faculty in UC Davis colleges, schools, and centers, in addition to other research institutions nationwide. One such example is the close collaboration between the CNPRC and the MIND Institute. I anticipate an even greater level of success as the CNPRC enters its next funding period.

Sincerely,

Excluded by Requester

Professor of Psychiatry and Behavioral Sciences

UNIVERSITY OF CALIFORNIA, DAVIS

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Excluded by Requester

July 7, 2014

Office of Research Infrastructure Programs
 Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
 9000 Rockville Pike
 Bethesda, MD 20892

Dear colleagues of the review panel,

In my capacity as the Senior Associate Dean for Research in the School of Medicine and the Director of the NIH funded Clinical and Translational Science Center (CTSC) at UC Davis, I am very pleased to express my strong and enthusiastic support for the application to renew the California National Primate Research Center (CNPRC) base grant. Ever since my arrival at UC Davis 12 years ago, I have been deeply engaged with the CNPRC. I have served as a member of the Research Advisory Committee (RAC) for many years and I have had very frequent meetings with [REDACTED] the retiring Director, and the CNPRC leadership to explore common areas of interest. These interactions have grown further after the NIH funding of our CTSC as part of the inaugural cohort of centers in 2006. Examples of the many and deep interactions between the CNPRC and the CTSC include shared workshops and symposia, joint pilot grant proposals, partnerships in core services and information technology, and in our respective educational missions. I am working very closely with [REDACTED] a CNPRC Core Scientist and Unit Leader of the Reproductive Sciences and Regenerative Medicine program. Dr. [REDACTED] is part of the CTSC leadership and oversees the CTSC Pilot and Collaborative Studies and Translational programs. We also share the oversight of the Pilot and Outreach program of the NIH-funded West Coast Metabolomics Center. Recently, I was appointed as one of the two co-Chairs for the search committee to identify the next CNPRC Director. We were very pleased by the high level of interest nationally and we had the pleasure to interact with many exceptionally strong candidates. At present, a top candidate has been identified and the search process is coming to a close. Participation in this process also provided excellent opportunities for me to set the stage for future interactions and to bring the many attributes of the CTSC to the attention of the candidates.

Both the School of Medicine and the CTSC are in strong support of the center application, which is critically important to the research portfolio in the School of Medicine as well as to the university at large. There are multiple examples of interaction between School of Medicine faculty, the CNPRC and the CTSC, and these interactions occur in all scientific areas of the CNPRC. One of the most recent examples involves multi-million dollar funding from the California Institute of Regenerative Medicine (CIRM) of preclinical studies for tracheal

regeneration in non-human primates jointly to [Excluded by Requester] from the School of Medicine and [Excluded by Requester]. Studies like these would not be possible without the CNPRC, and the results will accelerate the initiation of clinical studies in humans. I am very pleased that the CNPRC will be in an outstanding position to greatly benefit from the many available resources throughout UC Davis, including those of the CTSC, in achieving its goals. UC Davis will, in turn, greatly benefit from the presence of the CNPRC, which will promote new collaborations and cutting-edge science in areas of considerable institutional strength. These studies, and the impressive group of Core and Affiliated Scientists at the CNPRC, will continue to create dynamic partnerships throughout UC Davis colleges and schools. In this role, CNPRC, like the CTSC, will serve as a glue to bring an impressive range of collaborators together, and I am very pleased to see the high level of enthusiasm and creativity already at hand among the CNPRC faculty and leadership.

The translational science agenda with a focus on lifespan health outlined in the grant application is yet another reason for the CNPRC to be a natural partner for the CTSC. Together, we can make significant contributions to improvement in human health and to launch innovative and exciting projects. We are committed to bring the many resources of the UC Davis CTSC — including regulatory support and access to biostatistics, informatics and evaluation resources, education and mentoring, community outreach and technology transfer — to the CNPRC faculty and scientists. The CTSC has a long history of working collaboratively with many other NIH-funded centers and programs, including the recently funded West Coast Metabolomics Center

(PI: [Excluded by Requester]) as described above, and the Research Center for Minority Aging Research (PI: [Excluded by Requester]). In addition, the CTSC has a history of partnership with many translationally focused centers and programs in supporting exciting and innovative pilot studies, and we very much look forward to continue to work with the CNPRC in that regard as well.

I also am pleased to continue as a member of the Research Advisory Committee for the CNPRC should the application be successful. I am also very pleased to continue providing input on an as needed basis regarding the scientific cores, research projects, translational research agenda, and relationships to the broader scientific and UC Davis communities.

I strongly support this renewal application.

Sincerely,

[Excluded by Requester]

Director, Clinical and Translational Science Center (CTSC)
University of California, Davis

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July 9, 2014

Office of Research Infrastructure Programs
Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
9000 Rockville Pike
Bethesda, MD 20892

Dear colleagues of the review panel,

I am very pleased to write this letter of support for the important base grant renewal application for the California National Primate Research Center (CNPRC). The Center for Neuroscience (CNS), like the CNPRC, is a center that crosses school and college boundaries as it represents a partnership between the School of Medicine and the College of Biological Sciences. Many of our faculty members are already engaged in research projects focused on nonhuman primates, and the CNPRC is a natural partner for us.

The focus on neuroscience as articulated by President Obama and the national scientific leadership indicates the need to better understand cognition and the underpinnings of behavioral and mental disorders. In this regard, studies in nonhuman primates will be invaluable as this model closely reflects the situation in humans. The studies already under way at the CNPRC and the CNS, focused on neurodevelopmental and mental disorders, set the stage for future collaborative projects, as seen in the UC Davis intramurally funded Research Investments in Science and Engineering (RISE) awards. One of these awards is led by a CNS faculty

member, [REDACTED] and includes a CNPRC Core Scientist [REDACTED]. These initiatives serve as models for future interactions between the CNPRC and the CNS during the proposed funding period, and the CNPRC has been critical in providing the essential high-quality animals for CNS research, as well as expert veterinary expertise as needed. Other interactions include the many strengths in imaging capabilities, both at the CNS and the CNPRC.

I understand that the goals for the next CNPRC funding period are to address accessible state-of-the-art research opportunities for investigators and trainees that promote the study of lifespan health in the nonhuman primate model. This overarching vision is closely aligned with the goals of the CNS and we are very supportive of the CNPRC application. We look forward to a continued fruitful and productive interaction between the CNS and the CNPRC and together we will further advance the already extensive infrastructure, expertise, and support services in place to meet the growing needs of investigators and trainees locally and nationally. I offer my full support for the successful renewal of the UC Davis CNPRC.

Sincerely,

[REDACTED]

[REDACTED]

Director, Center for Neurosciences

Letters Of Support

UC DAVIS
COMPREHENSIVE
CANCER CENTER

A National Cancer
 Institute-Designated
 Comprehensive Cancer
 Center

July 7, 2014

Office of Research Infrastructure Programs
 Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
 9000 Rockville Pike
 Bethesda, MD 20892

Dear colleagues of the review panel,

I am extremely pleased to write this letter of support for the important base grant renewal application for the California National Primate Research Center (CNPRC). Like the CNPRC, the NCI-funded UC Davis Comprehensive Cancer Center constitutes an extraordinary university-wide asset and the two centers have overlapping areas of interest, setting the stage for productive and scientifically highly relevant partnerships. One of the components of the Comprehensive Cancer Center, the Biotechnology program, is co-led by Dr.

Excluded by Requester

a CNPRC Core Scientist. This offers unique opportunities to align imaging capabilities, and such interactions are already under way, as seen in several of the intramurally funded Research Investments in Science and Engineering (RISE) awards. Two of these awards are led by CNPRC Core Scientists and include members of our Comprehensive Cancer Center. I am personally involved in the RISE proposal led by Excluded by Requester also a CNPRC Core Scientist, and I am very committed to its success. These initiatives serve as models for future interactions between the CNPRC and the Cancer Center during the proposed funding period.

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The use of relevant animal models is of critical importance for the Comprehensive Cancer Center. We already have strong interactions with the School of Veterinary Medicine regarding tumors arising in companion animals. The CNPRC offers additional opportunities, in particular with regard to the role of the immune system and inflammation over the lifespan and the use of translational imaging approaches. We have led several institutional workshops focused on this concept with participation of CNPRC Core and Affiliate Scientists. This has made it clear that the CNPRC is a driving force in the use of highly relevant nonhuman primate models to explore critically important human disease conditions. In fulfilling these functions, the CNPRC continues to meet NIH strategic priorities by providing high-quality animals, facilities, tools, and services driven by the intellectual infrastructure of the Core Scientists who guide and conduct basic and translational research with nonhuman primates.

The goals for the next CNPRC funding period are to address accessible state-of-the-art research opportunities for investigators and trainees that promote the study of lifespan health in the nonhuman primate model. As seen above, this overarching vision is closely aligned with the goals of the Comprehensive Cancer Center.

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Letters Of Support

Page 264

Obtained by Rise for Animals.

Uploaded to Animal Research Laboratory Overview (ARLO) on 09/19/2020

We are very supportive of the CNPRC application that we believe will clearly strengthen the already impressive infrastructure, expertise, and extensive services in place to meet the growing needs of investigators and trainees locally and nationally.

During its long and fruitful history, the CNPRC has always adhered to the central goal of advancing nonhuman primate models for studying and treating human disease. This broad and encompassing vision has provided many opportunities for successful collaborations with faculty in UC Davis colleges, schools, and centers, in addition to other research institutions nationwide. I anticipate continued and an even greater level of success as the CNPRC enters its next funding period. I give my full support for the successful renewal of the UC Davis CNPRC.

Sincerely,

Excluded by Requester

Director, U.C. Davis Comprehensive Cancer Center

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July 10, 2014

Office of Research Infrastructure Programs
Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
9000 Rockville Pike
Bethesda, MD 20892

Dear colleagues of the review panel:

The UC Davis College of Agricultural and Environmental Sciences (CA&ES) addresses critical issues related to agriculture, food systems, the environment, and human and social sciences through cutting-edge research, top-ranked undergraduate and graduate education, and internationally recognized outreach programs. In 2013, UC Davis was ranked the No. 1 university in the world for teaching and research in the area of agriculture and forestry. CA&ES encompasses more than 2,300 acres devoted to agricultural teaching and research. UC Davis is the most published and cited U.S. research university in agricultural sciences, environment/ecology, and food science and nutrition. UC Davis researchers lead the nation in extramural funding in the agricultural sciences.

As dean of the CA&ES, I am impressed by the strong collaboration between CA&ES faculty and the California National Primate Research Center (CNPRC). Personal Info earlier this year and assuming the position as dean of CA&ES, I was excited to see the many opportunities at UC Davis, including the CNPRC. The role of CNPRC as a strong contributor to the National Primate Research Centers program nationwide is well acknowledged. The CNPRC continues to meet NIH strategic priorities by providing high quality animals, facilities, tools, and services driven by the intellectual infrastructure of the core scientists that guide and conduct basic and translational research with nonhuman primates. The CNPRC puts a strategic emphasis on multidisciplinary research teams that focus on developing and using nonhuman primate models of human health and disease. This partnership spirit resonates strongly with CA&ES goals. There are multiple avenues for interaction between CA&ES faculty and CNPRC. Two such expanding areas are nutrition and environmental sciences. Faculty in these areas have a history of partnering with CNPRC core scientists, and I am strongly committed to enhance and stimulate this partnership spirit. The recent intramurally funded Research Investments in Science and Engineering (RISE) award on mucosal immunity, co-led by Dr. Excluded by Requester a CA&ES faculty member and Director of the Foods for Health Institute, together with Excluded by Requester a CNPRC core scientist, serves as an outstanding model for fruitful and productive partnership. I am deeply committed to support such interactions leading to future partnerships.

In closing, I offer my strong support for the successful renewal of the CNPRC. The collaboration between CA&ES and the CNPRC is but one example of the strong, collaborative culture at UC Davis and I anticipate its continued success.

Sincerely,

 Excluded by Requester

Dean

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July 7, 2014

Office of Research Infrastructure Programs
Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
9000 Rockville Pike
Bethesda, MD 20892

Dear colleagues of the review panel,

UC Davis Health System (UCDHS), comprising the School of Medicine and the UC Davis Medical Center, is nationally recognized and excels at translating scientific discoveries and new technologies into improved patient care and community-wide health. UCDHS mission is to educate and train medical professionals; provide superior care to a large geographically dispersed population; contribute to the nation's basic, translational, and clinical research enterprises; and to further serve the public through outreach and health education programs. UCDHS is strongly aligned in multiple ways with the CNPRC and many of the Core Scientists who contribute to the center's research mission, including the Interim Director [REDACTED] have their departmental home in the School of Medicine (including [REDACTED]).

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Requester

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The partnership between the CNPRC and the School of Medicine goes back many years. From the inception of the NIH-funded UC Davis Clinical and Translational Science Center (CTSC) in 2006, the leaders of the CTSC and the CNPRC have interacted in multiple partnerships from joint pilot grant calls, workshops, symposia, joint committees and joint core facilities. In addition, both centers have a strong educational mission and partner with regard to their training programs. This close partnership has resulted in many scientific advances and a climate of trust and synergy. Notably, the CTSC Director [REDACTED] served as co-Chair for the search committee to identify the next CNPRC Director. Beyond the CTSC, multiple other centers housed in the School of Medicine, such as the NIH-funded Comprehensive Cancer Center, the Medical Investigations of Neurodevelopmental Disorders (MIND) Institute, the Center for Neuroscience, and the California Institute of Regenerative Medicine (CIRM)-supported Institute for Regenerative Cures, have established partnerships with the CNPRC (see separate letters of support). These partnerships extend to all the four scientific units of the CNPRC, and the School of Medicine is therefore deeply committed to the continued success of the CNPRC.

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Requester

One of the themes emphasized in the School of Medicine strategic plan is Regenerative Medicine and the School has provided over \$30 million in matching funds to establish a Translational Shared Research Facility located on-site at the CNPRC and at the Institute for Regenerative Cures (IRC), right next to the CTSC on the Medical Center campus. The Regenerative Medicine program combines unique capabilities for stem cell research with training in diseases that might be prevented, reversed, or ameliorated by stem cell therapy. Notably, the training program has

partnered with several other training programs housed in the CTSC to create a critical mass of trainees and to enhance curricular offerings. The IRC strives to link basic “discovery” efforts with translational investigations in nonhuman primates. An important asset for these activities is the Good Manufacturing Practices (GMP) facility, housed in the IRC, that enables researchers to readily move new stem/progenitor cell therapies into patients once they have been rigorously tested in nonhuman primates. The CNPRC Reproductive Sciences and Regenerative Medicine Unit is an integral component of these efforts, and Unit faculty conduct preclinical studies in nonhuman primates through research supported by the NIH and CIRM.

Another example of strategic partnerships at UC Davis is represented by the Center for Comparative Medicine (CCM), jointly overseen by the Schools of Medicine and Veterinary Medicine. The CCM is co-localized with the CNPRC and embraces the concept of “One Health” through interdisciplinary comparative medical research, teaching, and model development. Notably, the Interim Director of the CNPRC Excluded by Requester serves as Director for CCM.

Due to the importance of the CNPRC for the School of Medicine research portfolio and the outstanding opportunities offered through the center for translational research highly relevant to human disease, leaders of the School of Medicine have been deeply engaged in the transition of leadership at the CNPRC from Excluded by Requester to a new Director. The Vice Dean in the School of

Medicine, Excluded by Requester has worked closely with Excluded by Requester in the School of Veterinary Medicine and Vice Chancellor Lewin, the CNPRC base grant Principal Investigator, to develop a competitive recruitment package, which includes 4 faculty positions in the School of Medicine.

In addition, the CTSC Director Excluded by Requester has been involved in all aspects of the preparation of the base grant renewal process. All these efforts indicate the importance attested to the CNPRC by the School of Medicine.

In conclusion, I am delighted to underscore our commitment to the future success of the CNPRC in the strongest possible way. The CNPRC is important to UC Davis, to the entire University of California system, and to the nation, as it is one of only seven NIH-funded non-human primate research centers. We recognize the responsibility this carries and we remain fully supportive of the base grant application and committed to the continued success of the CNPRC.

Sincerely,

Excluded by Requester

Dean of the School of Medicine
University of California, Davis

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July 10, 2014

Office of Research Infrastructure Programs
 Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
 9000 Rockville Pike
 Bethesda, MD 20892

Dear colleagues of the review panel,

The California National Primate Research Center (CNPRC), located at the University of California, Davis (UC Davis), unifies key personnel, infrastructure, and services across research domains for a common goal: the advancement of nonhuman primate models for the study and treatment of human disease. The CNPRC brings together a strong team of Core Scientists, veterinarians, technicians, and administrative staff to capitalize on the depth and breadth of translational research with nonhuman primate models that cuts across the human lifespan. The CNPRC is embedded in the fabric of UC Davis and through this advantageous position enjoys virtually unlimited opportunities for cross-departmental and interdisciplinary interactions and partnerships. As seen throughout the present proposal, the CNPRC leadership and faculty have capitalized on this rich potential for outreach and the future plans are well integrated into the overall university research portfolio. It is clear to upper administration that the CNPRC brings a unique and critically important dimension to the pursuit of innovative therapeutic advances to improve human health. The exciting research projects described in the application, either initiated by CNPRC faculty or having CNPRC Core and Affiliated Scientists as key partners, will bring added value with regard to conditions mirroring those in humans. Results brought forward by these efforts will inform studies in humans and contribute to accelerate and catalyze discoveries and innovations.

The established CNPRC infrastructure includes experienced Core Scientists with joint appointments in academic departments in UC Davis schools and colleges (e.g., Schools of Medicine and Veterinary Medicine, Colleges of Engineering and Letters and Science) and integrates and leverages several key institutional Centers and programs. Through these partnerships, the CNPRC derives additional advantages that add to the already very strong program. During the current funding period, Core Scientists collaborated with 346 Affiliate Scientists and other investigators from institutions across the U.S. (128 from UC Davis), published approximately 400 manuscripts, and mentored 300 trainees (undergraduate to junior faculty). Extramural grants during the current funding period for all Units and facilities combined totaled approximately \$150 million.

Four broad Scientific Research Units (Brain, Mind, and Behavior; Infectious Diseases; Reproductive Sciences and Regenerative Medicine; Respiratory Diseases) include 20 Core Scientists that maintain active NIH-supported research, service, and training programs, and are collectively a resource for investigators and trainees nationwide. Working with nonhuman primates requires specialized

California National Primate Research Center

July 10, 2014

Page | 2

knowledge and expertise and Core Scientists provide the intellectual infrastructure for a range of collaborative opportunities, multidisciplinary partnerships, and novel services to support and facilitate research with nonhuman primates. We are deeply aware that the CNPRC is an established national resource with a primary mission to conduct nonhuman primate research at the highest quality level and to provide services and resources to the greater research community. UC Davis is deeply committed to the highest possible quality in all its missions and we take this responsibility very seriously.

In parallel with the base grant renewal application, a search for a new CNPRC Director has been conducted. The leaders of our Schools of Medicine and Veterinary Medicine assisted Vice Chancellor Lewin and me in developing a recruitment strategy, and quickly and enthusiastically mobilized the leadership and faculty of the many UC Davis colleges and schools that interact with the CNPRC. A search committee, led by Excluded by Requester has identified a strong leading candidate, and the UC Davis leadership has worked expeditiously to develop a recruitment package to ensure the continued success of the CNPRC. I am very pleased to state that UC Davis will make substantial institutional commitments to the Director for renovation of CNPRC facilities, faculty support and new instrumentation. These commitments, together with the creative leadership of a new director will serve to expand the already vibrant research program of the CNPRC.

I have conferred with the deans of selected colleges (Medicine, Veterinary Medicine, Biological Sciences, Engineering, Social Sciences) and the Primate Center leadership to identify thematic areas of scientific interest to the campus. Based on these areas, I have authorized or will authorize at least 10 joint faculty recruitments of Core Scientists in the CNPRC. The necessary infrastructure including space and equipment will be provided to these faculty members. I am very pleased that the new faculty positions are contributed by a very broad range of schools and colleges (School of Medicine, School of Veterinary Medicine, College of Biological Sciences, College of Engineering, and College of Letters & Sciences), recognizing the strategic importance of the CNPRC not only for UC Davis but for the entire University of California system. This broad and enthusiastic commitment is a clear indication of the importance of the CNPRC felt by faculty and students throughout the university.

In conclusion, I want to reemphasize our strong and unwavering support for the CNPRC. We are proud of the accomplishments of the CNPRC, we acknowledge our responsibility as housing one of the seven national primate research centers and we look forward with confidence to add to the national scientific arsenal in promoting discoveries to advance knowledge and human health.

Sincerely,

Excluded by Requester

Provost and Executive Vice Chancellor

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July 9, 2014

Office of Research Infrastructure Programs
Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
9000 Rockville Pike
Bethesda, MD 20892

Dear NIH Review Panel,

This letter serves to convey my enthusiasm to renew the base funding for the California National Primate Research Center (CNPRC) because of its enormous contribution to the UC Davis School of Veterinary Medicine (SVM), the campus as a whole, and the national research community. The UC Davis SVM is one of the premier veterinary schools in the world and the only veterinary school in the University of California system and it plays a crucial role to advance the health of animals, people, and the environment. The SVM serves the people of California by providing educational, research, clinical service, and public service programs of the highest quality to advance the health and care of animals, the health of the environment, and public health, and to contribute to the economy. We lead the nation among veterinary schools in total research funding and NIH funding; totally over \$65 million in total expenditures during the past fiscal year. School of Veterinary Medicine faculty members have earned a reputation for their broad expertise and shared commitment to solving some of society's most persistent health problems. The school's impact is evident in the accomplishments of clinicians who have developed novel treatments and basic scientists who continue to make major discoveries in animal, human and environmental health. Our educational mission is comprehensive and include a broad spectrum of students and trainees in our professional Doctor of Veterinary Medicine program, Master of Preventive Veterinary Medicine program, the most comprehensive clinical residency program in the world (in collaboration with the CNPRC), and exceptional graduate academic MS and PhD programs.

Prior to assuming the role as Dean of the SVM at UC Davis, I was very familiar with the many contributions of the CNPRC to the university and to the broader research community as a whole. I had the pleasure to serve as a member of the NIH site visit team in the previous renewal application cycle and was quite impressed with the achievements and the many areas of cutting-edge research focus of the CNPRC. As a long-term NIH funded investigator and member of the Institutes of Medicine (National Academy of Sciences), I feel very confident in helping evaluate and serve on the leadership team for the CNPRC. Since arriving at UC Davis, I have continued this interaction with the CNPRC and I have been very involved with facilitating the CNPRC leadership transition from [redacted] to the incoming director. Further, I am very pleased to note that many faculty members in the SVM are active in leading roles in the CNPRC as Core Scientists [redacted]. In addition, [redacted] Associate Director for Primate Services of the CNPRC, is a faculty

Excluded by
Requester

member in the SVM. This involvement attests to the close collaboration that exists between the CNPRC and the SVM.

The physical proximity of the CNPRC to the Center for Comparative Medicine (CCM) and the Pritchard Veterinary Medical Hospital (VMTH) facilitates novel research approaches that are highly comparative in nature and maximizes opportunities for collaboration in solving complex problems in disease transmission. At the CCM, SVM faculty work side-by-side with their counterparts affiliated with the School of Medicine to facilitate innovative approaches aimed at understanding the pathogenesis of complex human disease. Investigators are developing comparative experimental designs that integrate molecular engineering of new rodent models and naturally occurring veterinary diseases patients treated at the VMTH, thereby facilitating translation of study results to nonhuman primate models and human clinical trials.

The CNPRC is a central component and active contributor to the National Primate Research Centers program nationwide and continues to meet NIH strategic priorities by providing high-quality animals, facilities, tools, and services driven by the intellectual infrastructure of the Core Scientists who guide and conduct basic and translational research with nonhuman primates. The CNPRC places a strategic emphasis on multidisciplinary research teams that focus on developing and using nonhuman primate models of human health and disease. This strategic emphasis is directly in line with the mission of the SVM and we employ many companion animal models of human disease to achieve this goal. The goals for the next CNPRC funding period are to address accessible state-of-the-art research opportunities for investigators and trainees that promote the study of human health and healthy aging in the nonhuman primate model. This overarching vision builds upon expertise, productivity, and innovation; strong ties with institutional and national programs; and maximizes resources for NIH-funded research. The SVM will collaborate closely with the CNPRC to achieve this vision and to benefit veterinary medicine practices as well. Importantly, the SVM has committed several new faculty positions to the CNPRC as part of the recruitment of the new director. We believe that this strong level of support will jointly benefit the CNPRC and the SVM and continue the already strong synergy in promoting innovative scientific and educational initiatives.

During its long and fruitful history, the CNPRC has contributed to the success of many investigators within the CNPRC and outside of the center. The UC Davis SVM has developed a very strong, collaborative relationship with the CNPRC and I anticipate that this will continue to grow as the CNPRC enters its next funding period. I give my full support for the successful renewal of the UC Davis CNPRC.

Sincerely,

Excluded by Requester

Dean
School of Veterinary Medicine

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July 9, 2014

OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS

Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
9000 Rockville Pike
Bethesda, MD 20892

Dear colleagues of the review panel,

Since its founding in 1962, the UC Davis College of Engineering has focused on finding technical solutions to some of our nation's most challenging problems, while also preparing thousands of highly skilled engineers to join us in this challenge. In addition to finding engineering solutions to problems involving energy, environment, and physical infrastructure, our researchers and educators focus on specific areas of concern regarding human health and biology including biomedical imaging, biomedical engineering, data visualization, and information technology and management. Indeed, recent imaging technologies emerging from the UC Davis College of Engineering have allowed researchers to study biological processes at the cellular and molecular levels, regeneration and repair of tissues, nanomedicine and nanotherapeutics, and drug delivery systems that precisely target diseased cells.

The creation of the Department of Biomedical Engineering approximately 15 years ago added an important new dimension to the college and expanded opportunities for partnerships with faculty in life sciences. The department has rapidly grown to one of the most well-funded biomedical engineering departments in the University of California system, and its faculty is well recognized nationally. They have, since the inception of the department, developed very strong ties with faculty in the Schools of Medicine, Veterinary Medicine, and the California National Primate Research Center (CNPRC). Faculty from our college work with CNPRC scientists particularly in the area of biomedical imaging, which is

Excluded by Requester

enhanced by the participation of [redacted] one of our faculty members, in a leadership role of the CNPRC Multimodal Imaging Core. Assisted by the rich imaging opportunities provided, Core Scientists in the Reproductive Sciences and Regenerative Medicine Unit have unique strengths in gene- and cell-based therapy/regenerative medicine and tissue engineering. The unit has a long-standing commitment to the development and application of novel *in vivo* imaging technologies and tools including ultrasound, optical imaging, and positron emission tomography/computed tomography (PET/CT) as described in the Multimodal Imaging Core. The unit also provides a strong connection with the UC Davis Center for Molecular and Genomic Imaging directed by [redacted] the biomedical cyclotron at [redacted]

Excluded by Requester

biochemistry laboratory, led by [redacted] who has a joint faculty appointment in the College of Engineering and the School of Medicine, and the new UC Davis Radiochemistry Research and Training Facility that was developed cooperatively by the UC Davis Health System, PETNET Solutions Inc., and the Northern California PET Imaging Center. Led by [redacted] the unique partnership with PETNET functions as a pipeline for commercialization of the concepts and compounds that researchers develop.

Excluded by Requester

Office of Research Infrastructure Programs

July 9, 2014

Page 2

The goals for the next CNPRC funding period are to address accessible state-of-the-art research opportunities for investigators and trainees that promote the study of human health and healthy aging in the nonhuman primate model. This overarching vision builds upon expertise, productivity, and innovation; strong ties with institutional and national programs; and maximizes resources for NIH-funded research. The UC Davis College of Engineering will continue to collaborate closely with the CNPRC to achieve these goals and with a thoughtful plan for the addition of new imaging capabilities, including MRI, on-site at the Primate Center which will advance the CNPRC mission. In conclusion, I am very pleased to offer my full support for the successful renewal of the UC Davis CNPRC.

Sincerely,

Excluded by Requester



UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY · DAVIS · IRVINE · LOS ANGELES · MERCED · RIVERSIDE · SAN DIEGO · SAN FRANCISCO



SANTA BARBARA · SANTA CRUZ

Office of the Dean of Social Sciences
College of Letters and Science

One Shields Avenue
DAVIS, CALIFORNIA 95616

July 8, 2014

VICE CHANCELLOR HARRIS LEWIN

Office of Research

Dear Vice Chancellor Lewin,

The College of Letters and Science (L&S) is the largest of the schools and colleges at UC Davis. The college is made up of three divisions encompassing the broadest offering of disciplines at UC Davis: Humanities, Arts and Cultural Studies, Mathematical and Physical Sciences, and Social Sciences. The college is committed to providing the best higher education possible, cultivating a brighter future for generations to come. By providing critical thinking and fundamental education to students, it opens doors for future leaders, great thinkers, accomplished scholars, and strong global citizens. The college creates opportunities for undergraduate research and provides enhanced enrichment programs.

As Dean of Social Sciences in the UC Davis College of L&S, I am impressed by the strong collaboration between L&S faculty and the California National Primate Research Center (CNPRC). The CNPRC is a central component and driving force in the National Primate Research Centers program nationwide and continues to meet NIH strategic priorities by providing high-quality animals, facilities, tools, and services driven by the intellectual infrastructure of the Core Scientists that guide and conduct basic and translational research with nonhuman primates. The CNPRC puts a strategic emphasis on multidisciplinary research teams that focus on developing and using nonhuman primate models of human health and disease.

Several L&S faculty members serve as Core scientists in the CNPRC Brain, Mind, and Behavior Research Unit Excluded by Requester studying neuroanatomical organization, biobehavioral organization, neuroimmune interactions and the etiology of autism, social bonds and social development, the human-animal interface, and social networks. This team of investigators specializes in research on sociality, temperament, and development with a lifespan approach that utilizes measures from early stages to aged animals, including new primate models of human psychiatric diseases. The Unit Core Scientists lead vibrant research programs that contribute to the training of students and visiting scientists. Major focus areas include neurodevelopmental disorders, particularly those with social deficits such as autism. The effects of social development on lifespan health has been a central theme since inception of the Unit by Excluded by Requester whose early work on attachment in monkeys and its effects on later behavior was central to the field. The BioBehavioral Assessment (BBA) Program is a resource unique to the NPRC system. This program is based on more than three decades of psychobiological research documenting the existence of stable, individual differences in patterns of adaptation to the environment throughout the lifespan, which have been shown to be associated with genetics, brain function, neuroendocrine organization, patterns of neural innervation of lymphoid tissue, and immune function. These and related activities are also provided by Unit Core and Affiliate Scientists through the Behavior Research Services Core and the management of the CNPRC colonies in Primate Services through Behavior Management Services.

Vice Chancellor Lewin

July 8, 2014

Page 2

In closing, I offer my strong support for the successful renewal of the CNPRC. The collaboration between L&S faculty and the CNPRC is but one example of the strong, collaborative culture at UC Davis and I anticipate its continued success. To ensure a continued vibrant synergy between the CNPRC and the College of L&S, I am pleased to state that the College will contribute a new faculty position as part of the recruitment of the incoming CNPRC Director. This strong support underscores the importance of the ongoing CNPRC research studies for our college and the university as a whole.

Sincerely,

Excluded by Requester

Distinguished Professor of Psychology and Neurology
Dean of Social Sciences

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO



SANTA BARBARA • SANTA CRUZ

CENTER FOR COMPARATIVE MEDICINE
 SCHOOL OF MEDICINE
 SCHOOL OF VETERINARY MEDICINE
 (530) 752-7913
 FAX (530) 752-7914

ONE SHIELDS AVENUE
 DAVIS, CALIFORNIA 95616-8557

Vice Chancellor for Research Harris Lewin

July 10, 2014

Re: Letter of Support for the P51 renewal of the California National Primate Research Center

Dear Dr. Lewin,

I am writing to affirm the long-standing commitment of the Center for Comparative Medicine (CCM) to the highly productive and innovative collaboration between the CCM and the California National Primate Research Center (CNPRC). As you know, the primary mission of the CCM is the use of animal models of human diseases, and this concept embraces the concept of "One Medicine" through interdisciplinary comparative medical research, teaching, and model development. The research focus of the CCM is to investigate the pathogenesis of human disease, using experimental animal models and naturally occurring animal diseases. The recognition that animal diseases present unique opportunities to investigate the mechanisms of human disease pathogenesis is almost 90 years old. As first articulated in 1927 (Bradley, Proc Royal Soc Med. 21:129), *"Human and veterinary medicine are confronted with similar problems and employ similar means for their solution; and, taken together, they deal with a large group of animals sufficient to justify the contention that they are two branches of one medicine"*. Accordingly, UC Davis stands apart from all other institutions in enabling a translational pipeline from multiple veterinary species to human clinical practice, and the CCM represents the nexus between the Schools of Medicine and Veterinary Medicine.

The Center for Comparative Medicine will soon initiate new faculty recruitments for up to three Assistant/Associate Professor positions. The CCM has a balanced research portfolio between faculty who use nonhuman primate (NHP) and/or mouse models of human diseases, with an emphasis on infectious diseases. Of the three recruits to be considered, it is anticipated that one to two of these recruits will have research programs based on NHP models. Due to the long-standing interdigitation of the CNPRC and CCM research programs, our recruitments will be conducted with representation of the CNPRC Core Scientists on the search committee so that the recruitment processes harmonizes with the long-term goals of the CNPRC. While we are casting a wide net in our candidate search, one goal of the search is to recruit candidates with research programs involving infectious disease, mucosal immunity, vaccines, and/or microbial therapeutics. In particular, I would like to stress that recruitment of candidates with a subset of these areas as applied to respiratory biology will be a prime consideration to leverage the strong Respiratory Diseases program at the CNPRC.

The CNPRC is a critical resource nationally and for the UC Davis campus. The extensive and unique expertise for translational research with nonhuman primates by the core scientists, many of which are also faculty at the CCM, provides major strengths in intellectual and physical infrastructure shared between these adjacent facilities. With the current NIH strategic areas of focus related to infectious diseases and lifespan health, we envision expansion of many of the highly successful NIH supported programs in place within the CCM and CNPRC, and with the new recruitments planned in both programs.

Sincerely,

Excluded by Requester

Excluded by Requester

Associate Director, Center for Comparative Medicine;
 Associate Professor, Department of Anatomy, Physiology, and Cell Biology;
 School of Veterinary Medicine, University of California, Davis

Letters Of Support

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Obtained by Rise for Animals.

Uploaded to Animal Research Laboratory Overview (ARLO) on 09/19/2020

OVERVIEW

RESOURCE SHARING PLAN

Data and resources are regularly shared through collaborations, publications, presentations, outreach efforts, websites, and other collaborative and service opportunities provided through the California National Primate Research Center (CNPRC) and the National Primate Research Center (NPRC) Consortium *NPRC Research and Capabilities Inventory* website (see NPRC Consortium).

The overall objective is to: (1) Ensure that project datasets will be widely shared with the scientific community and public for research and training; (2) Ensure privacy and security for sensitive data; and (3) Ensure the long-term value and viability of data sets collected through proper metadata documentation and data archiving.

Data will be shared in several ways: (1) through dissemination of results, (2) through internal collaborations, (3) through collaborations with outside investigators, and/or (4) through online databases including those accessed through the CNPRC website, the Clinical and Translational Science Center (CTSC) *Facilities, Cores, and Resources* website that provides information to the research community on the opportunities for translational research at UC Davis, which includes the CNPRC Service Cores and other resource opportunities.

As soon as findings have been fully vetted and determined to accurately represent the data and the uncertainties therein, results will be disseminated through scientific presentations and to peer-reviewed journals. In general, dissemination to the public will usually occur only after acceptance of the article at the conclusion of peer review.

Following the NIH Public Access Policy (NOT-OD-08-033) all investigators funded by this program will submit or have submitted for them to National Library of Medicine PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. Because this program draws upon experts from diverse fields, the journals and professional meetings where research will be presented are also diverse.

The use of data made available by the CNPRC is subject to the following restrictions and qualifications: The data user will acknowledge the CNPRC in any publications, reports, or presentations that use data falling under the auspices of the program. Where such products result from the use of data secured through the program, the data user is strongly urged to consider collaboration and/or co-authorship with program investigators as appropriate for common practices regarding authorship. Data users will cite CNPRC data sets in a standard format.

Following peer-reviewed publication, data may be freely distributed to investigators at academic institutions requesting the information for non-commercial research. Requests for data from for-profit corporations to use the information commercially will be negotiated by the UC Davis Technology Transfer office. All licensing shall be subject to distribution pursuant to the home institution's policies and procedures on royalty income. The Technology Transfer office will report any invention disclosure submitted to them to the UC Office of the President.

Other data sharing occurs internally among investigators who are part of the CNPRC, for the purpose of furthering scientific goals. Use of data is decided by the component Leaders or the leaders of projects that are using CNPRC resources, and those uses that are not part of the original grant aims will be discussed by the Research Advisory Committee.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Administrative Overview

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename AO_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	AO_BibliographReferencesCited.pdf
10. Facilities & Other Resources	AO_FacilitiesOtherResources.pdf
11. Equipment	AO_Equipment.pdf

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

ABSTRACT

The Administrative Services of the California National Primate Research Center (CNPRC) provide administrative and business services across the entire program including those related to animal resources (Primate Services), Core Services, and Scientific Research Units, as well as the Pilot Research Program, Outreach, and NPRC Consortium activities. The CNPRC is an Organized Research Unit placed administratively under the UC Davis Vice Chancellor for Research, who also serves as Principal Investigator for the P51 base grant. The Vice Chancellor for Research is ultimately responsible for the CNPRC as a national resource, and the CNPRC Director is responsible for administrative functions including day-to-day management and scientific direction. The CNPRC Director is assisted in this role by Associate Directors (Administration and Operations, Primate Services, Research), Assistant Directors (Colony Management and Research Services, Information Technology Services), and the Research Unit Leaders (Brain, Mind, and Behavior Research Unit, Infectious Diseases Research Unit, Reproductive Sciences and Regenerative Medicine Research Unit, Respiratory Diseases Research Unit). The CNPRC is governed by two standing oversight committees, the National Scientific Advisory Board and the CNPRC Research Advisory Committee. Each provide a balanced perspective on external advice and review, and aid in more fully informing internal executive management and decision-making. Other CNPRC standing committees are responsible for the overall function and mission, and to address critical areas related to daily management and regulatory compliance. Several UC Davis centrally administered offices, including the Office of the Vice Chancellor for Research, provide key services to the CNPRC. The CNPRC facilities and administrative A-B-C rate structure is unique, and applies only to National Primate Research Centers. Services provided by UC Davis to support the CNPRC are included in the A-rate and income generated from A-rate recovery is returned to UC Davis with a portion shared with the CNPRC per UC policy. Income generated from the B- and C-rate is returned in its entirety to the CNPRC by the UC Davis administration. The Specific Aims for administrative services include: (1) Provide an overall structure for executive management and decision-making of the CNPRC, (2) Ensure administrative and operational responsibility for the CNPRC, (3) Support CNPRC technological and data management needs, and (4) Improve and maintain the infrastructure of CNPRC facilities.

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: There are 4 computers in the Director's Office. Laser printers and fax machines are also available.

Office: The Director's Office includes the office for the Director.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available.

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

EQUIPMENT

Not applicable

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	0.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	0.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AO_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
						Total Salary, Wages and Fringe Benefits (A+B)	0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	0.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	0.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AO_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:		File Name:					Total Senior/Key Person					0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	0.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	0.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AO_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:		File Name:									Total Senior/Key Person	0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	0.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	0.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AO_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months Effort	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional Base Salary		0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:		File Name:				Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	0.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	0.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	0.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AO_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW**BUDGET JUSTIFICATION****PERSONNEL**

All effort will be committed through the Director's Office, therefore effort listed in this component does not fully demonstrate the level of commitment to these activities.

		Percent (%) FTE devoted to CNPRC base functions by source			
Personnel	Role	P51	Program Income	Other	Total
Excluded by Requester	Interim Director	% Effort			
Excluded by Requester	Interim Director	EFFORT			
		months)	Excluded by Requester		

is Professor in the Department of Pathology and Laboratory Medicine, School of Medicine, and currently serves as the CNPRC Interim Director. He is responsible for the day-to-day management and scientific direction of the CNPRC.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None

TRAVEL

Not applicable

SUPPLIES

None

OTHER EXPENSES

None

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		0.00
Section B, Other Personnel		0.00
Total Number Other Personnel	0	
Total Salary, Wages and Fringe Benefits (A+B)		0.00
Section C, Equipment		0.00
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		0.00
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		0.00
Section H, Indirect Costs		0.00
Section I, Total Direct and Indirect Costs (G + H)		0.00
Section J, Fee		0.00

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OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

AO_SpecificAims.pdf

3. Research Strategy*

AdminOverviewFINAL.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

AO_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

SPECIFIC AIMS

The Administrative Services component of the California National Primate Research Center (CNPRC) provides services across the entire program through the Director's Office, Administration and Operations Services, Information Technology Services, and Facilities Improvement. The Specific Aims for the CNPRC administration are directly aligned with the components that comprise the central administration for the CNPRC as follows:

Specific Aim 1. Provide an overall structure for executive management and decision-making of the CNPRC.

Plan. This will be accomplished in the Director's Office by providing direction and leadership for research excellence, ensuring the successful operation of the CNPRC through consensus management and highly trained staff, mentoring and training the next generation of investigators with nonhuman primate expertise, and ensuring the highest standards of responsible conduct of research and animal care.

Specific Aim 2. Ensure administrative and operational responsibility for the CNPRC.

Plan. This will be accomplished through Administration and Operations Services that will provide business office services, human resources support, oversight of purchasing and stores, operations of facilities, and emergency response.

Specific Aim 3. Support CNPRC technological and data management needs.

Plan. This will be accomplished by Information Technology Services to ensure the efficient and cost-effective operations of Core and Affiliate Scientists research, colony management, and business operations as it pertains to information technology.

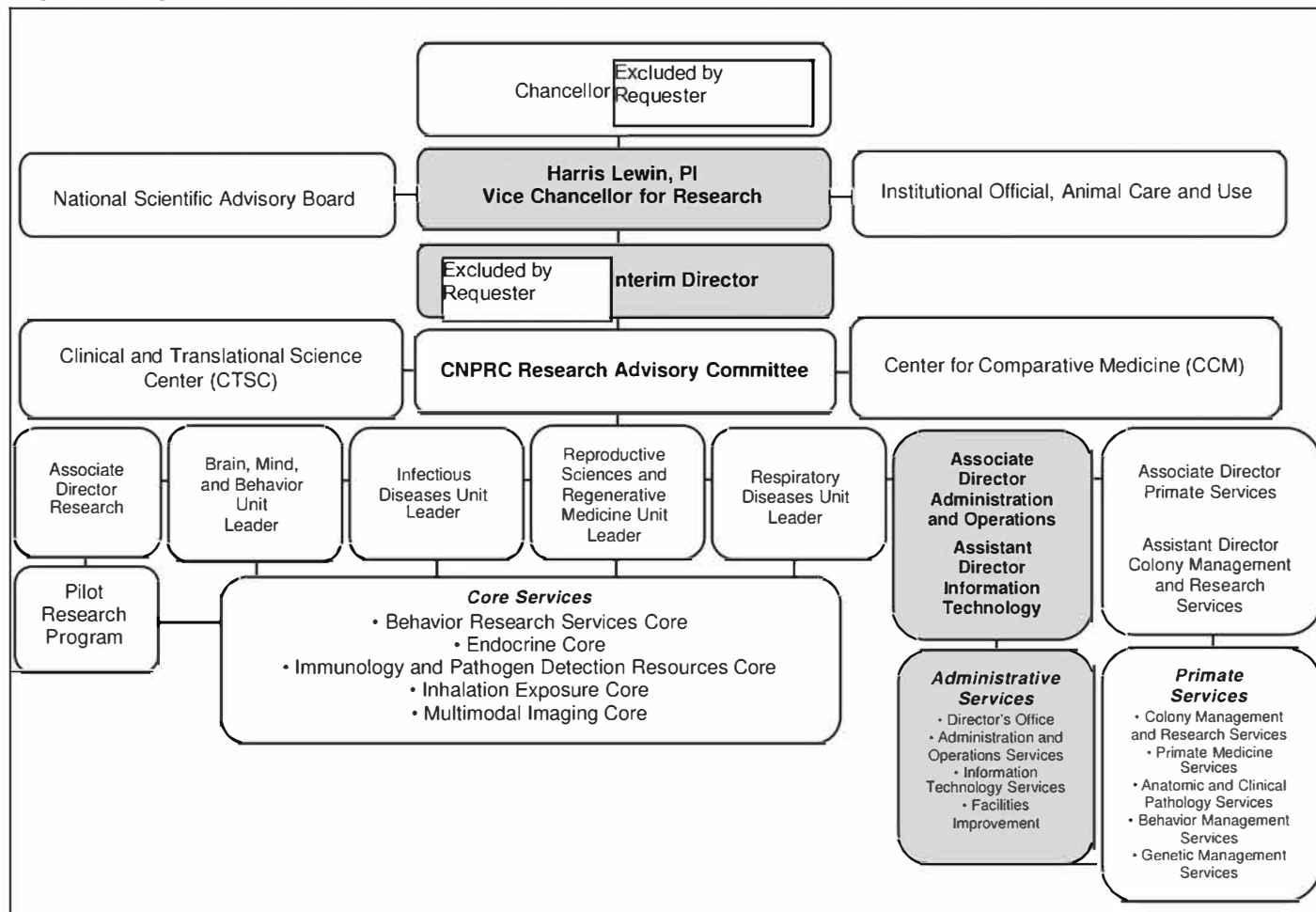
Specific Aim 4. Improve and maintain the infrastructure of CNPRC facilities.

Plan. This will be accomplished by directing Facilities Improvement funds to improve the overall infrastructure that supports the research enterprise by upgrading the facilities and replacing obsolete equipment to ensure the sustainability and overall mission of the CNPRC.

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

Introduction. The Administrative components of the California National Primate Research Center (CNPRC) provide services across the entire program. The components include: the **Director's Office, Administration and Operations Services, Information Technology Services,** and **Facilities Improvements** (Figure 1). The Administrative Overview provides an overall view of the CNPRC administrative functions within the context of the UC Davis campus.

Figure 1. Organizational Chart: Administrative Services



Functions and Qualifications of the CNPRC Principal Investigator (PI). Vice Chancellor Harris Lewin has ultimate responsibility for the conduct of CNPRC operations. As Vice Chancellor for Research, Dr. Lewin occupies a senior level position at UC Davis that assures administrative continuity of the CNPRC program. Vice Chancellor Lewin is directly responsible to **Excluded by Requester** for the following areas: Technology Management and Corporate Relations, Research Administration and Compliance, and Interdisciplinary Research and Strategic Initiatives (see below). Prior to his appointment at UC Davis, Vice Chancellor Lewin was faculty at the University of Illinois at Urbana-Champaign, and served as Director of the University of Illinois Biotechnology Center, Founding Director of the W.M. Keck Center for Comparative and Functional Genomics, and Founding Director of the Institute for Genomic Biology. He is a Fellow of the American Association for the Advancement of Science and a member of the U.S. National Academy of Sciences.

Administrative Relationships. The CNPRC is an Organized Research Unit placed administratively under the UC Davis Office of the Vice Chancellor for Research (see Organizational Chart, Figure 1). PI Lewin appoints the CNPRC Director in accord with UC Davis academic and personnel policies, approves appointments to the National Scientific Advisory Board, and is ultimately responsible for the CNPRC as a national resource. The CNPRC Interim Director **Excluded by Requester** is responsible through Vice Chancellor Lewin for the CNPRC P51 base grant to both the **University of California** and the National Institutes of Health (NIH) for administrative functions of the CNPRC. Interim **Excluded by Requester** addresses the day-to-day management and scientific direction of the

CNPRC. [Excluded by Requester] is an established investigator with a stellar track record of NIH funded research, and a Core Scientist in the Infectious Diseases Research Unit. As noted in the Overview [Excluded by Requester] will serve in this capacity until the new CNPRC director candidate currently under recruitment is in place. The CNPRC Director is assisted in this role by the Associate Directors, Assistant Directors, and the Research Unit Leaders. The Associate Director for Administration and Operations [Excluded by Requester] is responsible for all fiscal and administrative activities including budget, personnel, grants/contracts administration, business office, facilities management, central storehouse, purchasing, security, and administrative support to the Director's Office and the Scientific Research Units (see subsequent sections). The Associate Director for Primate Services (Dr. [Excluded by Requester]) is responsible for all Primate Services components, which includes Colony Management and Research Services, Primate Medicine Services, Anatomic and Clinical Pathology Services, and Behavior and Genetics Management Services. The Assistant Director for Colony Management and Research Services (Ms. [Excluded by Requester]) reports to the Associate Director for Primate Services in the areas of animal care, colony management, research-related support, and staff coordination. The Associate Director for Research [Excluded by Requester] oversees the Pilot Research Program and Service Cores. The Assistant Director for Information Technology [Excluded by Requester] is responsible for providing computing support and services for daily operations.

Research Unit Leaders provide administrative and scientific oversight for each of the four Research Units (Brain, Mind, and Behavior; Infectious Diseases; Reproductive Sciences and Regenerative Medicine; Respiratory Diseases). Core Scientists in these Research Units provide the essential scientific expertise to assist investigators nationwide in the use of the nonhuman primate model and related techniques and methodologies. Core Scientists are appointed by the CNPRC PI and the Director in strict conformance with the host institutions' academic and personnel policies and are approved by the NIH. Appointments of Core Scientists are made on the basis of whether demonstrated experience and expertise is appropriate to their proposed scientific and/or research service responsibilities within the CNPRC. Joint appointments of Core Scientists in academic departments at UC Davis ensure mutually beneficial relationships between the CNPRC and the host institution. Core Scientists represent a broad range of Schools and Colleges (e.g., Schools of Medicine and Veterinary Medicine, Colleges of Engineering and Letters and Science). Thus, administrative placement of the CNPRC within the Office of the Vice Chancellor for Research is highly advantageous. All [Excluded by Requester] scientists devote at least [Excluded by Requester] of their professional time to service that is directly related to supporting the [Excluded by Requester] research programs and activities at the CNPRC, and at least [Excluded by Requester] research effort to nonhuman primate research (see Overview, Service Cores, and Research Unit descriptions).

Oversight Committees. The CNPRC is governed by two standing oversight committees: the **National Scientific Advisory Board** (Table 1) and the **Research Advisory Committee** (Table 2).

Table 1. National Scientific Advisory Board Members

Members	Title	Department and Institution
[Excluded by Requester]	Professor	Department of Medicine, UC San Francisco
	Senior Director	Animal Resources, The Scripps Research Institute
	Professor	Department of Microbiology and Medicine Genetics, University of Pittsburgh
	Professor	Laboratory of Diagnostic Radiology Research, NIH
	Retired	Yerkes NPRC (Associate Director), Emory University
	Distinguished Professor	Department of Pathobiology and Diagnostic Investigation, Michigan State University
	Director	Department of Pathology and Comparative Medicine, Wake Forest University
	Professor	Division of Experimental Medicine, UC San Francisco
	Consultant	Private Consultant
	Professor	Center for Environmental Medicine, Asthma and Lung Biology, University of North Carolina
	Professor	Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh
	Associate Professor	Department of Neurobiology and Anatomy, University of Rochester
	Professor	Barshop Institute for Longevity and Aging Studies, University of Texas
	Professor	Department of Pediatrics, Indiana University

Each provide a balanced perspective of external advice and review, and to more fully inform internal executive management and decision-making. The role of the National Scientific Advisory Board is to provide advice and guidance to PI Lewin and Interim ^{Excluded by} ^{Donniester} on planning and program activities to support continued and balanced scientific growth of the CNPRC, and to ensure proper administrative organization and management. The National Scientific Advisory Board is composed of 14 nationally eminent scientists with experience using nonhuman primates for research, veterinarians, and administrative members who cover the range of CNPRC expertise and technical subjects. As a group, the National Scientific Advisory Board specifically addresses and reviews overall structure and function over a two-day period annually and provides a written report to PI Lewin and ^{Excluded by} ^{Donniester}. Under the direction of the PI, the Director's Office is responsible for implementing recommendations. National Scientific Advisory Board members are appointed annually and are typically reappointed for 3-5 consecutive terms. The most recent National Scientific Advisory Board meeting was held on February 26-27, 2013.

The CNPRC also has a standing **Research Advisory Committee** that provides advice to the CNPRC Director regarding prioritization of projects and resources, overall CNPRC function, and research needs. The Research Advisory Committee includes the four Research Unit Leaders, the Associate and Assistant Directors, the Senior Veterinary Managers for Primate Medicine Services and Anatomic and Clinical Pathology Services, and the Director's of the UC Davis Clinical and Translational Science Center (CTSC) and Center for Comparative Medicine (CCM); the committee meets every other week throughout the calendar year. The Research Advisory Committee also has a pre-proposal mechanism in place for the review of all proposed projects to be conducted at the CNPRC including all grant and contract submissions that propose to use CNPRC resources (see below). The Research Advisory Committee reviews the scientific merit of any new project proposals that have not undergone NIH peer review and propose to use CNPRC resources. Minutes from Research Advisory Committee meetings are maintained in the Director's Office.

The CNPRC has other standing committees that are responsible for the overall function and mission, and to address critical areas related to daily management and regulatory compliance (Table 2).

UC Davis Animal Care and Use Program. The CNPRC vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards for animal research at UC Davis and the CNPRC. The UC Davis AAALAC-accredited program has the most diverse and complex organization of any academic entity in the nation. Vertebrate animals are used in a wide array of biomedical/translational and agricultural research and teaching programs with educational efforts in areas such as basic biology, animal science and management, veterinary science, and training of veterinary and medical residents. Approximately 500 UC Davis investigators and instructors, plus an additional 2,000 supporting staff, use and care for approximately 346,000 animals, encompassing over 30 species. The campus devotes almost one million square feet in 280 buildings and structures to animal-related activities.

At UC Davis, a single **Institutional Animal Care and Use Committee (IACUC)** oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met across the campus. The IACUC, a faculty-based committee with 25 members (faculty, facility staff, campus Attending Veterinarian, IACUC staff, public non-affiliated members, non-scientists in addition to 12 alternate members) (Table 3) inspects all animal facilities, evaluates all aspects of the institutional animal care program, establishes policy and procedure for the UC Davis campus, and coordinates training, compliance, and occupational health programs. The IACUC meets every other week for a 2-hour period throughout the calendar year, and participates in inspections and subcommittee meetings. Approximately 600 protocols, over 1,000 amendments with significant changes, and approximately 4,000 administrative amendments are submitted on an annual basis; approximately 1,500 approved protocols currently support research and teaching activities. In addition to the IACUC Administrator there are 7 IACUC staff members to aid in facilitating the process. The IACUC has an on-line submission process for protocols and amendments.

Table 2. CNPRC Standing Committees

CNPRC Committee	Members	Frequency and Function
Research Advisory Committee	Director (Chair); Associate Director's for Administration and Operations, Primate Services, and Research; Assistant Director for Colony Management and Research Services; Assistant Director for Information Technology; Research Unit Leaders; Clinical and Translational Science Center Director; and Center for Comparative Medicine Director	<ul style="list-style-type: none"> • Biweekly • Address research needs and overall CNPRC function • Prioritizes projects and resources • Review proposed research projects; ~60 pre-proposals for submitted grants and contracts reviewed annually; discussed and evaluated in terms of scientific merit, resources available, animal availability, meeting the NPRC mission, applicability, and NIH priority
Senior Management Committee	Director (Chair); Associate Director's for Administration and Operations, Primate Services, and Research; Assistant Director for Colony Management and Research Services; Assistant Director for Information Technology; Primate Medicine and Pathology Senior Veterinary Managers	<ul style="list-style-type: none"> • Weekly • CNPRC programmatic, administrative, facility, and management topics many of which are brought in a more formal manner to the Research Advisory Committee for final review and approval
Colony Management Advisory Committee	Associate Director for Primate Services and Assistant Director for Colony Management and Research Services (Co-Chairs), Core Scientists, Staff Veterinarians	<ul style="list-style-type: none"> • Monthly • Issues impacting colony management (e.g., Specific Pathogen Free colony, reproductive colony, behavioral management and environmental enrichment, colony genetics)
Morbidity and Mortality Committee	Primate Medicine and Pathology Managers; UC Davis Attending Veterinarian; Associate Director for Primate Services; Assistant Director for Colony Management and Research Services; Unit Leader and UC Davis IACUC Co-Chair (Chair)	<ul style="list-style-type: none"> • Quarterly • Review spontaneous deaths in outdoor field corrals • Discuss colony-related topics and practices, identify action items
Environmental Enrichment Committee	Associate Director for Primate Services and Lead for Behavior Management Services (Co-Chairs); Assistant Director for Colony Management and Research Services; Staff Veterinarians; Behavior Management Services Staff	<ul style="list-style-type: none"> • Quarterly • Review ongoing practices, areas of focus or concern, new concepts and suggestions, and efficacy of current practices
Injury and Illness Prevention Program Safety Committee	Safety and Compliance Officer (Chair); representatives from Administrative components and Scientific Research Units	<ul style="list-style-type: none"> • Quarterly • Reviews any safety concerns, disseminates safety information including injury and illness prevention programs, emergency action plans, infection and exposure control practices, hazardous material procedures, biosafety guidelines, and medical waste procedures
Infection Control Committee	Associate Director for Primate Services; Assistant Director for Colony Management and Research Services; Core Scientists from the Infectious Diseases Research Unit (Core Scientist, Chair); Staff Veterinarians; Animal Resource Supervisor for infectious housing; Safety and Compliance Officer; Medical Director of the UC Davis Occupational Health Program	<ul style="list-style-type: none"> • Quarterly • Reviews ongoing practices including health surveillance for employees and visitors, vaccination policies, BSL3 polices and practices, and personal protective equipment (PPE) requirements

Table 3. UC Davis IACUC Membership

Name of Member/Code*	Degree/Credentials	PHS Policy Membership Requirements	UC Title
M001	PhD	Scientist: IACUC Co-Chair	Professor
Excluded by Requester	DVM, DACLAM	Attending Veterinarian (AV)	AV
M004	PhD	Scientist	Associate Professor
M005	PhD	Scientist: IACUC Chair	Professor
M007	MA	Non-Scientist	Librarian
M008	PhD	Scientist	Facility Manager
M009	DVM	Alternate for AV	Senior Veterinarian
M010	BS	Non-Scientist	Facility Manager
M013	BA, CPIA	Alternate for M014, M018 and M086	IACUC Specialist
M014	BA, CPIA	Member	IACUC Specialist
M016	BS	Non-Scientist	Facility Manager
M018	CPIA	Member	IACUC Specialist
M024	PhD	Scientist	Professor
M026	MD	Scientist	Associate Professor
M031	PhD	Alternate Scientific Member	Professor
M033	PhD	Scientist	Professor
M034	PhD	Scientist	Professor
M040	DVM	Alternate for AV	Veterinarian
M042	PhD	Scientist	Professor
M086	BS, CPIA	Member	IACUC Specialist
M087	PhD	Scientist	Professor
M090	PhD, DVM	Scientist	Professor
M091	PhD	Alternate for M024	Professor
M092	BS	Nonaffiliated	Retired Public Health
M093	PhD	Scientist	Professor
M094	BS, CPIA, CMAR	Alternate for M014, M018 and M086	Associate Director
M095	BS, CPIA, CMAR	Alternate for M014, M018 and M086	IACUC Specialist
M096	PhD	Scientist	Professor
M097	PhD, DVM	Scientist	Professor
M099	PhD	Alternate for M014, M018 and M086	IACUC Specialist
M100	PhD	Alternate for M034	Professor
M101	PhD	Scientist	Professor
M102	PhD	Scientist	Professor
M103	PhD	Alternate for M087	Professor
M104	PhD	Alternate Scientific Member	Professor
M105	DVM	Alternate for AV	Senior Veterinarian
M106	BS	Nonaffiliated	Retired Engineer

*IACUC members names are coded per University policy except for the Attending Veterinarian; CPIA=Certified Professional IACUC Administrator; CMAR=Certified Manager of Animal Resources

CNPRC Core Scientists are members of the UC Davis IACUC. Excluded by Requester Reproductive Sciences and Regenerative Medicine Research Unit Leader, serves as the IACUC Co-Chair and is also a member of the UC Davis **Animal Care Leadership Team** which consists of the Institutional Official (Vice Chancellor for Administration and Resource Management; Committee Chair), IACUC Administrator, IACUC Chair and Co-Chair, UC Davis Attending Veterinarian, Director of Research Compliance and Integrity, and the Associate Vice Chancellor for Safety Services. The campus Animal Care Leadership Team meets monthly to address a broad range of topics including security and future planning, and has quarterly meetings with the Deans of the Schools and Colleges to address overall subjects related to the UC Davis Animal Care Program.

Vice Chancellor Lewin and CNPRC Interim Excluded by Requester also participate in the quarterly campus **Animal Research Communication Coordination Committee**, which addresses campus topics of importance to the research community such as security, communications, and new programs. Members include the Institutional Official (Chair) and members from Government and Community Relations, the Office of Campus Council, Risk Management Services, News Service, the UC Davis Police Department, as well as the Deans of the Schools of Medicine and Veterinary Medicine and the College of Biological Sciences, the IACUC Chair and Co-Chair,

IACUC Administrator, UC Davis Attending Veterinarian, Director of Research Compliance and Integrity, and Associate Vice Chancellor for Safety Services.

UC Davis Administrative Functions and Services. As noted above, Vice Chancellor Lewin has primary responsibilities for Technology Management and Corporate Relations, Research Administration and Compliance, and Interdisciplinary Research and Strategic Initiatives which includes the following campus entities that provide assistance to faculty and staff as well as many key services.

- UC Davis **InnovationAccess** provides services to investigators in the areas of Technology Transfer and Business Development, particularly in developing new alliances through licensing to either existing companies or to UC Davis start-up companies to promote the commercialization of new discoveries. UC Davis researchers receive the full support of InnovationAccess, which has over 20 experienced professionals including 12 Intellectual Property Officers (including 4 patent and copyright attorneys, 3 patent agents) supported by 12 intellectual property paralegals. InnovationAccess is dedicated solely to protecting all UC Davis intellectual property through patents, copyrights, and trademarks and to ensuring that research discoveries benefit the public in accordance with the University's mission of public benefit through research and education. Each new invention disclosed to InnovationAccess receives full consideration regarding patentability and commercialization potential. Each filed patent application is broadly marketed internationally through postings on a searchable website. In addition, InnovationAccess conducts directed marketing of inventions to those companies that have specific interests in the commercial applications.

An example of the importance of InnovationAccess to the CNPRC is highlighted in the development of a novel scaffold that was patented by a member of the Reproductive Sciences and Regenerative Medicine Research Unit. A novel polysaccharide-based scaffold with a porosity of ~97% for generating three-dimensional organoids was developed; the properties of the scaffold make it an attractive biomaterial for engineering bone constructs for a variety of orthopedic applications as well as other tissue regeneration applications. This invention was initially disclosed to InnovationAccess with all relevant details, signatures of two qualified witnesses, and supporting documents. InnovationAccess evaluated the inventorship, ownership, possible patent rights, patentability, and marketability of the invention. A UC Davis intellectual property officer and external patent attorney worked closely with the inventor to develop the patent application. After submission, InnovationAccess announced a non-confidential description of the invention to the commercial sector and identified a potential commercial partner who engaged in technical and commercial discussions under a confidentiality agreement. After the evaluation of the technology (~1 year) and negotiation, the industry partner acquired the exclusive license for further preclinical and clinical development and commercialization.

- **Research Compliance and Integrity** promotes integrity through education and training and by developing and implementing policies and procedures to assure compliance with federal and state laws and regulations regarding the responsible conduct of research. This group provides administrative support and oversight for financial conflicts of interest in research, the responsible conduct of research program, and support for a variety of campus committees including the Committee for Research Integrity, Conflict of Interest in Research Committee, and the Stem Cell Research Oversight (SCRO) Committee. The Research Compliance and Integrity director also serves as a liaison to departments and research units to ensure compliance in biosafety, human subjects, and animal research, and provides the campus with expertise and training on complex federal, state, and university regulations and compliance areas. The Research Compliance and Integrity director has been very helpful to CNPRC faculty serving on committees such as SCRO, and in navigating the required NIH compliance documents for grant submissions.
- Another key aspect of support comes from **Sponsored Programs** which is the office responsible for the facilitation of grant proposal and award management processes. The program handles the review and submission of faculty grant applications, as well as the negotiation and administration of awards. The CNPRC Business Office regularly interacts with the Sponsored Programs office in conducting the pre- and post-award management of grants and contracts and is thus tightly integrated with this program.
- The Office of Research Central Administration also addresses **Business and Finance** which is responsible for financial analysis and reporting, budget and fiscal management, and review and approval of recharge

rates. Business and Finance works in partnership with the UC Davis community including administrators, faculty, staff, research unit directors, and managers to deliver financially sound and cost-effective business processes. The CNPRC Business Office has regular interactions with this office. Office of Research **Human Resources** also works directly with the CNPRC Human Resources Manager in the posting of positions and other activities related to employment. **Information Technology Services** provides information technology solutions and services for research administration, compliance, and risk management in support of researchers and administrators. CNPRC Information Technology Services staff work directly with campus staff in implementing and ensuring all of the information technology needs of the faculty and staff are met for those services that are handled at the campus level (see **Information Technology Services**).

Campus **Administrative and Resource Management** has responsibility for a number of services that are regularly utilized by the CNPRC. These include:

- The **Budget and Institutional Analysis** program which provides overall accounting and financial support, sets policy and procedures for these areas, and provides systems to support the accounting and budgeting work. This group provides the primary analytical support for campus rate analysis, and helps to guide the campus through audit processes when information is requested. The CNPRC Business Office interacts regularly with the Budget and Institutional Analysis team including to evolve financial models to account for the decreased NIH budget while continuing to support the needs of the biomedical research community.
- **Facilities Management** plays a significant role in the daily operation of the CNPRC. This group has primary responsibility for maintaining, repairing, and cleaning the campus's academic and administrative buildings, and provides basic maintenance, repair, and custodial services. Examples of additional services provided are road maintenance, telephone and cell phone service, energy conservation, alarm monitoring, lock service, moving services, major equipment repair, and grounds maintenance assistance, all of which are used by the CNPRC. When repairs or upgrades are in the planning process, the Facilities Management staff provide estimates regarding the cost of completing those repairs or upgrades (see **Facilities Improvement**). They also offer a broad array of professional facility services that can be based on recharge or service agreements. The CNPRC monitors facility needs and works with campus Facilities Management staff on a daily basis to ensure that any issues that may arise are addressed in a timely manner.
- If upgrades are major or construction of facilities is involved the **Design and Construction Management** group provides and coordinates project services ranging from project management to architectural, engineering, and specialty consultants. The CNPRC Administrative Services group has monthly meetings to review plans and conduct of minor capital projects at the CNPRC, and a monthly Project Advisory Committee meeting which reviews major capital projects (see **Administration and Operations Services**). This office continuously involves the CNPRC in campus planning for university or municipal projects that may affect the CNPRC or access to the CNPRC.
- A significant area of CNPRC concern is safety. UC Davis has a **Police Department** with which the CNPRC has partnered to ensure a safe and secure environment. The police and safety officers located on-site in a centrally located kiosk at the entry to the CNPRC grounds provide excellent planning and presence to address daily security needs and with any special events.
- **Safety Services** provides a comprehensive offering of services and support from laboratory safety to emergency management planning. CNPRC faculty and staff are provided support in environmental health and safety, occupational health, hazardous materials, and general safety management. Although some aspects of safety are unique to the CNPRC (such as Herpes B-virus exposure), the campus Environmental Health and Safety staff provide training, guidance, and support through these services, exercises, and classes which are shared with the CNPRC community. The CNPRC has an on-site Safety and Compliance Officer that is integrated with these campus entities and directly reports to the CNPRC Director (see **Director's Office**).
- **Contracting Services**, a component of UC Davis Materiel Management, provides support to facilitate the work of purchasing and stores operations. CNPRC purchasing is able to take full advantage of university agreements that have been competitively bid with outside vendors and provides reduced costs based on the

volume of campus purchases and favorable terms that have been negotiated. For example, last year the CNPRC purchased \$482,000 of consumable supplies from [REDACTED] Because of the UC system's strategic sourcing and contract the CNPRC received an approximate 20% discount which translated into \$96,000 in savings. CNPRC purchasing also works closely with Contracting Services to ensure that applicable policies and regulations are followed. They also provide support for the enterprise systems that facilitates the overall requisitioning, purchasing, and invoice payment process. This provides a further example of the institutional commitment towards efficient and effective use of resources to ensure maximum value to the research community and the CNPRC.

In addition to these campus entities, the CNPRC further benefits from being a part of UC System. For example, the **Office of General Counsel**, located in the UC Office of the President [REDACTED] provides the necessary legal services to the CNPRC. One area of ongoing support is related to the requests for information (e.g., Freedom of Information Act, FOIA). The Office of the General Counsel meets with the UC Davis Animal Care Program Leadership Team, other related administrators, and the CNPRC Director to consider these requests and to coordinate a response. The UC Office of the President also provides assistance through the **Government Relations** office. When requested they will assist the CNPRC in arranging for governmental official visits for events including the opening of new facilities such as the Respiratory Disease Center or in setting up appointments for direct input to government representatives and their staff on issues relevant to the CNPRC. The **Strategic Communications** office, housed in the UC Davis Chancellor's Office, also provides oversight and assistance with media relations and news releases.

CNPRC Rate Structure. The CNPRC Facilities and Administrative (F&A) rate structure is unique and applied only to National Primate Research Centers (NPRCs). As stated in the 7th edition of the National Primate Research Centers Program Guidelines: "*NPRCs have unique F&A mechanisms typically comprised of an A rate, a B rate, and a C rate. These rates are designed to reimburse the grantee institution for F&A type costs incurred in support of the NPRC through the A rate, to reimburse the NPRC for F&A type costs incurred in support of federal users of the NPRC through the B rate, and to reimburse the NPRC for F&A type costs incurred in support of non-federal users of the NPRC through the C rate. The B and C rates are considered program income to the P51 base grant and policies related to program income as stated in the NIH Grants Policy Statement apply to their use. It is expected that the program income will be added to the P51 base grant for use in further supporting approved NPRC activities.*"

Income generated from the B- and C-rate is returned in its entirety to the CNPRC by UC Davis administration. Services provided by UC Davis to support the CNPRC are included in the A-rate, and income generated from A-rate recovery is returned to UC Davis with a portion shared with the CNPRC per UC policy. Current CNPRC and UC Davis indirect cost rates are shown in Table 4. The UC Davis campus indirect cost rate is 54.5%. The CNPRC indirect cost rate for federal grants and contracts is 54.4% (A+B) and for industry contracts is 89.0% (A+B+C). As per NIH policy, this income is treated as program income with all of the appropriate procedures and processes in place.

Table 4. CNPRC Indirect Cost Rates

Rate	Details
A-Indirect Cost Rate	<ul style="list-style-type: none"> • Campus services provided to the CNPRC through the A-rate (22.7%) • A-rate recovery returned to UC Davis with portion shared with the CNPRC
B- and C-Indirect Cost Rate	<ul style="list-style-type: none"> • B-rate specific to NPRC Programs: reported as Program Income • Provided to offset expenses that cannot be directly recharged to grants • B-rate (31.7%) for federal grants and contracts • C-rate (34.6%) for non-federal grants and contracts

Access and Overall Process for Research Protocols. The CNPRC has unique and specialized resources, including Core Scientists with extensive expertise that routinely facilitate investigator and trainee research with nonhuman primates. Inquiries from investigators or for-profit companies interested in conducting research with nonhuman primates occur by a number of efficient pathways. The primary point-of-contact is the Core Scientists and they represent the route by which the majority of research conducted is initiated at the CNPRC. Core Scientists regularly establish new collaborations and serve as subcontract PI for many investigators nationally (see Research Unit descriptions). They serve as the primary facilitators based on their domain-

based expertise. New Affiliate Scientists identify research opportunities at the CNPRC through interactions with Core Scientists by direct contact or at meetings and other venues; through identification of research resources on the CNPRC website; by application to the CNPRC Pilot Research Program, as well as other pilot project programs and grant submissions. Core Scientists interact directly with Affiliate Scientists and provide assistance in preparation of pre-proposals for the Research Advisory Committee, in the entire grant submission process with all aspects of the application, and in the writing and submission of animal care and use protocols to the IACUC. Since the Research Advisory Committee meets biweekly, the process of pre-proposal review and approval is highly efficient and provides a means to review and confirm that the CNPRC can provide the requested resources for grant submissions. Priority is always given to NIH-funded research. Core Scientists also provide services through Cores and other outreach programs, and are the primary contacts for budget information and relevant grant application text. Inquiries that may come to the CNPRC through the website are directed to either the Director or the Associate Director for Research, who then directs interested investigators to the appropriate Core Scientist based on expertise. New investigators benefit greatly from collaborations with Core Scientists particularly when submitting grants and IACUC protocols. The number of grants with PIs from other institutions (with a Core Scientist as the on-site and subcontract PI) supports the level of engagement initiated by the Core Scientists and their facilitating access to the many resources at the CNPRC. In addition, programs such as the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases provides a national program that is widely advertised and ensures ready access to nonhuman primates, tools, and expertise (see Reproductive Sciences and Regenerative Medicine Research Unit).

Administrative Services. The sections that follow provide specific information related to each of the components of Administrative Services as follows:

- The **Director's Office** is responsible to both the NIH and the University for the overall administration of the CNPRC, including fiscal management, quality control of performance in all areas, compliance, and the development and implementation of short and long range plans.
- **Administration and Operations Services** functions with the UC Davis campus administration as noted with administrative and operational responsibility for business office services, human resources, purchasing and stores, facilities operations, and emergency response.
- The primary goal of **Information Technology Services** is to support all programs within the CNPRC, including Core and Affiliate Scientist research, colony management, and business operations to ensure efficient and cost effective operations.
- **Facilities Improvement** focus on overall infrastructure improvements that support the research enterprise. Facilities Improvement funds are used to upgrade the facility and to replace obsolete equipment to ensure sustainability and the overall mission of the CNPRC. There is extensive integration with campus services as noted above.

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

ADMINISTRATIVE SERVICES: ADMINISTRATION OVERVIEW

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

I: Indian/Native American Tribal Government (Federally Recognized)

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Director's Office

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: — 1 — 2 — 3 — 4 — 5 — 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename DOAbstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	DO_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	DOFacilitiesandotherresources.pdf
11. Equipment	DO_Equipment.pdf

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

ABSTRACT

Through the Principal Investigator, Vice Chancellor for Research Harris Lewin, the California National Primate Research Center (CNPRC) Director is responsible to the National Institutes of Health and the University of California for the overall administration of the P51 base grant including fiscal management, quality control of performance in all areas, and the development and implementation of short and long range plans. The CNPRC Director has the responsibility for the day-to-day management, scientific direction, and overall strategic planning for the programs and supporting facilities and resources. The Director also has primary responsibility for high quality veterinary care and research conduct; this oversight is enhanced through campus compliance activities, the UC Davis Institutional Animal Care and Use Committee, and on-site committees such as the Research Advisory Committee. The Specific Aims for the **Director's Office** are: (1) Provide direction and leadership for research excellence, (2) Ensure the successful operation of the CNPRC, (3) Mentor and train the next generation of investigators with nonhuman primate expertise, and (4) Ensure the highest standards of responsible conduct of research and animal care.

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: There are 4 computers in the Director's Office. Laser printers and fax machines are also available.

Office: The Director's Office includes the office for the Director, and shared office space for the Executive Assistant to the Director, the Safety and Compliance Officer, and the Administrative Coordinator.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available.

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

EQUIPMENT

Not applicable

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
Prefix:	First Name*: Harris	Middle Name A	Last Name*: Lewin	Suffix:
Position/Title*:	Vice Chancellor for Research			
Organization Name*:	University of California Davis			
Department:	Office of Research			
Division:	Office of Research			
Street1*:	One Shields Ave			
Street2:				
City*:	Davis			
County:				
State*:	CA: California			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	956165270			
Phone Number*: 530-754-7764	Fax Number:	E-Mail*: lewin@ucdavis.edu		
Credential, e.g., agency login:	eRA Commons User Name			
Project Role*: Other (Specify)	Other Project Role Category: Vice Chancellor for Research			
Degree Type: PhD	Degree Year: 1984			
File Name				
Attach Biographical Sketch*:				
Attach Current & Pending Support:				

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Harris	A	Lewin		Vice Chancellor for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
2.	Excluded by Requester							0.0	0.0	90,750.00	30,356.00	121,106.00
3.								0.0	0.0	18,150.00	7,239.00	25,389.00
4.								0.0	0.0	36,617.00	14,604.00	51,221.00
5.								0.0	0.0	48,206.00	19,226.00	67,432.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

265,148.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	EFFORT			53,160.00	28,122.00	81,282.00
1	Safety and Compliance Officer	4.2			25,987.00	13,748.00	39,735.00
3	Total Number Other Personnel					Total Other Personnel	121,017.00
						Total Salary, Wages and Fringe Benefits (A+B)	386,165.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	37,500.00
2. Foreign Travel Costs	0.00
Total Travel Cost	37,500.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	7,340.00
2. Publication Costs	0.00
3. Consultant Services	14,000.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Director's Office Copying and Printing	4,000.00
9. Annual Gene Symposium Expenses	5,000.00
Total Other Direct Costs	30,340.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	454,005.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	454,005.00	103,059.00
Total Indirect Costs			103,059.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	557,064.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: DOBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Harris	A	Lewin		Vice Chancellor for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
2.	Excluded by Requester					Interim Director		0.0	0.0	90,750.00	31,959.00	122,709.00
3.						Assoc Director for Primate Services		0.0	0.0	18,150.00	7,659.00	25,809.00
4.						Assoc Director for Research		0.0	0.0	38,082.00	16,071.00	54,153.00
5.						Assoc Director for Admin and Operations		0.0	0.0	49,652.00	20,953.00	70,605.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:					Total Senior/Key Person			273,276.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	EFFORT			54,754.00	30,288.00	85,042.00
1	Safety and Compliance Officer	4.2			26,539.00	14,680.00	41,219.00
3	Total Number Other Personnel					Total Other Personnel	126,261.00
Total Salary, Wages and Fringe Benefits (A+B)							399,537.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	38,625.00
2. Foreign Travel Costs	0.00
Total Travel Cost	38,625.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	7,560.00
2. Publication Costs	0.00
3. Consultant Services	14,420.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Director's Office Copying and Printing	4,120.00
9. Annual Gene Symposium Expenses	5,150.00
Total Other Direct Costs	31,250.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	469,412.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	469,412.00	106,557.00
Total Indirect Costs			106,557.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	575,969.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: DOBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Harris	A	Lewin		Vice Chancellor for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
2.	Excluded by Requester					Interim Director		0.0	0.0	90,750.00	33,048.00	123,798.00
3.						Assoc Director for Primate Services		0.0	0.0	18,150.00	7,929.00	26,079.00
4.						Assoc Director for Research		0.0	0.0	39,605.00	17,301.00	56,906.00
5.						Assoc Director for Admin and Operations		0.0	0.0	51,142.00	22,341.00	73,483.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

280,266.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	EFFORT			56,396.00	32,212.00	88,608.00
1	Safety and Compliance Officer	4.2			27,084.00	15,469.00	42,553.00
3	Total Number Other Personnel					Total Other Personnel	131,161.00
						Total Salary, Wages and Fringe Benefits (A+B)	411,427.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	39,783.00
2. Foreign Travel Costs	0.00
Total Travel Cost	39,783.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	7,787.00
2. Publication Costs	0.00
3. Consultant Services	14,853.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Director's Office Copying and Printing	4,244.00
9. Annual Gene Symposium Expenses	5,305.00
Total Other Direct Costs	32,189.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	483,399.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	483,399.00	109,732.00
Total Indirect Costs			109,732.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	593,131.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: DOBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Harris	A	Lewin		Vice Chancellor for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
2.	Excluded by Requester					Interim Director		0.0	0.0	90,750.00	34,046.00	124,796.00
3.						Assoc Director for Primate Services		0.0	0.0	18,150.00	8,164.00	26,314.00
4.						Assoc Director for Research		0.0	0.0	41,189.00	18,528.00	59,717.00
5.						Assoc Director for Admin and Operations		0.0	0.0	52,676.00	23,695.00	76,371.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:				Total Senior/Key Person				287,198.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	EFFORT			58,088.00	34,165.00	92,253.00
1	Safety and Compliance Officer	4.2			27,649.00	16,262.00	43,911.00
3	Total Number Other Personnel					Total Other Personnel	136,164.00
Total Salary, Wages and Fringe Benefits (A+B)							423,362.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	40,976.00
2. Foreign Travel Costs	0.00
Total Travel Cost	40,976.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	8,021.00
2. Publication Costs	0.00
3. Consultant Services	15,299.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Director's Office Copying and Printing	4,371.00
9. Annual Gene Symposium Expenses	5,464.00
Total Other Direct Costs	33,155.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	497,493.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	497,493.00	112,931.00
Total Indirect Costs			112,931.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	610,424.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: DOBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Harris	A	Lewin		Vice Chancellor for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
2.	Excluded by Requester							0.0	0.0	90,750.00	35,045.00	125,795.00
3.								0.0	0.0	18,150.00	8,416.00	26,566.00
4.								0.0	0.0	42,837.00	19,862.00	62,699.00
5.								0.0	0.0	55,884.00	25,911.00	81,795.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

296,855.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	EFFORT			59,831.00	36,258.00	96,089.00
1	Safety and Compliance Officer	4.2			28,222.00	17,103.00	45,325.00
3	Total Number Other Personnel					Total Other Personnel	141,414.00
						Total Salary, Wages and Fringe Benefits (A+B)	438,269.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	42,205.00
2. Foreign Travel Costs	0.00
Total Travel Cost	42,205.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	8,262.00
2. Publication Costs	0.00
3. Consultant Services	15,758.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Director's Office Copying and Printing	4,502.00
9. Annual Gene Symposium Expenses	5,628.00
Total Other Direct Costs	34,150.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	514,624.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	514,624.00	116,820.00
		Total Indirect Costs	116,820.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	631,444.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: DOBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Lewin, Harris, PhD	Principal Investigator (PI)	% Effort			
Excluded by Requester	Interim Director				
	Associate Director for Research				
	Interim Associate Director for Administration and Operations				
	Associate Director for Primate Services				
	Research Coordinator				
	Administrative Assistant to the Director				
TBN	Safety and Compliance Officer	35	65	0	100

TBN=to-be-named

Harris Lewin, PhD, PI [EFFORT] months - [% Effort] As the Vice Chancellor for Research, Dr. Lewin has supervisory authority over all Organized Research Units on the UC Davis campus including the CNPRC, and serves as the PI for the CNPRC P51 base grant. He provides administrative oversight and meets with the Director and Associate Director for Administration and Operations on a biweekly basis to review CNPRC operations. He is also the liaison with the UC Davis Schools and Colleges to promote the CNPRC program and facilitate sharing of resources. No salary is requested for Vice Chancellor Lewin (supported by UC Davis).

Excluded by Requester **Interim Director** [EFFORT] months - [% Effort] **Excluded by Requester** Professor in the Department of Pathology and Laboratory Medicine, School of Medicine, currently serves as the CNPRC Interim Director. He is responsible for the day-to-day management and scientific direction of the CNPRC. **Excluded by Requester** is a Core Scientist in the Infectious Diseases Research Unit and the Director of the Center for Comparative Medicine. **Excluded by Requester** efforts on the P51 base grant and funded extramural grants, he is currently re-negotiating the percent effort with the NIH and co-PIs to compensate for the [% Effort] as Interim Director. This re-negotiation of effort on extramurally funded grants is temporary (less than a year) and will be distributed across funded projects, thus having minimal impact on project progress and completion.

Excluded by Requester **Associate Director for Research** [EFFORT] months - [% Effort] **Excluded by Requester** is Professor in the Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine, and Core Scientist in the Respiratory Diseases Research Unit. The Associate Director for Research oversees for the Pilot Research Program and Core Services.

Excluded by Requester **Interim Associate Director for Administration and Operations** [EFFORT] months - [% Effort] **Excluded by Requester** is a veteran administrator who served as Vice Chancellor for Administration for UC Davis from 2003-2010, in other leadership positions in the Office of Administration since 1992, and as interim Vice Chancellor for Research from 2010-2011. His broad portfolio includes human resources, accounting and financial services, design and construction management, business services, facilities, safety services (including environmental health and safety, risk management, and the animal care program), and research administration. The Associate Director for Administration and Operations is responsible for assisting the Director in long range planning in the areas of financial, personnel, facility, and security needs, and coordinating activities related to the preparation of progress reports, and NIH and University of California reporting requirements.

Excluded by Requester **DVM, DACLAM, Associate Director for Primate Services** [EFFORT] months - [% Effort] **Excluded by Requester** is Associate Professor in the Department of Medicine and Epidemiology, School of Veterinary

Medicine, Associate Director for Primate Services, and Chief **Veterinarian**. As Associate Director he is responsible for oversight and management of Primate Services. [Excluded by Requester] has more than 30 years of experience in medicine and husbandry of nonhuman primates.

[Excluded by Requester]

Research Coordinator

EFFORT

months

% Effort

[Excluded by Requester]

works with the Director and the Associate Director for Administration and Operations by regularly collecting data and information on key components necessary for CNPRC reporting requirements such as lists of current publications and that these publications have acquired the necessary PMCID numbers. She also assists [Excluded by Requester] with special events and meetings, and provides technical assistance with research data for presentations and related documents.

[Excluded by Requester]

Administrative Assistant to the Director

EFFORT

months

% Effort

Under the direction of the Associate Director for Administration and Operations [Excluded by Requester] serves as the executive assistant to the director in managing the day-to-day activities in the Director's Office. [Excluded by Requester] provides high-level administrative support in all aspects of the Director's Office including scheduling activities, coordination of preparation of reports and manuscripts, preparing correspondence, coordinating special events and meetings, and responding to telephone calls and inquiries.

TBN, Safety and Compliance Officer (4.2 calendar months – 35%). The Safety and Compliance Officer develops and implements policies to ensure compliance with federal, state, and local environmental, health, and safety regulations, and ensures a safe workplace through integration with campus safety and compliance activities. The Safety and Compliance Officer is integrated with campus safety and compliance activities, chairs the CNPRC Injury and Illness Prevention Program Safety Committee, and monitors environmental safety programs, systems, and training. Training includes emergency preparedness, hazardous substances, and waste management.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None requested

TRAVEL

\$6,000 is requested for the Director to attend semi-annual NPRC Director's Meetings, and for two trips for administrative and NPRC Consortium activities necessary for the efficient operation of the CNPRC (4 x \$1,500).

\$9,000 is requested for the three Associate Directors to attend semi-annual NPRC Director's Meetings (6 x \$1,500).

\$1,500 is requested for research compliance activities and coordination with the NPRC Consortium.

\$18,000 is requested for travel for the National Scientific Advisory Board members to visit the CNPRC annually (12 x \$1,500).

\$3,000 is requested for two general consultants to visit the CNPRC on an as needed basis to provide input related to program guidance. It is occasionally necessary to seek advice on matters related to service, regulatory, administrative, and/or fiscal functions. When feasible local consultants are used (without cost); however, it is sometimes necessary to secure off-campus consultants.

CONSULTANT COSTS

\$12,000 is requested for consultant fees for the National Scientific Advisory Board members (\$500/day x 2 days x 12).

\$2,000 is requested for consultant fees for the general consultants (\$500/day x 2 days x 2).

SUPPLIES

\$7,340 is requested for the necessary office and administrative supplies to enable the successful management of the CNPRC. Cost estimates are based on historical usage.

OTHER EXPENSES

A total of \$9,000 is requested.

\$4,000 is requested for printing activities including brochures, reports, and other documents.

\$5,000 is requested to support the Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases, which has base support from the National, Heart, Lung, and Blood Institute (NHLBI), NIH.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		1,402,743.00
Section B, Other Personnel		656,017.00
Total Number Other Personnel	15	
Total Salary, Wages and Fringe Benefits (A+B)		2,058,760.00
Section C, Equipment		0.00
Section D, Travel		199,089.00
1. Domestic	199,089.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		161,084.00
1. Materials and Supplies	38,970.00	
2. Publication Costs	0.00	
3. Consultant Services	74,330.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	21,237.00	
9. Other 2	26,547.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		2,418,933.00
Section H, Indirect Costs		549,099.00
Section I, Total Direct and Indirect Costs (G + H)		2,968,032.00
Section J, Fee		0.00

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OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	96,300.00	B&C Rate F&A Return
2	101,597.00	B&C Rate F&A Return
3	107,185.00	B&C Rate F&A Return
4	113,080.00	B&C Rate F&A Return
5	119,299.00	B&C Rate F&A Return

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

DOSpecificAims.pdf

3. Research Strategy*

DOResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

DOResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

SPECIFIC AIMS

The Director's Office is responsible to the Principal Investigator (PI), Vice Chancellor Harris Lewin, for the P51 base grant and to the University of California and the NIH for the overall administration of the California National Primate Research Center (CNPRC). This includes fiscal management, quality control of performance in all areas, and the development and implementation of short and long range plans. The Specific Aims for the Director's Office are as follows:

Specific Aim 1. Provide direction and leadership for research excellence.

Plan. The Director is committed to a multidisciplinary approach to research and to the provision of outstanding animal care, facilities operations, and scientific expertise to ensure the goals of investigators nationwide can be achieved. The overarching objective is to promote the CNPRC resource and effectively facilitate and communicate the many research accomplishments, and the spectrum of opportunities for individual and institutional research partnerships. The Director meets regularly with UC Davis Organized Research Unit and Center Directors, and annually with the Council of Deans of the Schools and Colleges to discuss interdisciplinary research programs. The Director visits other academic institutions, the private sector, and the NIH campus to promote the CNPRC and highlight the depth and breadth of the infrastructure. The Director also works with the other National Primate Research Center (NPRC) Directors and the NIH to increase the recognition of the overall NPRC Program, particularly through the NPRC Consortium. The overall objective is to enhance growth of the CNPRC program through faculty recruitments, support for new programmatic initiatives that meet NIH strategic goals and priorities, and by forming new partnerships that advance translational research with the nonhuman primate model.

Specific Aim 2. Ensure the successful operation of the CNPRC.

Plan. The Director ensures that research goals are facilitated through an efficient process for proposal review for study conduct and grant/contract submissions, and by providing specialized facilities, expertise, and related nonhuman primate resources. The Director provides administrative oversight by consensus management that relies on faculty and staff participation in key advisory committees. The Director also ensures ready access to Core Scientists and research opportunities that advance the research mission.

Specific Aim 3. Mentor and train the next generation of investigators with nonhuman primate expertise.

Plan. The Director promotes mentoring and training of investigators in the performance of high quality research with nonhuman primates, and the conduct of multidisciplinary team-based investigations through Core Scientists, Veterinarians, and staff. Core Scientists participate in campus undergraduate and graduate education and training programs which provides essential mechanisms to cultivate emerging investigators dedicated to primatology and high quality nonhuman primate research.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

Plan. The Director provides vigorous oversight to ensure high quality veterinary care and research conduct. The Director's oversight is enhanced through campus compliance activities, the UC Davis Institutional Animal Care and Use Committee, participation in the campus Animal Research Communication Coordination Committee, the CNPRC Safety and Compliance Officer, and on-site standing committees such as the Research Advisory Committee, Colony Management Advisory Committee, Morbidity and Mortality Committee, and Infection Control Committee.

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

RESEARCH STRATEGY

INTRODUCTION

Through the Principal Investigator (PI), Vice Chancellor for Research Harris Lewin, the California National Primate Research Center (CNPRC) Interim Director Excluded by Requester is responsible to the NIH and the University of California for the overall administration of the P51 base grant (Figure 1). This includes fiscal management, quality control of performance in all areas, and the development and implementation of short and long range plans. The CNPRC Director has the responsibility for the day-to-day management, scientific direction, and overall strategic planning for the programs and supporting facilities and resources. To ensure the efficient and effective operation of the CNPRC, the Director delegates, monitors, and directs Core Scientists, Veterinarians, and staff in addressing these critical areas. Personnel in the Director's Office are shown in Table 1.

Figure 1. Organizational Chart: Director's Office

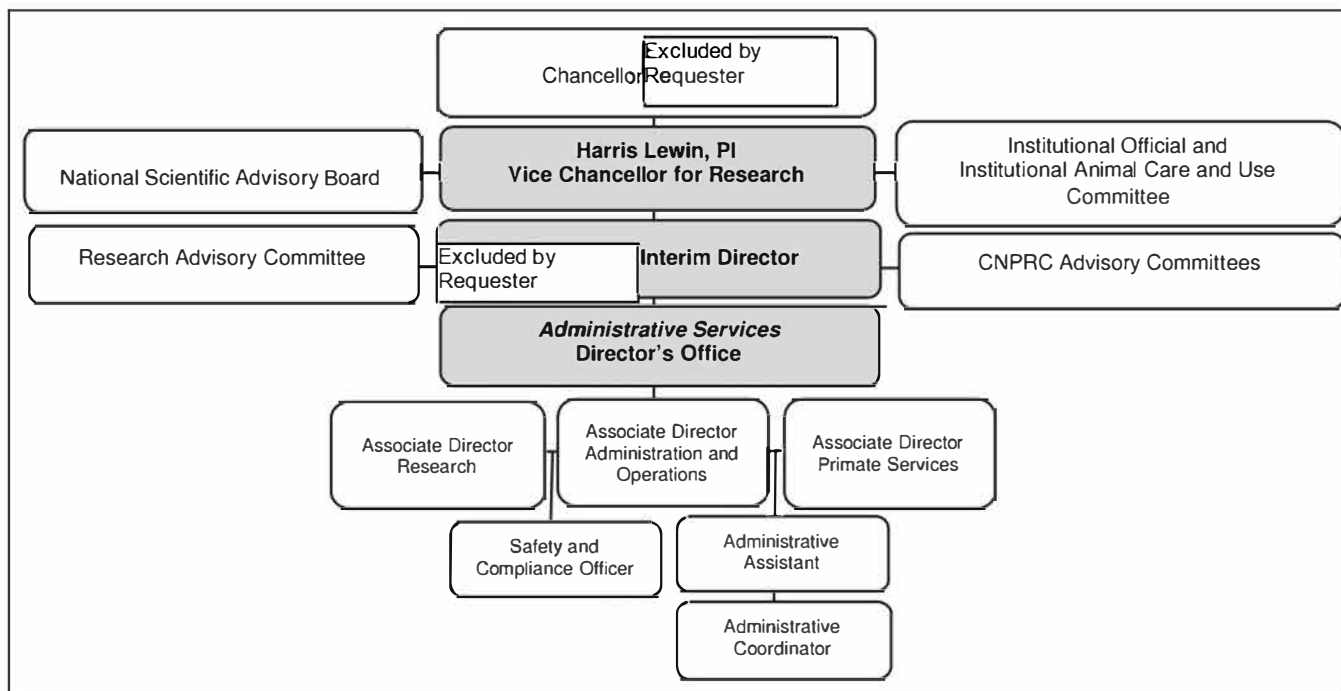


Table 1. Director's Office Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Harris Lewin, PhD	Office of the Vice Chancellor for Research, and Department of Evolution and Ecology, College of Biological Sciences	PI
Excluded by Requester	Department of Pathology and Laboratory Medicine, School of Medicine	Interim Director
	Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine	Associate Director for Research
	CNPRC	Interim Associate Director for Administration and Operations
	Department of Medicine and Epidemiology, School of Veterinary Medicine	Associate Director for Primate Services
	CNPRC	Research Coordinator
	CNPRC	Administrative Assistant to the Director
TBN	CNPRC	Safety and Compliance Officer

TBN=to-be-named

The sources of support for the Director's Office in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 2. Support for the Director's Office

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$438,738	\$454,005
Program Income from P51	\$91,485	\$96,300
Other Sources	\$132,484	\$132,484
TOTAL	\$662,707	\$682,789

Response to the Summary Statement:

reviewers' comments

reviewers' comments

SIGNIFICANCE

The Director's Office administrative responsibilities include monitoring compliance with required procedures of the NIH and the University of California; authorizing and reviewing budgetary and program reports; directing the preparation of the P51 base grant renewal and noncompeting continuation applications; authorizing and directing special applications such as C06 and G20 grant submissions, and other funding mechanisms to provide support for CNPRC initiatives; and to encourage and assist CNPRC Core and Affiliate Scientists in the development of extramural grants and contracts to support research. The Director ensures that access to CNPRC resources is strongly promoted through Core Scientists, Outreach, the Pilot Research Program, collegial professional relationships, and interactions with Schools and Colleges, campus programs, academic institutions, and professional associations. The Director plays a key role in the interactions with the Vice Chancellor for Research, the Deans of the UC Davis Schools and Colleges, and other UC leadership to promote and prioritize operations and expansion of the CNPRC within UC Davis.

The Director is the primary contact for the NIH regarding the conduct of the P51 base grant, and authorizes and manages the roles of key individuals in their National Primate Research Center (NPRC) Consortium activities (see **NPRC Consortium**). This authorization and managing role includes ad hoc efforts, such as the development of white papers in coordination with other NPRC Directors, the appointment and oversight of individuals in the various Consortium Working Groups, and authorizing and supporting specific inter-NPRC initiatives, such as the Animal Research Management System (ARMS) initiative which will provide a compatible animal records system among the NPRCs. This requires a team effort with the Research Unit Leaders, Core Services, Primate Services, and Administrative Services as described in the **Overview**.

The Director has a formal structure that includes three Associate Directors. The Associate Director for Administration and Operations is responsible to the Director for Administrative Services and to address fiscal and administrative activities including budget, personnel, grant/contract administration, purchasing and storehouse, accounting, administrative support, and facilities management. In addition, the Associate Director for Administration and Operations provides input to the Director and the Research Advisory Committee regarding long range fiscal planning. The Associate Director for Primate Services is responsible to the Director for colony management and overall animal well-being, and for providing research support through Primate

Services to investigators. The Associate Director for Research is responsible to the Director for the Pilot Research Program and Core Services. Two Assistant Directors, the Assistant Director for Colony Management and Research Services and the Assistant Director for Information Technology Services, provide additional support to the Director and Associate Directors.

The Safety and Compliance Officer is responsible for providing oversight of safety and compliance with regulatory agencies, and integrates in this capacity with UC Davis Safety Services including Environmental Health and Safety (EH&S).

The CNPRC **Research Advisory Committee** provides advice to the CNPRC Director regarding prioritization of projects and resources, overall CNPRC function, and research needs. The Research Advisory Committee includes the four Research Unit Leaders, the Associate and Assistant Directors, the Senior Veterinary Managers for Primate Medicine Services and Anatomic and Clinical Laboratory Services, and the Director's of the UC Davis Clinical and Translational Science Center (CTSC) and Center for Comparative Medicine (CCM), with meetings every other week throughout the calendar year. The Research Advisory Committee has a pre-proposal mechanism in place for the review of all proposed projects to be conducted at the CNPRC including all grant and contract submissions that propose to use CNPRC resources (see below). The Research Advisory Committee reviews the scientific merit of any new project proposals that have not undergone NIH peer review and that propose to use CNPRC resources. Minutes from Research Advisory Committee meetings are maintained in the Director's Office.

The Director's Office has standing advisory committees that address the function and activities within the CNPRC. The goal is to ensure sustainability, compliance, and to address needs and new opportunities. Committees that participate in the overall function and mission of the CNPRC are shown in Table 3.

UC Davis Animal Care and Use Program. The CNPRC vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited Animal Care Program. The entire campus recently participated in an AAALAC site visit and received **Full Accreditation** with no recommendations for improvements recognizing the long-standing commitment to high quality animal care at UC Davis and the CNPRC. A routine visit from the Office of Laboratory Animal Welfare (OLAW) was also highly complementary to the UC Davis program overall and the CNPRC.

At UC Davis, a single IACUC oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met (see **Administration Overview**). The IACUC reviews all submitted protocols for compliance with the requirements of the Animal Welfare Act, the NIH *Guide for the Care and Use of Laboratory Animals*, the Public Health Service Policy on the Humane Care and Use of Laboratory Animals, and UC Davis Policies and Guidelines. The IACUC submits reports and recommendations to the Institutional Official, Senior Associate Vice Chancellor [REDACTED]. The UC Davis IACUC is a based committee with 25 members (faculty, facility staff, UC Davis Attending Veterinarian, IACUC staff non-affiliated members, non-scientists in addition to 12 alternate members) and inspects all animal facilities, evaluates all aspects of the institutional animal care program, establishes policy and procedure for the UC Davis campus, and coordinates training, compliance, and occupational health programs for all of UC Davis including the CNPRC.

Excluded by
Requester

Vice Chancellor Lewin and the CNPRC Director also participate in a quarterly campus **Animal Research Communication Coordination Committee**, which addresses campus topics of importance to the research community such as security, communications, and new programs. Members include the Institutional Official (Chair) and members from Government and Community Relations, the Office of Campus Council, Risk Management Services, News Service, the UC Davis Police Department, as well as the Deans of the Schools of Medicine and Veterinary Medicine and the College of Biological Sciences, the IACUC Chair and Co-Chair, IACUC Administrator, UC Davis Attending Veterinarian, Director of Research Compliance and Integrity, and Associate Vice Chancellor for Safety Services. This provides an excellent opportunity for critical interactions on timely topics related to the animal care program, security, and the CNPRC.

Table 3. CNPRC Standing Committees

CNPRC Committee	Members	Frequency and Function
Research Advisory Committee	Director (Chair); Associate Director for Administration and Operations, Primate Services, and Research; Assistant Director for Colony Management and Research Services, Assistant Director for Information Technology Services; Research Unit Leaders; Clinical and Translational Science Center Director; and Center for Comparative Medicine Director	<ul style="list-style-type: none"> • Biweekly • Address research needs and overall CNPRC function • Prioritizes projects and resources • Review proposed research projects; ~60 pre-proposals for submitted grants and contracts reviewed annually; discussed and evaluated in terms of scientific merit, resources available, animal availability, meeting the NPPRC mission, applicability, and NIH priority
Senior Management Committee	Director (Chair); Associate Director for Administration and Operations, Primate Services, and Research; Assistant Director for Colony Management and Research Services, Assistant Director for Information Technology; Primate Medicine and Pathology Managers	<ul style="list-style-type: none"> • Weekly • CNPRC programmatic, administrative, facility, and management topics many of which are brought in a more formal manner to the Research Advisory Committee for final review and approval
Colony Management Advisory Committee	Associate Director for Primate Services and Assistant Director for Colony Management and Research Services (Co-Chairs), Core Scientists, Staff Veterinarians	<ul style="list-style-type: none"> • Monthly • Issues impacting colony management (e.g., Specific Pathogen Free colony, reproductive colony, behavioral management and environmental enrichment, colony genetics)
Morbidity and Mortality Committee	Primate Medicine and Pathology Managers; UC Davis Attending Veterinarian; Associate Director for Primate Services; Assistant Director for Colony Management and Research Services; Research Unit Leader and UC Davis IACUC Co-Chair (Chair)	<ul style="list-style-type: none"> • Quarterly • Review spontaneous deaths in outdoor field corrals • Address colony-related topics and practices
Environmental Enrichment Committee	Associate Director for Primate Services and Lead for Behavior Management Services (Co-Chairs); Assistant Director for Colony Management and Research Services; Staff Veterinarians; Behavior Management Services Staff	<ul style="list-style-type: none"> • Quarterly • Review ongoing practices, areas of focus or concern, new concepts and suggestions, and efficacy of current practices
Injury and Illness Prevention Program Safety Committee	Safety and Compliance Officer (Chair); representatives from Administrative components and Scientific Research Units	<ul style="list-style-type: none"> • Quarterly • Reviews any safety concerns, disseminates safety information including injury and illness prevention programs, emergency action plans, infection and exposure control practices, hazardous material procedures, biosafety guidelines, and medical waste procedures
Infection Control Committee	Associate Director for Primate Services; Assistant Director for Colony Management and Research Services; Core Scientists from the Infectious Diseases Research Unit (Core Scientist, Chair); Staff Veterinarians; Animal Resource Supervisor for infectious housing; Safety and Compliance Officer; Medical Director of the UC Davis Occupational Health Program	<ul style="list-style-type: none"> • Quarterly • Reviews ongoing practices including health surveillance for employees and visitors, vaccination policies, BSL3 policies and practices, and personal protective equipment (PPE) requirements

CNPRC Access. The Director ensures access to the CNPRC and specialized resources, including the Core Scientists that have extensive expertise and are committed to facilitate investigator needs with nonhuman primates. The primary point-of-contact for studies with nonhuman primates is the Core Scientists as they represent the route by which the majority of research conducted is initiated at the CNPRC. Core Scientists serve as subcontract PI for many investigators nationwide (see Research Unit descriptions). They serve as the primary facilitators based on their domain-based expertise. New Affiliate Scientists may also identify research opportunities at the CNPRC through interactions with Core Scientists at annual meetings and at other venues; through identification of research resources on the CNPRC and related websites; and by submitting applications to the CNPRC Pilot Research Program and other outreach opportunities available in Service Cores and other NIH-supported resource programs at the CNPRC. Core Scientists interact directly with Affiliate Scientists and aid in preparation of pre-proposals for timely submission to the Research Advisory Committee, the grant submission process, and in the writing and submission of IACUC protocols. Since the Research Advisory Committee meets biweekly, the process of pre-proposal review and approval is highly efficient. Priority is always given to NIH-funded research. Core Scientists facilitate research at the CNPRC by serving as the on-site PI for a range of projects. They also provide a service function through Cores and outreach programs. Inquiries that may come to the CNPRC are directed to the Director or the Associate Director for Research, who then in turn directs interested investigators to the appropriate Core Scientist based on expertise. New investigators benefit greatly from the expertise of Core Scientists when submitting nonhuman primate NIH and pilot project applications.

EH&S and Compliance. The Senior Associate Vice Chancellor oversees resource planning and finance, facilities and land management, and Safety Services. Responsibilities include planning, designing, operating, and stewarding the campus's physical and natural resources; and providing for the health and safety of the campus community. Safety Services includes programs and services related to animals, biological safety, chemical and laboratory safety, emergency management and mission continuity, ergonomics and body mechanics, environmental management, fire prevention, general health and safety, hazardous materials and hazardous waste management, injury and illness prevention, occupational health, radiological safety, and risk management. Under the auspices of the campus Safety Services program the CNPRC has a dedicated Safety and Compliance Officer that works with the UC Davis campus in the implementation and assurance of the overall safety program. While there are central compliance requirements for all UC Davis faculty and employees in general, the responsibility to ensure environmental and safety regulations are followed remains with departments and Organized Research Units such as the CNPRC, PIs, and the on-site safety coordinators. All work together to ensure appropriate policies and procedures are followed including participation in mandatory training sessions. Similar to departments, the CNPRC is required to have the following plans and programs in place:

- **Biological Safety.** Research that involves recombinant DNA technology; work with materials that are infectious (or potentially infectious) to plants, animals, or humans; any material that falls under the Cal-OSHA Bloodborne Pathogen Standard, which includes human cell lines, human blood or blood products, human body fluids, nonhuman primate cells or cell lines, and nonhuman blood or blood products, as well as storage of biohazardous materials require PIs to obtain a Biological Use Authorization (BUA). Shipment of hazardous materials must also comply with state and federal laws (training classes are provided). Other authorization programs include **Radiation Use Authorization (RUA)** and Laser Use Authorization.
- **Chemical Hygiene Plan.** EH&S provides resources, training, and consultation in the use of chemicals and offers regular chemical and laboratory safety training with online access to chemical safety information. Each laboratory is required to have a laboratory-specific chemical hygiene plan that describes the hazards in the laboratory and how workers should protect themselves from these hazards. All employees must be trained, at least annually, on the hazards to which they might be exposed and how to protect themselves from those hazards. Employees also need to be trained on the provisions of the laboratory-specific chemical hygiene plan. All training must be appropriately documented.
- **Chemical Inventory System (CIS) and Self-Audit Program.** Annual hazardous materials inventory reporting is required through the CIS program. The Yolo County program monitors this inventory, and inspects campus laboratories to verify compliance with hazardous materials and waste storage and handling, as well as the required training. The campus is also required to report use of California-regulated carcinogens annually through the CIS program. Material Safety Data Sheets are accessible to all employees who might use chemicals.

- **Emergency Management and Mission Continuity.** Planning for natural and man-made emergencies requires an integrated approach to the management of programs and activities for all four phases of Emergency Management: mitigation, preparedness, response, and recovery. The campus has emergency policies relating to emergency planning and alert notifications. Comparable to all programs at UC Davis, the CNPRC has an emergency action plan.
- **Integrated Hazardous Waste Management.** This office provides cost effective disposal options for radioactive, biological, and chemical hazardous wastes in accordance with Federal State and local regulations. The campus has a Hazardous Chemical Use, Storage, Transportation, and Disposal policy in place for these activities.
- **Injury and Illness Prevention Program.** The program establishes a management framework for reducing the risks associated with workplace injuries and illnesses, and identifying activities required to promote safety and health. Cal-OSHA regulations require UC Davis to establish, implement, and maintain an effective Injury and Illness Prevention Program in writing. The CNPRC has an on-site document that addresses the requirements of this program.

The CNPRC also has an on-site Safety and Compliance Officer that follows the UC Davis SafetyNet #125 on Program Guidelines for Department Safety Coordinators. In addition, the Scientific Research Units each have dedicated Safety Coordinators that meet regularly with the Safety and Compliance Officer who is responsible for developing, implementing, and monitoring environmental and safety programs for the CNPRC to ensure compliance with federal, state, and local environmental, health, and safety regulations, and a safe workplace. This individual also engages managers, supervisors, and employees in creating a safe work environment and trains in the campus-wide dangerous goods course.

Progress and Major Accomplishments: Contributions to the CNPRC Mission

During the current funding period, Core Scientists collaborated with 346 Affiliate Scientists and other investigators from institutions across the U.S. (128 from UC Davis), published over 400 manuscripts, and mentored 290 trainees (undergraduate to junior faculty). Extramural grants during the current funding period totaled approximately \$150 million. The following lists CNPRC-wide accomplishments under the Director's leadership and oversight:

- Obtained funding for and completed the Respiratory Diseases Center Building. This is further addressed in the **Facilities Improvement** section, and represents a major expansion of the CNPRC Respiratory Diseases capability through the leadership of the prior director. Excluded by Requester The opening ceremony was held February 27, 2014.
- Appointment of the following:
 - Excluded by Requester Unit Leader of Infectious Diseases Research Unit
 - Excluded by Requester Core Scientist with a joint appointment in the Infectious Diseases and Reproductive Sciences and Regenerative Medicine Research Units
 - Excluded by Requester Core Scientist in the Infectious Diseases Research Unit
 - Excluded by Requester Associate Director for Primate Medicine
 - Excluded by Requester Associate Director for Research
 - Excluded by Requester Interim Director
 - Excluded by Requester Interim Associate Director for Administration and Operations
- Realignment of the Analytical Resource Core and transition to the Endocrine Core and Immunology and Pathogen Detection Resources Core with appointment of Core Leads Excluded by Requester and Excluded by Requester Excluded by Requester respectively
- Transition from the Computational Imaging Core to the Multimodal Imaging Core with addition of a new PET/CT imaging facility and expanded imaging services

NPRC Consortium. The Director is an active participant in the NPRC Consortium, which strengthens communications, leverages CNPRC-wide resources, and facilitates sharing of information and best practices across NPRCs and their host institutions. The CNPRC is an active participant in these NPRC director-driven activities (see **NPRC Consortium**) (Table 4).

Table 4. NPRC Consortium Activities

Working Group	CNPRC Representative	Examples of Activities
Behavioral Management	Excluded by Requester Management Services (Primate Services)	• Standardized terminology and behavior assessment tools • Development of a common categorization system for factors underlying single housing
Breeding and Colony Management	Excluded by Requester Assistant Director Colony Management and Research Services	• Establishment of colony management best practices through surveys
Clinical and Surgical Techniques	Excluded by Requester Senior Veterinary Manager Primate Medicine Services (Primate Services)	• Conducted x CAST webinars • Established Institutional Guidelines for Common Research Procedures survey
Consortium Project Management and Informatics Group	Excluded by Requester Assistant Director Information Technology Services	• Meeting coordination, web conference hosting, website support, and security administration for working groups • Project management, application development, system integration, testing, training, and documentation support • Colony Health Benchmarks data collection and analysis, yielding data-intensive sharing of husbandry practices between NPRCs
Data Access Guidelines	Excluded by Requester Interim Associate Director of Administration and Operations	• Development of overall content guidelines and approval processes
Genetics and Genomics	Excluded by Requester and Genetics Management Services	• Development, validation, and successful use of new Single-Nucleotide Polymorphisms (SNP)-based genetic tests for parentage and geographic ancestry in rhesus macaques across NPRCs
Integrity and Compliance	Excluded by Requester Interim Associate Director of Administration and Operations	• Conducted 5 quarterly web conferences to address topics such as post approval monitoring and response to USDA citations
Occupational Health and Safety	Excluded by Requester PhD, Immunology and Pathogen Detection Resources Core	• Review Herpes B-virus testing practices and specifics related to human cases
Outreach	Excluded by Requester Information Officer	• Design, production, and implementation of a new NPRC logo, word mark, and public outreach brochure
Pathology	Excluded by Requester ACVP, Senior Veterinary Manager Anatomic and Clinical Pathology Services (Primate Services)	• Tripled the number of curated cases in the Primate Pathology Image Database
Training	Excluded by Requester Senior Veterinary Manager Primate Medicine Services (Primate Services)	• Monthly Virtual Grand Rounds expanded to 9 external institutions

In addition to the formal consortium activities, CNPRC Core Scientists and staff consult regularly with their counterparts at the other NPRCs via telephone conferences and listservs to discuss issues and to problem solve. The Associate Directors for Administration, Public Information Officers, Information Technology Managers, Veterinarians, Safety Officers, Enrichment Program Managers, and Security Managers are examples of groups from each of the NPRC's that regularly teleconference. Face-to-face meetings by members of these groups are periodically held in conjunction with the semi-annual NPRC Directors' meetings and occasionally during the weekly Director's conference calls as part of the evaluation process for the Consortium working groups. The semi-annual face-to-face meetings are two-day agenda-rich meetings that interface with representatives from the Office of Research Infrastructure Programs (ORIP) and discuss common issues critical to all of the NPRCs (e.g., NPRC/Center for AIDS Research collaborations, development of a NPRC website of capabilities and phenotypes, and strategic planning). The weekly NPRC

Director's conference call allows for timely follow-up on issues discussed at the semi-annual meetings as well as collaborative projects among the NPRCs. Through these activities of collaborative leadership, strategic growth, increased linkages, and the commitment to Consortium success, the foundation is laid for successful growth and research accomplishments during the next funding period.

INNOVATION

In order to best leverage the resources of the UC Davis campus, the Director reports to the Vice Chancellor for Research; the CNPRC is one of the eight Organized Research Units overseen by the Vice Chancellor. One of the strengths provided by reporting directly to the Vice Chancellor for Research is that there is broad and unified campus representation of CNPRC-related issues presented to the upper echelons of campus administration. While the majority of Core Scientists are affiliated with home departments in the Schools of Medicine and Veterinary Medicine, Core Scientists also have their home departments in the Colleges of Engineering and Letters and Sciences. Further engagement with all of the Schools and Colleges contributing to new faculty FTE that have been designated as a result of the search for a new Director will provide important and innovative opportunities for the growth of the CNPRC program as aligned with NIH and campus strategic initiatives. This brings unique advantages as the Director is in an excellent position to reach out across multiple colleges and schools to spearhead interdisciplinary initiatives.

The Director is an active participant in the NPRC Consortium. These activities result in white papers (e.g., nonhuman primate phenotypes of human disease to genotype identification of specific therapeutic targets), plan NPRC-wide initiatives (e.g., CNPRC joined forces with Wisconsin and Yerkes NPRC to enhance managing animal records), and development of the NPRC-wide website listing of resources and capabilities (Figure 2).

A primary area of CNPRC innovation reflected in this renewal is the overarching theme of **Lifespan Health**. This is a common theme that is a thread throughout all of the CNPRC Scientific Research Units, and all stages of development, maturation, and aging are well represented in the nonhuman primate colonies maintained at the CNPRC. This accomplished group of CNPRC Core Scientists provides a rich environment for the development, validation, and study of nonhuman primate models of human disease. All of the Scientific Research Units at the CNPRC include programs that address the human and nonhuman primate age spectrum. The Overview and individual Unit descriptions present details related to these research and training activities, contributions, and collaborative partnerships that address roadblocks to improving human health while furthering the study of nonhuman primate development, health, aging, and disease.

Figure 2. NPRC website



APPROACH

Plans for the Next Funding Period

The CNPRC has significant strengths and an array of scientific achievements that, when coupled with key UC Davis initiatives, can build and enhance research excellence and opportunities. Key resources and core facilities in genomics, metabolomics, and bioinformatics linked with the unique nonhuman primate models in place at the CNPRC provides a strong foundation for the future, setting the stage for innovative initiatives. The goals for the next funding period are reflected in the Specific Aims that focus on providing readily accessible state-of-the-art research opportunities to investigators and trainees for studies that promote human health and healthy aging. Through targeted opportunities and key UC Davis initiatives, the Director's Office will actively promote the recruitment of faculty to the program, and continue to provide and expand the necessary infrastructure, expertise, and essential services to meet the growing needs of investigators and trainees as they advance the research frontier to improve human health.

Specific Aim 1. Provide direction and leadership for research excellence.

The Director will support research programs and grant submissions in response to NIH strategic priorities and promote research opportunities that focus on human health across the lifespan. This will be accomplished

through expanding opportunities for collaboration across UC Davis including campus programs central to the mission (e.g., Clinical and Translational Science Center, MIND Institute, Stem Cell Program, Center for Comparative Medicine, Center for Health and the Environment, Center for Comparative Lung Biology and Medicine), other UC campuses, national outreach, and through the Pilot Research Program and related pilot project programs. The Director will provide leadership and expertise in short and long range planning to ensure that resources are made available to the scientific community and the use of nonhuman primate models is sustained, promoted, and expanded, consistent with the Strategic Plan of the Office of the NIH Director. Through the NPRC Consortium and other NPRC Directors, the CNPRC Director will foster and encourage resource collaborations amongst the seven NPRC's. CNPRC Core Scientists possess critical intellectual and practical expertise, and they provide an essential conduit through which investigators can address novel experimental concepts and/or therapies in a primate system that most closely simulates humans. During the next funding period the CNPRC will continue to build collaborations and promote translational research through collaborative funding opportunities, joint support of research seminars and symposia, and through a dynamic, informational, and regularly maintained CNPRC website that serves as a portal for investigators.

Efforts in the NPRC Consortium on genetics/genomics are very timely as there is a major effort underway to strengthen this concept at the institutional level. Precision genomics and personalized medicine will be critical to improve human health care, and the School of Medicine Human Genomics Initiative is poised to capitalize on infrastructure already in place to address the national priority of human genomics to manage chronic illnesses. This program will link closely with the CNPRC. The NPRC Consortium has recently drafted a white paper that provides the rationale to enhance nonhuman primate resources through the application of genomics to nonhuman primate phenotypes of human disease using DNA sequencing. There currently exists in the NIH-supported rhesus monkey colonies tens of thousands of naturally occurring genetic variants and numerous disease phenotypes that are directly relevant to human disease mechanisms providing ideal translational models. As the research frontier moves forward and the ability to link genotypic and phenotypic information improves, the nonhuman primate model is likely to provide critically important insights that will inform studies in humans. The CNPRC is in an outstanding position to take full advantage of this confluence of knowledge, given the close and vibrant relationships with other UC Davis Centers, Schools, and Colleges.

Specific Aim 2. Ensure the successful operation of the CNPRC.

The Director is dedicated to the enhancement of research through a supportive environment of specialized facilities, expertise, and resources unique to nonhuman primates for the investigation of the regenerative medicine, neuroscience, behavior, infectious diseases, respiratory diseases, and reproductive and developmental disorders throughout the lifespan. Core Scientists, veterinarians, and staff provide unique services through their relative components including Core Science Services. The Director's administrative oversight approach is by consensus management, which relies on faculty and staff participation on a number of committees as described above.

The CNPRC Director will foster an environment that emphasizes scientific expertise, which is critical to carry out the mission of the CNPRC. Internal and external research collaborations will be promoted utilizing the extensive expertise of Core Scientists who will actively participate in developing the resource including best practices for colony management. The increasing commitment of the Director and CNPRC faculty and staff to the NPRC Consortium is also expected to result in more outcomes that improve husbandry, scientific infrastructure, and overall support for the NIH research community. The established Primate Center Cores (Behavior Research Services Core, Endocrine Core, Immunology and Pathogen Detection Resources Core, Inhalation Exposure Core, Multimodal Imaging Core) are all dedicated to providing a spectrum of services and research opportunities to investigators nationwide. All of the Scientific Research Units also have specialized repositories of nonhuman primate cells, tissues, and data that collectively provide important opportunities for entrepreneurial research synergies, training, pilot projects, and new NIH grant submissions. The Director will also capitalize on campus investments and growth areas such as "-omics", bioinformatics, and "Big Data". The Research Investments in Science and Engineering (RISE) proposals highlight opportunities to study the microbiome and the development of advanced imaging tools which links with campus efforts in translational imaging. Notably, many of these initiatives have representation of CNPRC Core Scientists, illustrating the key position of the CNPRC in the overall UC Davis campus. This is recognized by the UC Davis leadership, which is making significant resources available to improve and renovate the CNPRC infrastructure as part of the recruitment plans for a new Director.

Specific Aim 3. Mentor and train the next generation of investigators with nonhuman primate expertise.

The Director vigorously promotes the mentoring and training of new investigators in the development of primate expertise, the design and study of nonhuman primate models of human health and disease, and the conduct of multidisciplinary translational investigations through the collaborative efforts of the Core Scientists, veterinarians, and staff. The Director will encourage Core Scientists to participate in UC Davis Training Grants that provide an important mechanism in the mentoring and training of emerging investigators in nonhuman primate investigations (Table 5). Through these efforts, the CNPRC will continue to integrate the training of undergraduate and graduate students and postdoctoral and clinical fellows (human and veterinary) in research programs and projects, and ensure the development of expertise in primatology and the successful conduct of translational team science.

Table 5. Examples of UC Davis Training Grants Led by CNPRC Core Scientists (May 1, 2010 to April 30, 2014)

Training Grant	School	Core Scientist (Research Unit)
NIH Animal Models of Infectious Diseases Training Program	Medicine	Excluded by Requester Infectious Diseases)
NIH Interdisciplinary Training for Autism Researchers	Medicine	Excluded by Requester (Brain, Mind, and Behavior)
California Institute for Regenerative Medicine (CIRM) Stem Cell Training Program	Medicine	Excluded by Requester (Reproductive Sciences and Regenerative Medicine)

The CNPRC has a staff of well-trained and dedicated scientists, administrators, veterinarians, veterinary pathologists, and research and husbandry technicians whose continued professional development needs to be nurtured. Mentoring and training of students, fellows, junior investigators, and related research personnel will be essential in order to ensure a pipeline of investigators and staff committed to supporting the CNPRC colonies and to provide services to the research community. The CNPRC provides the “complete primate experience” for trainees at all levels based on the resources and research programs of the Core Scientists and their integration with campus educational and training programs. The link with CTSC educational and training programs will ensure the success of academic programs while promoting national core competencies.

A 2014 publication in the Proceedings of the National Academy of Science highlights several key points related to the research enterprise and impact on trainees. While there remains hope that federal funds for scientific research will increase, UC Davis has several training programs and initiatives that support trainees with mentoring focused on the use of the nonhuman primate as a model for human health and disease. In addition, the CNPRC has a long history of providing research opportunities for trainees that ensures successful and alternative career paths (see Research Unit descriptions). While the current funding environment presents challenges, opportunities are available to participate in CNPRC research programs as, for example, a senior scientist or project manager.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

The Director is directly involved in oversight of high quality veterinary care and research support. The rhesus monkey production colony offers research subjects that span the entire life history, and all of these age groups are utilized in current research programs and projects. All requests for animals, specialized procedures, veterinary, and technical support are evaluated biweekly by the Research Advisory Committee and through other standing committees (e.g., Colony Management, Morbidity and Mortality).

The CNPRC Public Information Officer provides outreach materials and addresses questions and requests from within UC Davis, the media, the scientific community, and the general public on behalf of the CNPRC. The CNPRC takes the responsibility to inform the public seriously and these activities will continue with the integration of the campus Strategic Communications office and Animal Care Program leadership team.

The CNPRC has experienced a significant increase in the number of Freedom of Information Act requests from animal rights organizations and is working closely with campus administration, the UC Office of the President, and at the level of the NIH, USDA, and other regulatory bodies regarding these activities. The Director continues to work with campus administration in the review and interpretation of NIH, OLAW, State of California, University of California, and various other regulatory policies to ensure that the CNPRC's activities remain in full compliance.

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

ADMINISTRATIVE SERVICES: DIRECTOR'S OFFICE

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Administration and Operations Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename AOSAbstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	AOS_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	AOSFacilitiesandOtherResources.pdf
11. Equipment	AOSEquipment.pdf

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES

ABSTRACT

The California National Primate Research Center (CNPRC) **Administration and Operations Services** functions in coordination with the UC Davis campus administration and maintains administrative and operational responsibility for the CNPRC in the areas of business office services, human resources, purchasing and stores, facilities operations, emergency response, and support for the Director's Office. The Specific Aims for Administration and Operations Services include: (1) Ensure effective and efficient operation of the CNPRC infrastructure to optimize the conduct of nonhuman primate research, (2) Work with Core Scientists, the UC Davis campus, and the NIH to evaluate infrastructure needs and facilitate research, and (3) Share best practices across the NPRC Consortium.

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: There are 13 computers in Administration and Operations Services. Each individual has a PC computer that is linked to the CNPRC server, which automatically backs up work on a daily basis, and all are networked to Campus Accounting, Payroll, and Personnel databases. There are also workstations for specified functions such as reception and Human Resources orientation. Three guest computers are provided in the copier/supply room. Laser printers and fax machines are also available.

Office: The Administration and Operations Services staff is housed in offices that encompass 1,135 sq. ft. Purchasing/shipping/receiving has 184 sq. ft. of offices within the Central Supply/Locker Building. The 135 sq. ft. Facility Security

Other: The CNPRC has a 1,879 sq. ft. Central Supply/Receiving Building for stores, shipping, and receiving. A 203 sq. ft. copier/supply room provides copy, guest computer, printer, scanning, and shredding capabilities.

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES

EQUIPMENT

Facility Security

The copy/supply room in Administration and Operations Services provides a high-speed copier, three guest workstations, network printers, and shredders. There are also shared-use document scanners available to all staff.

Shipping and receiving has a pallet jack, hand trucks, a safe, a $\leq -80^{\circ}\text{C}$ freezer, $\leq -20^{\circ}\text{C}$ freezer, two 4°C refrigerators, and access to two forklifts from the colony operation when needed.

Two UC Davis vehicles are available to Administration and Operations Services providing transportation options for pick-ups, deliveries, and meetings on the Davis and Sacramento campuses.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	24,103.00	9,613.00	33,716.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						33,716.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			11,719.00	6,199.00	17,918.00
1	Business Office Manager				27,415.00	14,503.00	41,918.00
4	Business/Finance Staff				52,748.00	27,903.00	80,651.00
3	Storehouse Staff				32,751.00	20,032.00	52,783.00
3	Human Resources Staff				53,389.00	28,243.00	81,632.00
12	Total Number Other Personnel						
					Total Other Personnel		274,902.00
					Total Salary, Wages and Fringe Benefits (A+B)		308,618.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	20,500.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	3,000.00
Total Other Direct Costs	23,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	332,118.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	332,118.00	75,391.00
		Total Indirect Costs	75,391.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	407,509.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	24,826.00	10,477.00	35,303.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					35,303.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			12,070.00	6,677.00	18,747.00
1	Business Office Manager	Excluded by Requester			28,238.00	15,620.00	43,858.00
4	Business/Finance Staff	Excluded by Requester			54,329.00	30,053.00	84,382.00
3	Storehouse Staff	Excluded by Requester			33,734.00	21,363.00	55,097.00
3	Human Resources Staff	Excluded by Requester			54,991.00	30,419.00	85,410.00
12	Total Number Other Personnel					Total Other Personnel	287,494.00
Total Salary, Wages and Fringe Benefits (A+B)							322,797.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>Total Participant Trainee Support Costs</u>
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	21,115.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	3,090.00
Total Other Direct Costs	24,205.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	347,002.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	347,002.00	78,769.00
		Total Indirect Costs	78,769.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	425,771.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	25,571.00	11,170.00	36,741.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

36,741.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			12,432.00	7,101.00	19,533.00
1	Business Office Manager		Excluded by		29,085.00	16,612.00	45,697.00
4	Business Office Staff		Excluded by		55,959.00	31,963.00	87,922.00
	Excluded by Requester						
3	Storehouse Staff		Excluded by Requester		34,721.00	22,653.00	57,374.00
	Excluded by Requester						
3	Human Resources Staff		Excluded by		56,640.00	32,351.00	88,991.00
	Excluded by Requester						
12	Total Number Other Personnel				Total Other Personnel		299,517.00
						Total Salary, Wages and Fringe Benefits (A+B)	336,258.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	21,749.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	3,183.00
Total Other Direct Costs	24,932.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	361,190.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	361,190.00	81,991.00
Total Indirect Costs			81,991.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	443,181.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester					Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	26,338.00	11,848.00	38,186.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	38,186.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			12,805.00	7,531.00	20,336.00
1	Business Office Manager	Excluded by Requester			29,957.00	17,620.00	47,577.00
4	Business/Finance Staff	Excluded by Requester			57,638.00	33,903.00	91,541.00
3	Storehouse Staff	Excluded by Requester			35,788.00	24,043.00	59,831.00
3	Human Resources Staff	Excluded by Requester			58,339.00	34,313.00	92,652.00
12	Total Number Other Personnel					Total Other Personnel	311,937.00
Total Salary, Wages and Fringe Benefits (A+B)							350,123.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	22,401.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	3,278.00
Total Other Direct Costs	25,679.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	375,802.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	375,802.00	85,307.00
Total Indirect Costs			85,307.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	461,109.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	<div>Excluded by Requester</div>				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	27,128.00	12,578.00	39,706.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						39,706.00

B. Other Personnel

Number of Project Role* Personnel*		Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		13,189.00	7,993.00	21,182.00
1	Business Office Manager:	Excluded by			30,856.00	18,699.00	49,555.00
4	Business Office Staff:	Excluded by			59,367.00	35,977.00	95,344.00
	Excluded by Requester						
3	Storehouse Staff:	Excluded by Requester			36,862.00	25,515.00	62,377.00
	Excluded by						
3	Human Resources Staff:	Excluded by			60,090.00	36,415.00	96,505.00
	Excluded by Requester						
12	Total Number Other Personnel				Total Other Personnel		324,963.00
					Total Salary, Wages and Fringe Benefits (A+B)		364,669.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	23,073.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	3,376.00
Total Other Direct Costs	26,449.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	391,118.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	391,118.00	88,784.00
		Total Indirect Costs	88,784.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	479,902.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: AS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Interim Associate Director for Administration and Operations	% Effort			
	Business Office Manager				
	Business Office Finance Assistant				
	Grants and Contracts Manager				
TBN	Grants and Contracts Analyst	25	75	0	100
Excluded by Requester	Administrative Services Support	% Effort			
	Human Resources Manager				
	Assistant Human Resources Manager				
	Human Resources Representative				
	Storehouse Manager				
	Business Services Representative				
	Storehouse Purchasing Agent				
	Storehouse Assistant				
<i>Security Guards (6)</i>	<i>Security Guards</i>	0	100	0	100

Individuals shown in italics are not supported by the P51 base grant; their salary support is provided by Program Income

TBN=to-be-named

Excluded by Requester **Interim Associate Director for Administration and Operations** EFFORT months - % Effort

Excluded by is a veteran administrator who served as Vice Chancellor for Administration for UC Davis from 2003-2010 and in other leadership positions in the Office of Administration since 1992. His broad portfolio includes human resources, accounting and financial services, design and construction management, business services, facilities, safety services (including environmental health and safety, risk management, and animal care and use), and research administration. Under the direction of the CNPRC Director and in coordination with the base grant PI, Vice Chancellor for Research Harris Lewin, the Associate Director for Administration and Operations is responsible for overall direction of the operational, financial, and business services areas which includes budgeting, finances, purchasing, shipping, receiving, and stores; grants management; human resources; and day-to-day aspects related to the facilities.

Excluded by Requester **Business Office Manager** EFFORT months - % Effort Under the direction of the Associate Director and in coordination with the Vice Chancellor's Office and Accounting and Financial Services, Excluded by is responsible for the day-to-day financial operation of the P51 base grant and other sources of funding, supervising billing, grants management, and accounting activities to assure compliance with UC Davis policy and procedure and regulatory agencies, and for the development of per diem rates, services rates, and the development of the F&A rates. He has direct responsibility for the Business Office.

Excluded by Requester **Business Office Finance Assistant** EFFORT months - % Effort Under the direction of the Business Office Manager, Excluded by is responsible for both pre-award and post-award activities related to the P51 base grant and related program income accounts, preparation of the annual budgets, review of monthly transactions, and she serves as a resource for base grant financial activity analysis and transaction processing.

Excluded by Requester **Grants and Contracts Manager** EFFORT months - % Effort Under the direction of the Business Office Manager and in coordination with the Office of the Vice Chancellor for Research, Ms. Excluded by is responsible for the pre- and post-award administration at the CNPRC. She serves as the resource on grant related policies and procedures, assists Core Scientists with grant and contract

submissions, and maintains and oversees the CNPRC grants management database and award-related reporting. She is also responsible for training and mentoring staff in pre- and post-award management.

TBN, Grants and Contracts Analyst (3.0 calendar months – 25%). Under the direction of the Grants and Contracts Manager, this position assists in pre- and post-award administration and provides support to CNPRC investigators.

Excluded by Requester **Administrative Services Support** EFFORT months – % Effort Excluded by Requester facilitates the CNPRC main receptionist area including visitor access and security control. She also provides assistance to the Business Office, and processes travel support documents.

Excluded by Requester **Human Resources Manager** EFFORT months – % Effort In coordination with UC Davis's Human Resources office, supported by the Assistant Human Resources Manager, is responsible for managing all personnel and payroll activities at the CNPRC. Activities include recruitment support, classification, performance evaluation facilitation, corrective action assistance, benefits administration, labor relations coordination, and union contract and Human Resources policy application. Excluded by Requester is also a resource for CNPRC staff and Core Scientists.

Excluded by Requester **Assistant Human Resources Manager** EFFORT months – % Effort Excluded by Requester supports the Human Resources Manager in recruitment, classification, performance evaluation, corrective action assistance, benefits administration, UC Davis Human Resources policy, and payroll.

Excluded by Requester **Human Resources Representative** EFFORT months – % Effort Under the direction of the Human Resources Manager, Excluded by Requester is responsible for the coordination of payroll activities, as well as data entry into the UC Davis Personnel Payroll System, processing and checking forms related to areas such as health check clearance and volunteer approvals, production of access badges, and other Human Resources and Payroll related duties.

Excluded by Requester **Storehouse Manager** EFFORT months – % Effort In coordination with UC Davis Purchasing Contract Services, Excluded by Requester is responsible for all aspects of central supply; garment control for uniforms, laboratory coats, and locker assignments; shipping and receiving operations; along with purchasing/accounts payable; and equipment inventory control. He supervises the processing of all purchase orders and invoice payments and serves as a resource to CNPRC staff and Core Scientists regarding vendors, commodities, and procurement approaches for cost savings.

Excluded by Requester **Business Services Representative** EFFORT months – % Effort Under the direction of Mr. Excluded by Requester is responsible for assisting with coordination of all purchasing and accounts payable activities, for problem solving, developing processing improvements, and assisting with long-range planning efforts.

Excluded by Requester **Storehouse Purchasing Agent** EFFORT months – % Effort Under the direction Mr. Excluded by Requester is responsible for processing purchase orders, initiating payment of vendor invoices, and assisting with receiving and central supply operations.

Excluded by Requester **Storehouse Assistant** EFFORT months – % Effort Under the direction of the House Manager, Excluded by Requester is responsible for shipping and receiving, CNPRC deliveries, and g in central supply operations.

The CNPRC has Security Guards (6) that are responsible for the security of the CNPRC entry point and the overall grounds. The Security Guards are supported by Program Income.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis's federally negotiated rates, which are applied by title code and fiscal year (July through June)

EQUIPMENT

None

TRAVEL

None

CONSULTANTS

None

SUPPLIES

A total of \$20,500 is requested.

\$10,000 is requested for the necessary office and administrative supplies to enable the organization of materials and information in support of the P51 base grant and related grant activities. Cost estimates are based on historical usage.

\$6,500 is requested in grounds maintenance supplies. This includes yard tools, mower maintenance supplies, sprinkler system parts, and other ground maintenance needs.

\$4,000 is requested to purchase new and replacement shop tools. This includes tools such as grinders, drills, air tools, saws, welding wire and other welding consumables, hand tools, and safety equipment that primarily supports the upkeep and care of colony-related equipment.

OTHER EXPENSES

\$3,000 is requested for copy expenses related to reports and other documents.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		183,652.00
Section B, Other Personnel		1,498,813.00
Total Number Other Personnel	60	
Total Salary, Wages and Fringe Benefits (A+B)		1,682,465.00
Section C, Equipment		0.00
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		124,765.00
1. Materials and Supplies	108,838.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	15,927.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,807,230.00
Section H, Indirect Costs		410,242.00
Section I, Total Direct and Indirect Costs (G + H)		2,217,472.00
Section J, Fee		0.00

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OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	1,719,500.00	B&C Rate F&A Return
2	1,814,073.00	B&C Rate F&A Return
3	1,913,847.00	B&C Rate F&A Return
4	2,019,109.00	B&C Rate F&A Return
5	2,130,160.00	B&C Rate F&A Return

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

AOSSpecificAims.pdf

3. Research Strategy*

AOSResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

Resource_Sharing_Plan.pdf

Appendix (if applicable)**14. Appendix**

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES

SPECIFIC AIMS

Administration and Operations Services functions in coordination with the UC Davis campus administration, and has administrative and operational responsibilities for the California National Primate Research Center (CNPRC) in business office services, human resources, purchasing and stores, facilities operations and emergency response, and provides administrative support for the Director's Office.

Specific Aim 1. Ensure effective and efficient operation of the CNPRC infrastructure to optimize the conduct of nonhuman primate research.

Plan. The CNPRC physical infrastructure includes the land, physical buildings, and shared equipment. The effective operation of these physical resources to optimize the scientific mission of the CNPRC is carried out by teams of employees and professional staff providing assistance and support in areas such as Administration, Facilities, Business Office Services, Information Systems, Emergency Operations, Primate Services, and Core Services. The Administration and Operations Services will continue to oversee, manage, and provide the support needed to ensure an optimal and efficient operation of the CNPRC.

Specific Aim 2. Work with Core Scientists, the UC Davis campus, and the NIH to evaluate infrastructure needs and facilitate research.

Plan. Administration and Operations Services plays a central role in identifying and accessing expertise as needed for the effective operation of infrastructure resources. Interactions with Core Scientists, the UC Davis campus administration, and with the NIH Office of the Director are instrumental in enhancing physical resources and identifying funding streams to support the CNPRC.

Specific Aim 3. Share best practices across the NPRC Consortium.

Plan. The challenges of National Primate Research Centers (NPRCs) are unique in terms of funding and compliance. An optimal sharing of information on rates, policies, procedures, compliance, and benchmarks across the NPRCs provides an efficient mechanism to identify and distribute best practices. Efforts will continue in order to exchange experiences with administrative counterparts within the NPRC Consortium in order to define and implement best practices throughout the NPRC system.

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES

RESEARCH STRATEGY

INTRODUCTION

The Administration and Operations component of Administrative Services provides central administrative and operational support for the California National Primate Research Center (CNPRC) (Figure 1).

This component specifically coordinates activities with the central UC Davis campus administration and has administrative and operational responsibility for the CNPRC in the areas of Business Office Services, Human Resources, Purchasing and Stores, Facilities Operations, and support for the Director's Office.

Staff and resources are committed to the mission of the CNPRC and view excellence in research and husbandry as a primary goal (Table 1). The sources of support for Administration and Operations Services in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Figure 1. Organizational Chart: Administration and Operations Services

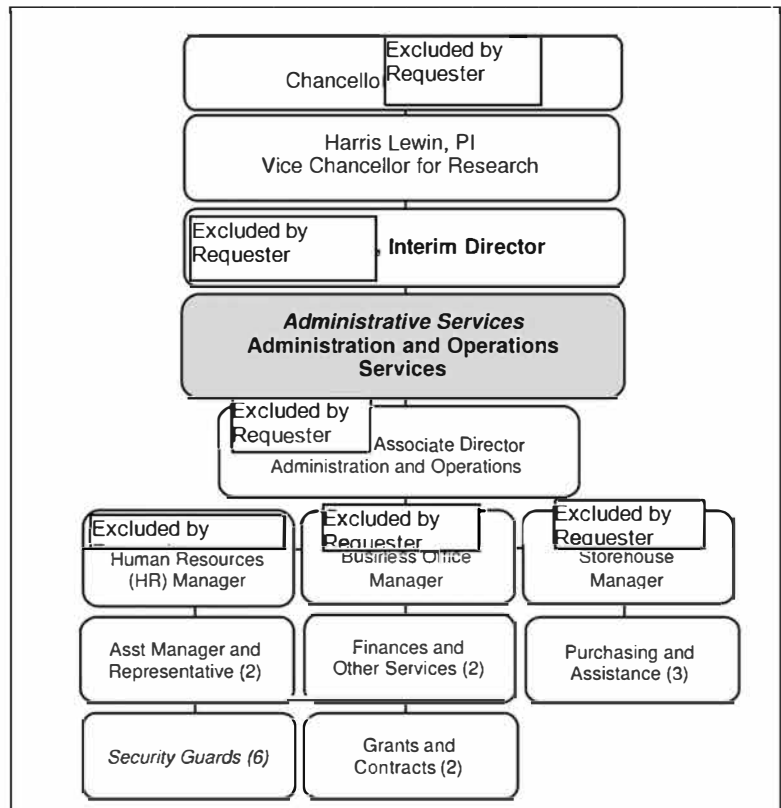


Table 1. Administration and Operations Services Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Excluded by Requester	CNPRC	Interim Associate Director Administration and Operations
	CNPRC	Business Office Manager
	CNPRC	Business Office Finance Assistant
	CNPRC	Grants and Contracts Manager
TBN	CNPRC	Grants and Contracts Analyst
Excluded by Requester	CNPRC	Administrative Services Support
	CNPRC	Human Resources Manager
	CNPRC	Assistant Human Resources Manager
	CNPRC	Human Resources Representative
	CNPRC	Storehouse Manager
	CNPRC	Business Services Representative
	CNPRC	Storehouse Purchasing Agent
	CNPRC	Storehouse Assistant
Security Guards (6)	Police Department	Security Guards

TBN=to-be-named

Table 2. Support for Administration and Operations Services

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$321,651	\$332,118
Program Income from P51	\$1,632,525	\$1,719,500
Other Sources	\$0	\$0
TOTAL	\$1,954,176	\$2,051,618

Response to Summary Statement.

reviewers' comments

reviewers' comments

SIGNIFICANCE

The P51 base grant provides central support to ensure infrastructure resources are available for nonhuman primate research. A significant part of this infrastructure is provided through Administration and Operations Services which, in coordination with the UC Davis main campus, has administrative and operational responsibility for the CNPRC, and provides support for the Director's Office. Partnerships with entities on the UC Davis campus as well as with external entities are shown in Table 3.

The following reflects the day-to-day activities of the Administration and Operations Services.

Business Office Services

- Daily financial administration of the CNPRC and the P51 base grant
- Ensures accounting and cost accounting services and compliance in coordination with Accounting and Financial Services and external rules and regulations
- Facilitates the conduct of audits such as the financial audit, A-133
- Develops, implements, and monitors budgetary and financial performance
- Strategically plans the financing of the CNPRC through mechanisms such as indirect costs (F&A) and recharge rates
- Ensures planning, management, and financing for the infrastructure resources that support nonhuman primate colonies and research
- Provides management of the NPRC Consortium budget for these efforts at the seven NPRCs
- Provides for daily infrastructure operation of the CNPRC ensuring that the various services facilitate the day-to-day business in coordination with university services
- Safeguards the resources of the CNPRC in association with UC Davis Central Services
- Works to bring industry best practices into administrative services, facilities operations, and construction and renovation projects
- Meets regularly with counterparts at the other six NPRC's to share information, practices, and collaborate on finding ways to improve the administrative, operational, and physical infrastructures

Table 3. Reporting Structure and UC Davis Campus Relationships

Position	Supervisor	Campus Entities	External Entities
Associate Director for Administration and Operations	Director	<ul style="list-style-type: none"> • Administrative and Resource Management • Campus Counsel • Design and Construction Management • Office of the Vice Chancellor for Research • Police Department / Security Service 	<ul style="list-style-type: none"> • NIH / Office of the Director • NPRC Consortium
Business Office Manager	Associate Director for Administration and Operations	<ul style="list-style-type: none"> • Accounting and Financial Services • Office of the Vice Chancellor for Research and Sponsored Programs • UC Davis Schools, Colleges, Centers, Organized Research Units 	<ul style="list-style-type: none"> • Public and private customers
Human Resources Manager	Associate Director for Administration and Operations	<ul style="list-style-type: none"> • Disability Management Services • Employee and Labor Relations • Human Resources and Payroll • Office of the Vice Chancellor for Research • Other Academic Units • Occupational Health, Risk Management, Safety Services, Workman's Compensation 	<ul style="list-style-type: none"> • UC Office of the President • Nonprofit and Public Job Placement Agencies • International Students
Storehouse Manager	Associate Director for Administration and Operations	<ul style="list-style-type: none"> • Capital Assets / Equipment Management Safety Services • Contracting Services • Furniture and Surplus Programs • Mail Services • Other Academic Units • Purchasing 	<ul style="list-style-type: none"> • Laundry suppliers • Shipping companies • Vendors

Grants and Contracts

- Ensures grants administration and compliance in association with the Office of the Vice Chancellor for Research

Support for the Director's Office

- Provides support services as requested from the Director's Office
- Participate in the CNPRC short-term and long-range financial planning process
- Assists with outreach to the local community
- Assists as needed with Freedom of Information Act (FOIA) requests in coordination with the General Counsel's Office

Human Resources

- Ensures effective Human Resource Services and compliance in coordination with UC Davis campus Human Resources
- Ensures CNPRC compliance and cooperation with union represented employees in coordination with UC Davis Labor Relations

Storehouse

- Ensures that effective and efficient purchasing services are provided and that opportunities for cost savings are obtained
- Ensures that the Stores operation provides readily available supplies for CNPRC use
- Ensures that shipping and receiving services and laundry services are provided

Facilities Administration

- Oversight of visitor reception area and related daily security issues
- Ensures that construction and renovation projects meet goals and comply with applicable federal interest rules, and meet the space and resource needs of the CNPRC
- Coordinates resources for the security of the physical facilities and during events with the UC Davis Police, Facilities Management, and Design and Construction Management
- Provides essential support for CNPRC emergency response in coordination with UC Davis campus emergency response
- Mechanical shop staff (see **Colony Management and Research Services**, Primate Services section) respond efficiently and promptly to repair any caging needs, and for heating, ventilation, and air conditioning (HVAC) issues to determine if the problem requires additional campus expertise

With the exception of facility services, the CNPRC has functioned in an efficient way essentially as a financially independent entity within UC Davis. The CNPRC has historically received a small operational budget from UC Davis (less than 1%) in addition to the return of indirect costs. The majority of operational support is provided by the P51 base grant and program income. Program income includes recharge activities and the F&A B-rate and C-rate, which are returned to the CNPRC and used according to the program guidelines. A portion of the A-rate is returned to the CNPRC in accordance with UC Davis F&A return policies. All facility services are provided by UC Davis campus Facilities Management, and these costs are funded primarily through the A-rate and other campus sources. The CNPRC is invited to submit requests to the UC Davis budgeting planning process and through this opportunity UC Davis has generously assisted in supporting major building and renovation projects and other activities. A summary of UC Davis project support (\$9,537,888) during the current funding period is provided in Table 4. All improvements are presented in **Facilities Improvement**.

Table 4. Facility Improvements with UC Davis Matching Funds

Improvement	P51 (\$)	Campus (\$)	Other (\$)	Total Cost (\$)
Cage Washer	0	801,086	NIH G20: 498,644 Non-federal: 193,917	1,493,647
HVAC Units for Freezer Building Upgrade	92,549	25,000	0	117,549
Respiratory Diseases Center Building	0	3,999,802	NIH ARRA C06: 14,228,198	18,228,000
Upgrade 6 Perimeter Cameras (to pan-tilt zoom)	0	28,000	0	28,000
Virology and Immunology Building	0	4,684,000	NIH C06: 3,800,000 Non-federal: 200,000	8,684,000
TOTALS	\$92,549	\$9,537,888	\$18,920,759	\$28,551,196

Budgeting. The Associate Director for Administration and Operations is the chief budgeting officer for the CNPRC. Major budget adjustments such as those made in Year 52 of the current award, due to sequestration, reflect decision-making at the Director's level in consultation with the Research Advisory Committee. Table 5 provides a summary of operational budget revisions in 2013-2014 to allow the CNPRC to efficiently operate at lower funding levels due to a reduced award and contracted program income.

Table 5. Operational Budget Changes (2013-2014)

Action	Component	Positions	Total (\$)
Budgeted positions not filled	Colony Management and Research Services	3	214,044
Retirement positions not replaced	Colony Management and Research Services	2.4	165,035
Layoffs	Administration	3	277,631
	Facilities	1	102,148
Contract positions to reduce costs	Colony Management	-	36,000
Supplies and travel cuts	All	-	127,110
TOTALS		9.4	\$921,968

Another in-depth financial analysis will be completed after the 2014 year-end close is completed. This exemplifies needed adjustments undertaken after careful consideration by the Director, guided by the Research Advisory Committee, emphasizing a dynamic process to ensure the maintenance of critically needed support and infrastructure despite variances in the financial environment.

Progress and Major Accomplishments: Contributions to the CNPRC Mission

During the current funding period the following progress has been made:

- Implemented changes to the billing system to streamline the monthly billing process and consistently track the funding mechanisms for all services provided to off-site users. The implementation of the Animal Research Management System (ARMS), in collaboration with the Yerkes and Washington NPRCs, will include a billing module that greatly improves efficiencies related to both input and output.
- A review of UC Davis document routing systems to reduce the use and retention of paper documents has been completed. For purchasing, a pre-purchasing approval document is under evaluation which will eliminate paper records. The CNPRC has eliminated the retention of documents such as packing slips and vendor invoices. For timesheets, UC Davis has implemented an online time reporting system which eliminates paper timesheets, and facilitates direct reporting, calculating, and issuance of payroll checks.
- All staff are strongly encouraged to attend monthly Research Administration Forums presented by UC Davis as well as other UC Davis Staff Development sponsored classes.

Additional accomplishments for service areas include the following:

Business Office Services

- Successful cooperative conduct of financial and A-133 audits with no findings during this period
- Oversight in cooperation with Purchasing and Stores of the pre-purchasing system implementation
- ARMS system evaluation of Business aspects working toward a successful implementation
- Successful Kuali implementation (new campus-wide financial system implemented in phases)
- Revision of financial reporting allowing for more relevant information and eliminating unnecessary data
- Improvement of the Grants Management Database for tracking pending, current, and expired grants

Human Resources

- Transition of the CNPRC to the new Time Recording System
- Transition of the CNPRC to the new online Employee Performance Appraisal Report system
- Creation and implementation of a new facilities access request and approval process
- Implementation of background checks for volunteers
- Implementation of changes in the annual health clinic to increase efficiencies
- Participation and input into CNPRC restructuring
- Preparation planning for threatened strikes to ensure CNPRC services remain uninterrupted

Purchasing and Stores

- Accurately processed and managed the purchase of supplies and equipment with a value totaling over \$25 million while ensuring procurement met state and federal guidelines, regulations, and policies
- Implemented a web based order request approval system for processing procurement activities
- Initiated a FedEx shipping station which allows for printing of waybills and paperless billing
- Negotiated a contract with Life Technologies with discounts totaling 20-30% off list
- Maintained a physical inventory of equipment assets with a bi-annual audit valued over \$16.5 million
- Hosted on-site Pipette clinic to assist laboratories in calibration of pipettes and record retention
- Initiated a project to identify hospital supply vendors for generic medical supplies

Facilities

See **Facilities Improvement** section for information on major capital improvements

- Cage wash proposal funded and planning initiated (proposed start date 09/21/14)
- Clean cage storage funded through a C06 application (proposed start date 08/15/14)
- Corn Crib replacement prototype completed and operational
- Two modular units for animal housing installed and operational

- Respiratory Disease Center completed
- Construction completed for the Virology and Immunology building, now occupied
- Completed modifications for 3 field corrals
- Animal Wing Renovation – Worked with Design and Construction Management and contractor to resolve warranty claim in animal rooms and hallway
- Enrichment preparation renovation completed
- Quarantine Controls renovation in progress
- Bird netting for new shop and administration building
- Propane conversion to natural gas for modular buildings and new shop facility
- Wireless network in progress
- Butler Building renovations
- Freezer Building HVAC renovation
- Installed auto close system in security Kiosk for “lockdown”
- Perimeter fence alarm upgraded
- Facility Security
- Monthly spill prevention, control, and counter measures plan for all generators in operation
- Recharge for the maintenance shop mechanics research support services (Table 6)

Table 6. Maintenance Shop Services (May 1, 2010 to April 30, 2014)

Table of Maintenance Shop Services (May 1, 2010 to April 30, 2014)					
Grant Year	Service Type	# Users	Investigators (N)	Service Cost (\$)	Total Cost (\$)
2010 - 2011	Research Support	15	Core Scientists (6)	5,975	79,676
			UC Davis (2)	50,210	
			External (7)	23,491	
2011 - 2012	Research Support	15	Core Scientists (4)	3,287	31,926
			UC Davis (5)	18,083	
			External (6)	10,556	
2012 - 2013	Research Support	13	Core Scientists (4)	2,758	48,677
			UC Davis (4)	38,968	
			External (5)	6,950	
2013 - 2014	Research Support	10	Core Scientists (3)	949	32,350
			UC Davis (5)	29,687	
			External (2)	1,714	
TOTAL					192,629

INNOVATION

During the current funding period, the NIH guidelines for NPRCs were updated and the NPRC Consortium further developed. The ability to share best practices across the NPRCs allowed the Associate and Assistant Directors responsible for infrastructure resources to work together and craft a statement on program income and the A-B-C F&A rate methodology to ensure consistency across the NPRCs.

The Southwest NPRC enlisted the aid of a cost accountant in 2013. The Assistant Director at the Southwest NPRC and the cost accountant visited the CNPRC for a day to review cost accounting and rate setting practices at the CNPRC with the Business Office Manager, [Excluded by Requester]. This meeting provided an effective format for sharing practices and discussing NPRC cost accounting for operational success. Other practices under consideration include a review of monthly PI reports to determine if a new report format to complement the online PI ledger should be developed, to improve operating efficiencies. The CNPRC Business Office continues to evaluate operational procedures to ensure optimal services to faculty and staff.

As noted above, the Business Office has been deeply involved in maintaining an optimal and efficient operation at the CNPRC while adjusting to sudden changes in the fiscal environment. Through the close relationship with the Director's Office and the respective Cores and Research Units through the Research Advisory Committee, the Business Office was able to expeditiously adjust the operational needs to the award reduction through the sequestration implemented by Congress. The Business Office anticipates a similar efficient operation and a close involvement with the incoming CNPRC Director during the proposed funding period. In addition, the close and mutually beneficial collaborative partnership between the CNPRC and the UC Davis campus administration continues to serve both partners well.

APPROACH

Plans for the Next Funding Period

Extensive progress has been made during the current funding period as noted above and plans are underway for further enhancements during the proposed funding period.

Specific Aim 1. Ensure effective and efficient operation of the CNPRC infrastructure to optimize the conduct of nonhuman primate research.

During the proposed funding period, Administration and Operations staff will focus on excellence in their respective support areas and on increasing the ability of the CNPRC Core and Affiliate Scientists to compete for contracts and awards. This effort will involve strategic improvements in the following areas:

- Better tools to document the costs associated with services at the CNPRC. Web pages are being updated and reworked for consistency of presentation and clarity of information.
- Enhancements to the CNPRC website to support the mission of the CNPRC.
- Continue staff improvement efforts, particularly in grants management and human resources. All new grants management staff will attend the Research Administration courses offered by UC Davis Staff Development.
- Continue to improve the Grants Management and Billing Activities databases to enhance the reporting capabilities of activities.
- Continue to evaluate operating procedures to assure appropriate controls and compliance with the goal of improving operational efficiencies.
- Work closely with the Director and the Research Advisory Committee to continuously improve operational efficiencies and reduce barriers.
- Continue ongoing interactions with the Office of the PI, the Vice Chancellor for Research, to evolve and refine financial underpinnings for the CNPRC.

Specific Aim 2. Work with Core Scientists, the UC Davis campus, and the NIH to evaluate infrastructure needs and facilitate research.

Administration and Operations staff play a central role identifying external expertise for the effective operation of infrastructure resources. The relationships with Core and Affiliate Scientists, the Central Campus administration, and with the Office of the Director at NIH are key in this operation.

Examples of Core Scientists interacting with administration to improve facilities is represented by the new

Excluded by Requester	imaging facility initiated by [REDACTED] through the funding of an S10 High-End Instrumentation and the successful funding of the C06 Facilities Grant for the Respiratory Disease Center building
Excluded by Requester	[REDACTED] Both of these facilities greatly enhance research opportunities for Core and Affiliate Scientists, and investigators nationwide.

Another example is the relation between the Associate Director for Administration and Operations and the UC Davis Administrative Services staff and the Director of Finance in the Vice Chancellor's Office to ensure that CNPRC financial needs are addressed through appropriate means. The CNPRC interacts with this office to establish appropriate rates for recharge services, provide annual financial reporting with regular updates that occur quarterly, plan needed budgetary requests, and provide an annual qualitative report on the CNPRC operations. Through this well-established and mutually beneficial relationship, the CNPRC is provided a regular external evaluation and assistance in identifying and addressing financial opportunities and challenges.

Specific Aim 3. Share best practices across the NPRC Consortium.

Administrative and Operational staff works closely with the Director to ensure the financial success of the CNPRC. The direct award and budgeting practices support the entire organization and regulate program income and its allocation. The external relationships that are fostered through this component provide for stability, external evaluation, and create conditions optimizing the continued financial success of the CNPRC, creating a stable foundation for the CNPRC scientific enterprise and for the innovative work performed by CNPRC Core Scientists. Some examples of potential positive outcomes of shared practices across the NPRC Consortium include:

- Adoption of common methods and best practices established by the NPRC Consortium Working Groups to increase capabilities across the NPRCs.

- Consortium Working Group initiatives resulting in cost savings through collaborative development of common shared methods and materials. For example, the collaborative development of common NPRC Outreach materials has the potential to serve multiple NPRCs.
- Assist in expanding capabilities for NPRC Core and Affiliate Scientists to create dynamic social networking tools.

ADMINISTRATIVE SERVICES: ADMINISTRATION AND OPERATIONS SERVICES

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

ADMINISTRATIVE SERVICES: ADMINISTRATIVE AND OPERATION SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Information Technology Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename ITAbstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	FI_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	ITFacilitiesandOtherResources.pdf
11. Equipment	ITEquipment.pdf

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES

ABSTRACT

The primary mission of **Information Technology (IT) Services** is to support all programs within the California National Primate Research Center (CNPRC), including research projects carried out by Core and Affiliate Scientists, colony management, and business services to ensure the most efficient and cost effective approach to operations. IT Services manages all software and hardware of the information system, maintains local network and databases, provides technical support for personal computers and printers, develops database and web applications, and provides complex database queries in support of business operations, animal care, and regulatory review. In addition, IT staff maintains the security camera system and environment monitoring system ensuring the safety and integrity of the CNPRC. Further, the IT group supports research by providing complex database queries, and assisting investigators with data analysis and data sharing. IT Services actively participate in National Primate Research Center (NPRC) Consortium activities, and collaborate with colleagues at other NPRCs to share data and best practices. The goals of IT Services include the provisions of efficient information and computing tools for data collection, management, access, reporting, analysis and publication, to facilitate communication and streamline processes, and to assist investigators to meet the CNPRC mission. To achieve these goals, IT Services will build on strengths in implementing an investigator portal, a laboratory information management system, enhance the animal records system, and automate business processes through the following Specific Aims: (1) Provide effective data management, streamlined data access, and bioinformatics assistance in support of the CNPRC research mission, (2) Ensure investigators have access to efficient IT systems and tools, (3) Aid in the training of the next generation of investigators with nonhuman primate expertise, and (4) Support nonhuman primate colony management and animal care.

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: Each of the Information Technology staff members has a desktop computer with standard office software and specialized programming software.

Office: The Information Technology Services staff are located in a 943 sq. ft. space that is subdivided with sound attenuating panels into individual workspaces. Part of this space also serves as a work area for staff that provides desktop support (e.g., repairs, configuring new computers). Excluded
by
Requester has an office within this space.

Other: The computer room is air-conditioned by two APC-100 in-row cooling units; chilled water is supplied by a Legacy 96D chiller that is located on a concrete pad outside the server room. A 15kVA battery backup UPS supplies conditioned power for the computer room servers.

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES

EQUIPMENT

All servers are located in the CNPRC computer room.

Database Systems:

Proprietary Info

Proprietary Info

Windows Domain Systems:

Proprietary Info

Proprietary Info

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assistant Director for IT Services	Institutional Base Salary	EFFORT	0.0	0.0	71,319.00	28,444.00	99,763.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						99,763.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	IT Services Manager	Excluded by Requester		EFFORT	57,836.00	30,595.00	88,431.00
1	IT Project Manager	Excluded by Requester			49,416.00	26,141.00	75,557.00
1	IT Systems Administrator	Excluded by Requester			40,049.00	21,186.00	61,235.00
2	IT Programmers	Excluded by Requester			70,103.00	37,085.00	107,188.00
2	IT Support Specialists	Excluded by Requester			44,325.00	23,448.00	67,773.00
7	Total Number Other Personnel					Total Other Personnel	400,184.00
					Total Salary, Wages and Fringe Benefits (A+B)		499,947.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,000.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	46,310.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	250.00
9. IT Expenses	1,920.00
Total Other Direct Costs	48,480.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	557,427.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	557,427.00	126,536.00
Total Indirect Costs			126,536.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	683,963.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ITBudgetJustifications.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assistant Director for IT Services	Institutional Base Salary	EFFORT	0.0	0.0	71,319.00	30,097.00	101,416.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						101,416.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	IT Services Manager	Excluded by Requester	EFFORT		59,571.00	32,953.00	92,524.00
1	IT Project Manager	Excluded by Requester			50,898.00	28,155.00	79,053.00
1	IT Systems Administrator	Excluded by Requester			41,250.00	22,818.00	64,068.00
2	IT Programmers	Excluded by Requester			72,205.00	39,942.00	112,147.00
2	IT Support Specialists	Excluded by Requester			45,655.00	25,255.00	70,910.00
7	Total Number Other Personnel					Total Other Personnel	418,702.00
					Total Salary, Wages and Fringe Benefits (A+B)		520,118.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,270.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	9,270.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	47,699.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	258.00
9. IT Expenses	1,978.00
Total Other Direct Costs	49,935.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	579,323.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	579,323.00	131,506.00
Total Indirect Costs			131,506.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	710,829.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ITBudgetJustifications.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assistant Director for IT Services	Institutional Base Salary	EFFORT	0.0	0.0	75,662.00	33,052.00	108,714.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					108,714.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	IT Services Manager	Excluded by Requester	EFFORT		61,358.00	35,046.00	96,404.00
1	IT Project Manager	Excluded by Requester			52,425.00	29,943.00	82,368.00
1	IT Systems Administrator	Excluded by Requester			42,487.00	24,267.00	66,754.00
2	IT Programmers	Excluded by Requester			74,371.00	42,478.00	116,849.00
2	IT Support Specialists	Excluded by Requester			47,024.00	26,858.00	73,882.00
7	Total Number Other Personnel					Total Other Personnel	436,257.00
Total Salary, Wages and Fringe Benefits (A+B)							544,971.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,548.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,548.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	49,130.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	266.00
9. IT Expenses	2,037.00
Total Other Direct Costs	51,433.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	605,952.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	605,952.00	137,551.00
Total Indirect Costs			137,551.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	743,503.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ITBudgetJustifications.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Assistant Director for IT Services	Institutional Base Salary	EFFORT	0.0	0.0	77,932.00	35,056.00	112,988.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:		File Name:					Total Senior/Key Person					112,988.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	IT Services Manager	Excluded by Requester	EFFORT		63,198.00	37,171.00	100,369.00
1	IT Project Manager	Excluded by Requester			53,998.00	31,760.00	85,758.00
1	IT Systems Administrator	Excluded by Requester			43,762.00	25,739.00	69,501.00
2	IT Programmers	Excluded by Requester			76,602.00	45,055.00	121,657.00
2	IT Support Specialists	Excluded by Requester			48,436.00	28,488.00	76,924.00
7	Total Number Other Personnel					Total Other Personnel	454,209.00
Total Salary, Wages and Fringe Benefits (A+B)							567,197.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,834.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,834.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	50,604.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	274.00
9. IT Expenses	2,098.00
Total Other Direct Costs	52,976.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	630,007.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	630,007.00	143,011.00
Total Indirect Costs			143,011.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	773,018.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ITBudgetJustifications.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assistant Director for IT Services	Institutional Base Salary	EFFORT	0.0	0.0	80,270.00	37,219.00	117,489.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	117,489.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	IT Services Manager	Excluded by Requester	EFFORT		65,094.00	39,447.00	104,541.00
1	IT Project Manager	Excluded by Requester			55,618.00	33,705.00	89,323.00
1	IT Systems Administrator	Excluded by Requester			45,075.00	27,315.00	72,390.00
2	IT Programmers	Excluded by Requester			78,901.00	47,814.00	126,715.00
2	IT Support Specialists	Excluded by Requester			49,889.00	30,232.00	80,121.00
7	Total Number Other Personnel					Total Other Personnel	473,090.00
Total Salary, Wages and Fringe Benefits (A+B)							590,579.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,129.00
2. Foreign Travel Costs	0.00
Total Travel Cost	10,129.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	52,122.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	283.00
9. IT Expenses	2,161.00
Total Other Direct Costs	54,566.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	655,274.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	655,274.00	148,747.00
Total Indirect Costs			148,747.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	804,021.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ITBudgetJustifications.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Assistant Director IT Services	% Effort; Excluded by Requester			
	IT Services Manager				
	IT Systems Administrator				
	IT Project Manager				
	Programmer				
	Programmer				
	IT Support Specialist				
	IT Support Specialist				

Excluded by Requester **PhD, Assistant Director for Information Technology (IT)** EFFORT months – % Effort Excluded by Requester

is the daily operation of the IT Services. He is responsible for centralized IT and informatics management oversight, long range IT planning, research and scientific computing support, business process development and optimization, and IT external relations. Excluded by Requester has a PhD in Animal Genetics and an MS in Computer Science. He has over 14 years working experience and 10 years of experience in leadership roles in IT and Biomedical Informatics. His research background includes bioinformatics, association study of Single-Nucleotide Polymorphisms (SNP) and quantitative phenotypes, genome analysis and annotation, SNP and transcript variance analysis, and drug target identification. Previously, as a bioinformatics scientist and manager of a cancer informatics facility at the Moffitt Cancer Center, he supported many research projects in population science, biological science, and drug discovery, as well as translational research.

Excluded by Requester **IT Services Manager** EFFORT months – % Effort Excluded by Requester is responsible for managing the infrastructure of the information system, and has primary responsibility for database design and administration. He supervises desktop support operations and server administration staff and oversees computer hardware, software, and network resources. He monitors information system performance, manages the security monitoring system, ensures data backup and plans for system upgrades, and disaster recovery.

Excluded by Requester is responsible for management and extension of the extensive colony database, with over 350 data tables including 25 million rows of data associated with 150+ data entry screens, and more than 100 reports used in recording and reporting on all aspects of the nonhuman primate colonies. He interacts with UC Davis departments to improve network and information capabilities linking the CNPRC and the UC Davis campus.

Excluded by Requester has a BS in Computer Science and has undergone intensive training Specific Private Vendor database administration and database programming. He has worked in data services at the CNPRC for 36 years. Specific Private Vendor designed the database, developed database procedures, and developed reports, forms, and applications. His continuing education is in the area of Java programming database administration.

Excluded by Requester **IT Systems Administrator** EFFORT months – % Effort Excluded by Requester is responsible for server and network administration and security. He has the overall responsibility for computer server configuration and maintenance, new account setup, and user access controls for more than 350 users. Excluded by Requester administrator for the CNPRC anti-virus capabilities, system backup, electronic mail, and web server. researches and recommends new hardware and software options to all members of the CNPRC staff, maintains the network database, and requests network changes or new installations. He provides both one-on-one and classroom training to familiarize investigators and staff with new software or hardware. Excluded by Requester has been working in system administration, network administration, and security for 13 years. He has attended continuing education classes on advanced Active Directory configuration and security management.

Excluded by Requester **IT Project Manager** EFFORT months – % Effort Excluded by Requester is an IT Project Manager for the Animal Resource Management Services (ARMS) Project. He is responsible for coordination with other NPRCs

and the [Specific Private Vendor] on the further development of the ARMS animal record system. His responsibilities include gathering user requirements, organizing online conferences with end users from all NPRCs, communicating with consulting companies and ensuring user requirements are implemented in future development. In addition, he is also responsible for developing web applications as needed that cannot be implemented in the ARMS program. He serves as a technical lead on Java programming and database design and provides mentoring to junior web application developers. [Excluded by Requester] has an MS in Computer Science and over 15 years of computer programming experience in the areas of database design and administration, database-driven web application, system analysis, and system architecture.

[Excluded by Requester] Programmer [EFFORT] months – [Excluded by Requester] joined the CNPRC in June 2013 and is focusing on web application development using the web portal platform. After identifying an optimal portal framework he has taken the lead in developing web portal applications for the animal information system, business operations, and research data management, providing easy access to data and automation of business processes. In addition, he provides group and one-on-one training to users on the web portal applications. [Excluded by Requester] has been a programmer for 9 years and has a BS in Computer Science.

[Excluded by Requester] Programmer [EFFORT] months – [Excluded by Requester] provides programming and operational support for the CNPRC information systems. He develops and maintains the CNPRC web interfaces to the databases and web based data entry/reporting database applications for the animal records data. He develops and maintains the public website for the CNPRC and for research groups that request external interactions. He provides database queries for researchers and serves as the technical backup for maintenance of the portable barcode data entry systems and applications that are used daily for animal health reporting. His future focus will be on implementing a Laboratory Information Management System (LIMS) for the Service Cores and research groups. [Excluded by Requester] has a BS in Computer Science and has attended continuing education classes on PHP, C#, and Java programming. He has 13 years of programming experience using PL/SQL, and Reports, as well as [Specific Private Vendor]

[Excluded by Requester] IT Support Specialist [EFFORT] months – [Excluded by Requester] provides technical support for Macintosh, PC desktops, printers, projectors, and network connections for the CNPRC user community. He configures and installs new hardware and software, troubleshoots user problems, provides upgrades, and monitors teleconference equipment. He assists with server maintenance, new account setup, and user access controls; he also provides one-on-one and classroom training for new software and hardware. In addition, Mr. [Excluded by Requester] provides web programming for the internal administrative website, and is responsible for maintenance of the computer equipment inventory. He has been working in desktop support for 10 years.

[Excluded by Requester] IT Support Specialist [EFFORT] months – [Excluded by Requester] provides technical support for Macintosh, PC desktops, printers, projectors, and network connections for the CNPRC user community. These abilities are shared with [Excluded by Requester] (see above). She configures and installs new hardware and software, and troubleshoots user problems. She also assists with life cycle and asset management. In addition, she provides one-on-one and classroom training for new software and hardware. She assists in programming and maintenance of desktop applications and Access database applications, [Specific Private Vendor] and Reports. Ms. [Excluded by Requester] has been working in desktop support for 7 years.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Equipment requests are included in the **Facilities Improvement** section.

TRAVEL

\$9,000 is requested for domestic travel (6 x \$1,500). These travel and training expenses are to ensure programming and support staff remains current with programming techniques and strategies. As the CNPRC databases grow in size and complexity, new technologies are employed for database maintenance and data retrieval. It is necessary to be conversant with efficient methods for handling large amounts of data, and presenting it to staff and investigators in the most useful manner.

A total of \$46,310 is requested.

\$18,470 is requested for yearly software maintenance costs for Specific Private Vendor maintenance and licensing (e.g., Corporate Time-Named User, Internet Application Server Enterprise Edition, Specific Private Vendor Edition, Tuning Pack, Diagnostic Pack), Toad Data Modeler, SAS desktop Analytical Suite, SQL*XL ADO-SQL to Excel database connector/formatter, Symantec Backup management package, VMWare license, Data Center Standby Services, Ipswitch IMail Secure Server software update support and license, FileMaker software maintenance and licensing, SAP Business Object, Microsoft Consolidated Campus Agreement (MCCA) licensing, and Adobe Acrobat licensing agreement.

\$5,680 is requested for computer supplies annually. Examples include the following: Computer supplies, keyboards, mice, adapters, power supplies, fans, external hard disk or removable media drives, monitors, equipment stands, scanners, and enclosures; maintenance supplies (workbench tools and test equipment, cleaner, printer maintenance kits), memory upgrades, and networking supplies and upgrades.

\$16,160 is requested for purchase of replacement desktop computers at \$1,100 each, and five printers at \$600 each for Administration and Primate Services users. Over 200 PCs and 30 printers are used by CNPRC staff. The replacement schedule is based upon a 6-year lifespan.

\$6,000 is requested for new software tools, other equipment, and necessary administrative supplies such as software purchases (utilities, domain management components, database tools, operating systems, office productivity suites) for evaluation or installation on new servers or IT desktop systems, and programming books and manuals.

OTHER EXPENSES

\$1,920 is requested for study materials and self-study courses necessary for staff to keep current on technologies; examples of self-study courses include Specific Private Vendor SAP Business Objects Administration and Data Services Subscription Course Library, SAP Business Objects Business Intelligence Subscription course library, Specific Private Vendor online training; examples of books

Specific Private Vendor

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		540,370.00
Section B, Other Personnel		2,182,442.00
Total Number Other Personnel	35	
Total Salary, Wages and Fringe Benefits (A+B)		2,722,812.00
Section C, Equipment		0.00
Section D, Travel		47,781.00
1. Domestic	47,781.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		257,390.00
1. Materials and Supplies	245,865.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	1,331.00	
9. Other 2	10,194.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		3,027,983.00
Section H, Indirect Costs		687,351.00
Section I, Total Direct and Indirect Costs (G + H)		3,715,334.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

Excluded by
Requester**2. Human Subjects**

Clinical Trial?

☒ No ☐ Yes

Agency-Defined Phase III Clinical Trial?*

☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***

Is program income anticipated during the periods for which the grant support is requested?

☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	631,500.00	B&C Rate F&A Return
2	666,233.00	B&C Rate F&A Return
3	702,876.00	B&C Rate F&A Return
4	741,534.00	B&C Rate F&A Return
5	782,318.00	B&C Rate F&A Return

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

ITSpecificAims.pdf

3. Research Strategy*

ITResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

Resource_Sharing_Plan.pdf

Appendix (if applicable)**14. Appendix**

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES

SPECIFIC AIMS

The primary mission of Information Technology (IT) Services is to support all programs within the California National Primate Research Center (CNPRC), including research, colony management, and business services to ensure efficient and cost effective operations.

Specific Aim 1. Provide effective data management, streamlined data access, and bioinformatics assistance in support of the CNPRC research mission.

Plan. The goal is to build a data center to manage research data, develop an investigator portal to provide Core Scientists and research staff easy access to all related data through a single entry site, and assist Core and Affiliate Scientists with data analysis through strategic linking with UC Davis campus programs and resources.

Specific Aim 2: Ensure investigators have access to efficient IT systems and tools.

Plan. Implement a Laboratory Information Management System (LIMS) to track samples and capture research data from the Service Cores, enhance the CNPRC internal website to provide dynamic data and online services, assist the CNPRC Public Information Officer with the external website for easy access of CNPRC information, and automate business practices such as work order processing and billing in order to increase efficiencies, facilitate communications, and reduce paper use.

Specific Aim 3: Aid in the training of the next generation of investigators with nonhuman primate expertise.

Plan. Assist Core and Affiliate Scientists in the training of new investigators in the use of modern IT and informatics tools, and to perform basic bioinformatics analyses.

Specific Aim 4: Support nonhuman primate colony management and animal care.

Plan. Improve the animal records system to include electronic health records, colony information, genetic characterization, breeding records, and pathology findings; integrate with other animal related data, such as behavior and clinical pathology results; develop portal applications to allow Core Scientists, Veterinarians, and Colony Management and Research Services staff easy access to data related to individual animals through a single web entrance; develop mobile applications and assist users to select mobile devices to ensure that data can be entered at the point-of-service, and that real-time data can be accessed at the cageside; and automate processes to facilitate communications among animal care groups and with Core and Affiliate Scientists.

By achieving the above Specific Aims, the IT Services staff will be able to ensure strong support of the ongoing state-of-the-art research at the CNPRC, of high quality animal care, and streamlined business operations by providing point-of-service data entry, cageside data access, real-time information exchange and communications, automated processes, integrated presentation of related data, and computing support for research projects. These efforts will ultimately improve CNPRC operations in virtually all areas, and serve as a foundation to increase efficiency and economy of scale.

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES

RESEARCH STRATEGY

INTRODUCTION

Information Technology (IT) Services at the California National Primate Research Center (CNPRC) includes seven staff members and the Assistant Director for IT, (Figure 1, Table 1).

IT Services provides user support for all aspects of IT including management of computer hardware and software, servers, network communication, database, and security monitoring systems. IT Services support daily CNPRC activities including the use of all computers and printers, enabling high-speed communications, improving efficiency, reducing paper use, managing data, facilitating collaborations, automating business processes, assisting with resource planning, promoting data sharing, and improving quality of animal care and regulatory compliance.

The sources of support for IT Services in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Figure 1. Organizational Chart: Information Technology (IT) Services

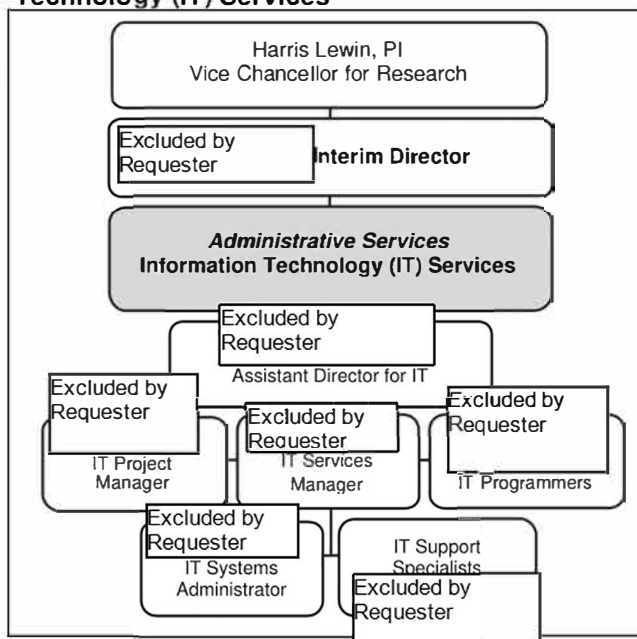


Table 1. Information Technology (IT) Services Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Excluded by Requester	CNPRC	Assistant Director IT Services
	CNPRC	IT Services Manager
	CNPRC	IT Systems Administrator
	CNPRC	IT Project Manager
	CNPRC	Programmer
	CNPRC	Programmer
	CNPRC	IT Support Specialist
	CNPRC	IT Support Specialist

Table 2. Support for Information Technology Services

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$540,802	\$557,427
Program Income from P51	\$599,925	\$631,500
Other Sources	\$0	\$0
TOTAL	\$1,140,727	\$1,118,927

IT Services support 390 computers and 68 printers, and address approximately 1,500 support requests annually; manages servers and networks; monitors security and environmental monitoring systems; manages electronic mail, files, databases, websites, and related applications; manages software licenses and upgrades; develops and maintains databases, Specific Private Vendor web data entry and database query applications; performs complex database queries and generates well-formatted reports for research and regulatory analysis; assists and participates in short-term and long-term strategic planning for the CNPRC; and collaborates with other National Primate Research Centers (NPRCs) to identify solutions and share ideas and best practices.

Response to Summary Statement.

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

Recognizing the universal importance of a well functioning IT system, the IT team has been reinforced with [redacted] new members [redacted] joined the CNPRC as the Assistant Director of IT November 1, 2010, [redacted] extensive experience in IT and biomedical informatics to identify solutions and participate in the strategic planning for the CNPRC's future growth. In addition to the IT Support Specialist, a Web Application Developer (Programmer) was recruited to develop web portal applications. An experienced Project Manager was also hired to replace a database programmer. The Project Manager leads IT projects to develop web applications and coordinates with other NPRCs on the implementation and development of the Animal Research Management System (ARMS). A working relationship with the UC Davis [redacted] Specific Private Vendor [redacted] has been established to provide advanced troubleshooting services as needed. The team is currently well positioned for strategic innovation and to address future needs.

Figure 2. Screen view of the first page of the WebVitals database query web application.

The screenshot displays the 'CNPRC Web Vitals' web application. At the top, there is a search bar and a 'Submit' button. Below the search bar, a navigation menu includes links for Home, Animal Selection, and MH Files. The main content area is titled 'Animal Summary' and shows details for a specific animal, including its location, weight, body condition, TB test, serum bank, harvest date, and various flags. The summary is dated May 22, 2014, 09:20 AM. The interface also includes a sidebar with links to various database sections like Assignment, BB Assessment, Conception, Enrichment, Diarrhea, Fostering, Immunization, Morning Health, Pairing, Pedigree, Project, Relocation, Reproductive, Serum Bank, SNOMED, Virology, and Weight TS. The bottom of the page shows the CNPRC logo and contact information.

IT Services continue to improve information systems and tools to facilitate data access. The web application WebVitals (Figure 2) has been improved and migrated to [redacted] Specific Private Vendor [redacted]

[redacted] Specific Private Vendor [redacted] WebVitals is widely used by the Core Scientists, research staff, Veterinarians, and Colony Management and Research Services staff. After an animal identification number is submitted, the Animal Summary page presents demographics, project assignment, and other important information about an individual animal. The Assignment page shows the full history of research projects to which a particular animal has been assigned. The BioBehavioral Assessment is also included. Similarly, the other links on top of the page presents data related to the animal's conception history, enrichment information, diarrhea incidence, fostering, immunization, morning health observations, pairing, pedigree, project assignments, relocation history, reproductive records, serum bank samples, SNOMED, virology, weights, and tuberculin test

dates and outcomes. A web query application has also been developed for the Business Office to examine accounts and billing information. More complex queries or data mining are performed by IT staff upon request.

Generating reports from the database is another method for data access. Well-defined reports have been developed for various purposes using [Specific Private Vendor] To provide users with a powerful reporting function, a business intelligence software package from SAP entitled Business Object Edge has been licensed [Specific Private Vendor] tallied to provide reporting functions from the [Specific Private Vendor] User training has been conducted for the [Specific Private Vendor] the Business Object software tools. Reporting structure will be developed for the users to customize the final reports as needed.

[Specific Private Vendor] am enhanced [Specific Private Vendor] applications to allow efficient data entry. In addition to colony data, entry of [Specific Private Vendor] ent information has been added to the applications. Treatment plans can be entered easily using data entry forms with the function of automatically calculating drug dosage based on the formulation and animal weight in the database. This function was shared with the **NPRC Consortium** and resulted in requests for a similar capability from veterinarians at the Washington and Yerkes NPRCs. The drug formulation database and the programming source code have been shared with IT colleagues at these NPRCs for implementation. Morning Health is another application developed in-house to capture animal health observations using a barcode scanner. A list of predefined health conditions are coded with bar codes and printed on hard cardboard. Barcode scanners are used by animal technicians to scan barcodes when they perform morning health checks. These observational records are uploaded to the central database and reports are generated automatically to notify animal care services and investigators on the morning health outcomes. This is an example of another efficient way of capturing data that has been shared with other NPRCs.

The IT team has also enhanced applications for pathology analysis. The pathology database has been improved to capture pathology findings and generate pathology reports from **Anatomic and Clinical Pathology Services**. A new web application has been developed to manage necropsy scheduling and biospecimen distribution. It models the workflow of the process and automates communications with requesters for tissues. An investigator can request specific types of tissues by filling out online forms. The request is recorded in a first-come-first-serve queue in the database. The application records the necropsy schedule and has access to information related to the animals on the list of the scheduled procedures. The system matches tissues requested with the animals scheduled for the next week. If a match is identified, the requester is notified by an e-mail message including a link back to the web page where he or she can confirm the acquisition. If an investigator declines or does not respond within 24 hours, the request is rotated to the lowest end of the queue and the opportunity is given to the next requester matched in the queue. This application enforces a fair process, makes full use of precious biospecimens, saves staff time and paper, and streamlines billing by maintaining distribution records. The IT team will continue to develop similar applications that model operational processes, manage records, and facilitate communications to support research and services needs.

In order to provide network access in the indoor animal rooms and outdoor animal areas, wireless network and access points have been installed. Network access in these areas enables cageside data access and point-of-service data entry. A sample set of mobile devices has been acquired and tested. Animal care staff will be using mobile devices as mobile applications are developed.

Supporting CNPRC Service Cores is another important component of IT Services. A home-built record management system has been maintained for the **Immunology and Pathogen Detection Resources Core** for laboratory technicians to enter and manage assays, test results, and access billing information. A web application has also been developed to manage freezer space. Another data management and billing application is under development for the **Inhalation Exposure Core**.

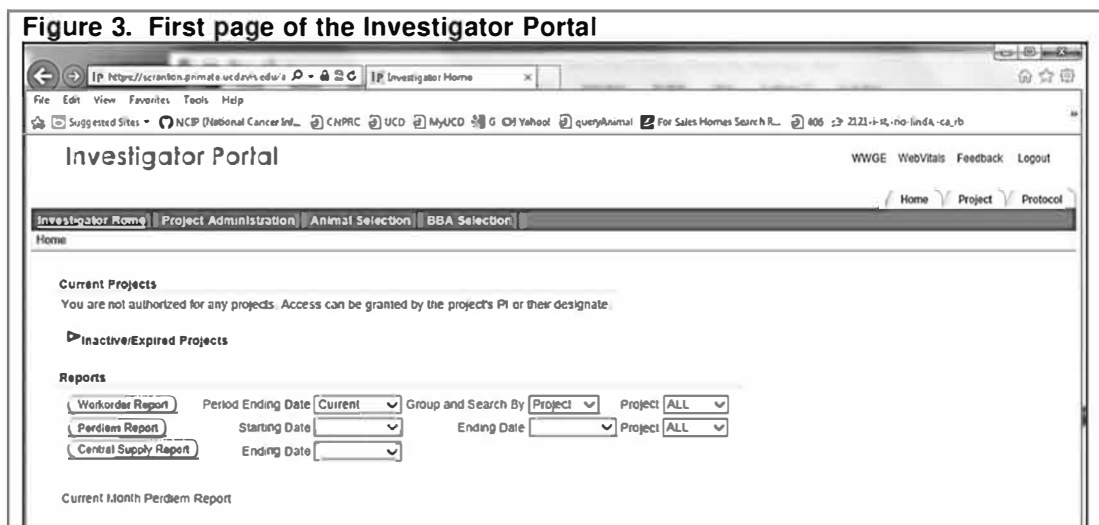
With increasingly tight schedules and complex analyses, the CNPRC Service Cores require more IT functions, including sample tracking, inventory management, scheduling of equipment usage and staff time, recording analytical results, and billing for tests completed. A full-featured LIMS will be needed to provide such functions. A request for proposal (RFP) through the UC Davis Office of Acquisition for LIMS solutions had received 13 responses, but none were viable due to high costs. Many LIMS packages have been evaluated, including caLIMS from the National Cancer Institute. An open-source LIMS package, [Specific Private Vendor] has been s [Specific Private Vendor] because it does not require a licensing fee and can be freely shared, and it has features meeting the n [Specific Private Vendor]

Cores and other services. It is currently being implemented and tested in the CNPRC **Clinical Pathology Laboratory (Anatomic and Clinical Pathology Services)**. Once the tests have been evaluated and if found effective, [redacted] will be implemented for Service Cores that may benefit from the program features [redacted] a management.

Working with the Director's Office, IT Services has migrated the CNPRC internal website to a content management system [redacted] hosted by the UC Davis campus Information and Educational Technology. This system provides a user-friendly interface for average users to publish and update content on the internal website. CNPRC staff and Core Scientists can find up-to-date information on the internal website. The IT team is also assisting the Public Information Officer to migrate and enhance the external website.

To support research and help Core Scientists to keep track of their projects, budgets, and animals, a prototype of an investigator portal was built using [redacted] server (Figure 3). This preliminary prototype helps Core Scientists to manage access to project information, and to track work orders, per diem costs, central supplies used, number of animals assigned to specific projects, and available animals in the colony. The data presented is specific to the logged-in user. No other users can access the project data if a Core Scientist has not granted permission.

Figure 3. First page of the Investigator Portal



In order to integrate more data and automate processes, a full-featured portal framework will be needed to develop the investigator portal. After evaluating and testing several popular portal frameworks, the IT team has [redacted] an open-source web portal framework [redacted] to develop web applications and to integrate data and [redacted] ses. Open-source products offers significant advantages due to the low cost and ease of sharing with other NPRCs. Web applications will be developed incrementally on this platform and made available to users as soon as possible.

CNPRC Core Scientists are adopting more “-omics” technology that will require increasing biomedical informatics support. A small Linux cluster of 4 computer nodes and 20 TB disk space has been built to store genomics data and perform bioinformatics analysis for investigators. [redacted] has established a [redacted] transfer research data, such as Single-Nucleotide Polymorphism (SNP) genotypes of nonhuman prim [redacted] CNPRC storage. SNP genotyping data from the **CNPRC Consortium** Genetics and Genomics Working Group are currently being collected across the NPRCs, and whole exome and whole genome sequence data will be downloaded to the CNPRC bioinformatics server and integrated with phenotype data as they emerge for CNPRC investigators to analyze. An enhanced data center and biomedical informatics support will be needed for future translational research. In this regard, a quarterly meeting is held with [redacted] Associate Director of the UC Davis Clinical and Translational Science Center (CTSC) Biomedical Informatics Program to share ideas and resources. The REDCap (Research Education Data Capture) application, which allows users to build and manage online databases quickly and securely, is hosted by the CTSC, and is used extensively by Core Scientists.

In addition to these projects, the IT team has maintained the current applications and supported the daily operations of the CNPRC. The following upgrades and improvements have been completed:

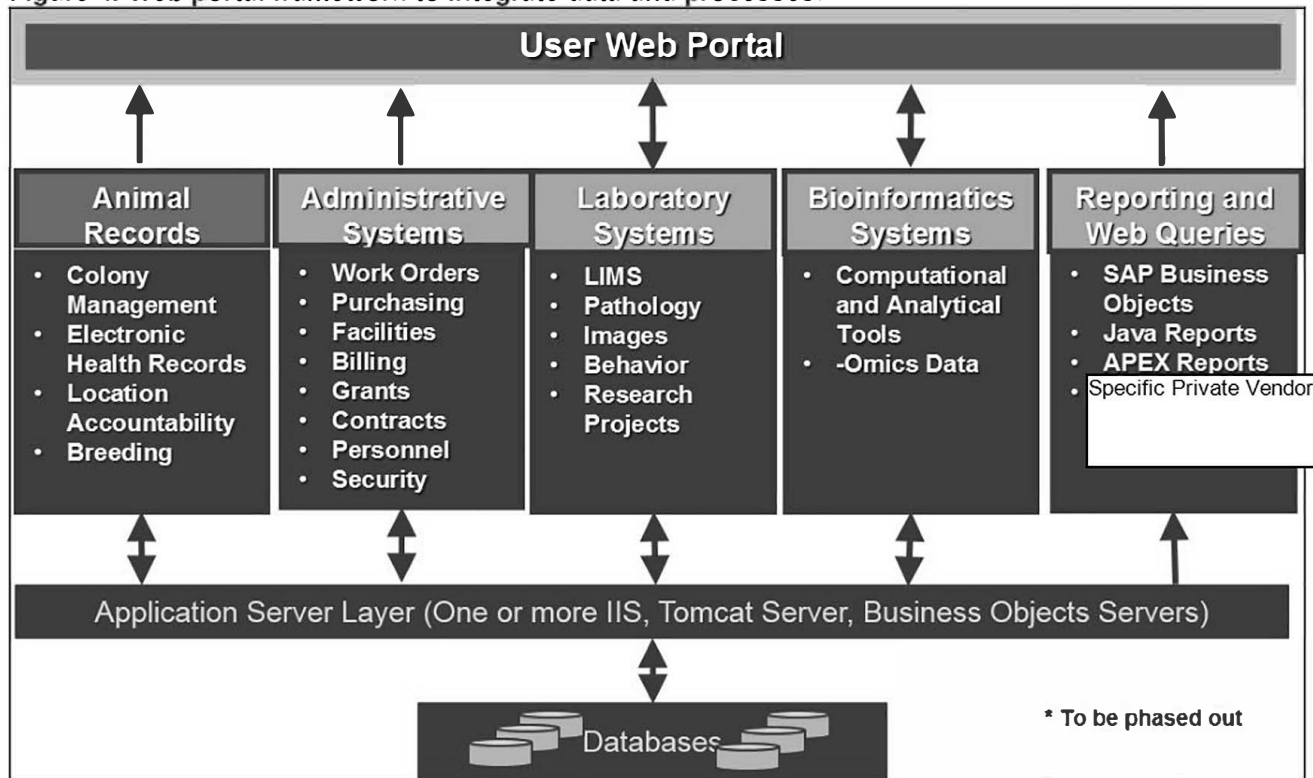
- Acquired new servers for electronic mail, shared files, image archives, backup, and security monitoring
- Implemented VMWare® to ensure full use of hardware servers
- Replaced the heating, ventilation, and air conditioning (HVAC) system in the computer server room
- Upgraded over 30 printers
- Upgraded [Specific Private Vendor]
- Converted the Microsoft® license to a full-time-user basis
- Upgraded firewall and network connections to provide connectivity to a number of outlying areas and improve access in other areas
- Installed videoconferencing equipment in a conference room and upgraded video presentation equipment in the CNPRC Seminar Hall
- [Specific Private Vendor]
- Assisted with the acquisition of automatic drug dispensers and built message communications with the database to record controlled substance usage (see **Colony Management and Research Services**)
- Selected and installed a barcode printer and barcode generation software
- Built a database and web interface for pathology images and case records
- Built an online drug formulary application
- Streamlined monthly billing processes and wrote numerous reports for business and grants management
- Developed web applications for Service Cores to upload data to a central database

Excluded by Requester [redacted] worked with [redacted] the Informatics Consultant of the **NPRC Consortium**, to establish a local Pathology and Image Database for sharing pathology cases across NPRCs

INNOVATION

The IT team proposes innovative methods to support operations and research at the CNPRC. One major area of innovation is in software application development, and by adopting a web portal framework to develop web applications, integrate data, and automate processes (Figure 4).

Figure 4. Web portal framework to integrate data and processes.



The web portal is a good framework from which to develop web applications that will increase efficiency and save developers significant time by providing basic functions such as user management and consistent layout. Developers will only need to focus on the specific application, allowing incremental development and

deployment of web applications to replace current [Specific Private Vendor] applications. Users will be able to readily view the new features or functions on the web without waiting for developers to write code. In addition, the web portal framework provides a mechanism to present different content or functions to users on the same website and is able to host multiple websites. Users can personalize the look and layout of their login pages without assistance.

Importantly the portal framework allows seamless integration of data and processes. Data from different sources can be integrated at the application layer and presented seamlessly to the end users as one unified view, regardless of where the data is stored. A veterinarian, for example, could in an integrated fashion assess an animal's demographic information and medical history from the animal records system, laboratory results from LIMS, reports from the pathology database, and radiographs or images from other sources. Workflow and communications among colleagues can be implemented smoothly using the workflow engine or via web services that the web portal framework supports. Business processes can be automated using the workflow engine to reduce paper use and to improve efficiency, communications, and record management. As an example, a work order can be entered online and triaged to the performing areas and staff. Communications will be triggered by the system as the process progresses, and status updates or results will be available in a timely manner. When completed, the series of records can be processed for billing.

Furthermore, the web portal framework provides social and collaborative functions, such as document sharing, discussion forums, a wiki, message boards, instant messages, shared calendars, polls, announcements, and alerts. These tools can be used out-of-the-box to facilitate collaborations and improve communications and efficiency. Users can set up their own groups to share information, documents, and ideas without programming. Posts and notes that do not need to be recorded in the database can be posted on the online message board to bring an individual's attention to specific issues.

APPROACH

Plans for the Next Funding Period

A user panel was formed with representative members from all CNPRC research and service groups to identify the needs for information and computing support for daily operations. The current list of needs includes the following: capturing colony and medical data at point-of-service, tracking samples and recording results from Service Cores promptly, providing real-time access to animal records from all sources at cageside, integrating and automating processes such as work orders and billing, and supporting research with biomedical informatics services. The IT team has proposed an overarching solution, which was approved by the senior management team, to adopt a web portal framework to integrate the animal records system, administrative applications, LIMS, report generation, and biomedical informatics applications.

The IT team has aligned extremely well with the needs of the CNPRC and with strategic planning to implement solutions. Good working relationships with other IT resources on the UC Davis campus have been established allowing extensive leverage. When a specific advanced technique is needed, the IT team can seek assistance from a UC Davis service group, such as the [Specific Private Vendor] to troubleshoot problems. UC Davis Networking Support manages the computer network to the CNPRC. Information and Educational Technology Software Licensing on campus provides discounted software licenses negotiated with vendors, such as [Specific Private Vendor] and [Specific Private Vendor]. The progress achieved in ARMS, the web portal, LIMS, and bioinformatics tools have laid a solid foundation for continued implementation of the solutions detailed in the following Specific Aims.

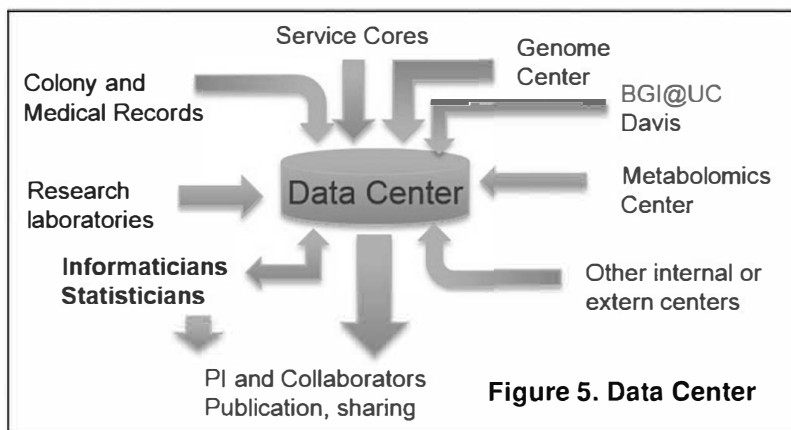
Specific Aim 1. Provide effective data management, streamlined data access, and bioinformatics assistance in support of the CNPRC research mission.

Modern biomedical research employs many high throughput technologies, such as microarrays, that generate tens of millions of data points in each experiment. Biomedical informatics, which applies IT, computing, and biomedical knowledge to support research, plays an important role throughout the whole life cycle of a research project, starting from the research hypotheses to publication and data sharing. Informaticians assist investigators with database searches and analyses of in-house and published data to help develop novel research hypotheses and draft grant proposals. Informaticians can also assist with experimental design, data collection, data management, data processing, and data sharing among collaborators. At the conclusion of the project, informaticians manage and analyze data, draft data related sections for publication, and facilitate sharing of data with the greater scientific community. The importance of biomedical informatics support

remains a component in the future success of the CNPRC and is an outstanding example of the team science spirit at the CNPRC.

UC Davis has a depth of expertise in Biomedical Informatics through the School of Medicine and the CTSC, as well as individual Centers and programs such as the Genome Center and West Coast Metabolomics Center. [REDACTED] has established working relationships with these campus entities to share resources and ideas. The Informatics Core in the Genome Center and BGI@UCDavis both have established bioinformatics services

for analysis. CNPRC Core Scientists can access these services through specific projects on a recharge basis. These service providers do not archive research data. Therefore, this will need to be accomplished at the CNPRC and integrated with other animal data in a central data repository. The integrated data from nonhuman primates accumulated throughout their lifetime become a valuable asset for future research and new discoveries. Data owned by individual investigators will be integrated but not widely accessible unless the investigator in question grants permission or releases the information.



The current Linux cluster with four computer nodes and 20 TB raw storage space can store primate genomics data and provide basic analytical computing functions. With more “-omics” data and medical images accumulating rapidly, the storage and computing capacity will need to be expanded. A Data Center with 100 TB storage space, two servers, and five additional computing nodes will be needed in the next five years to manage and integrate data from various sources (Figure 5).

Data from high throughput services, e.g., sequencing or SNP genotype data, will need to be transferred to a data center storage location and integrated with data from other sources. Animal records including medical and phenotypic observations, analytic results, medical images, and “-omics” data, will be managed in the Data Center. The data repository will be a valuable asset to investigators for future discoveries. Informaticians will help investigators to mine the data to form new research hypotheses. Access to the Data Center will be governed by the CNPRC and the NIH data sharing policy.

An investigator portal will be developed to provide Core Scientists with a single entrance to data and services. One cost-effective way of integrating the data from various sources is using the web portal framework, which allows data and processes to be integrated at the middle tier or at the presentation layer. By entering one animal identification number on the query form, demographic data and medical records from the colony database, data from the behavior database, laboratory results from LIMS, and “-omics” data from the bioinformatics server can all be presented to the investigator on one screen, as described above. Investigators will also be able to order tests for project animals through the portal and determine progress on previous requests. Data sources, functions, and communication procedures can be added incrementally to the portal. Access to data and process is highly customized to the user. Investigator-generated data will be accessible only to the investigator, staff, and collaborators unless the data have been released to the CNPRC database to be shared with other investigators. The IT team uses an open source portal framework, [REDACTED] to [REDACTED] Specific Private Vendor web interfaces and applications. The design and source codes will be shared with other NPRCs.

Analysis of biomedical data integrated in a data center will require assistance of informaticians. Local biomedical informatics specialists will help scientists extract and reformat the data, perform preliminary analysis, and coordinate with specialized biostatisticians. Sophisticated bioinformatics analysis, such as gene expression and genome-wide association studies, will require specialized biostatisticians from specialized service centers on campus.

Specific Aim 2. Ensure investigators have access to efficient IT systems and tools.

To enable service units to optimize the management of resources, IT staff will continue to develop and enhance software tools for resource management, including animals, biospecimens, equipment, staff training,

freezers, and other resources at the CNPRC. Specialized database and web applications will be enhanced or developed for these functions. This will bring increased efficiency and result in better and more cost-effective services.

The Service Cores need a full-featured LIMS for efficient resource management, daily workflow, data tracking, scheduling, and billing functions. The IT team is implementing the open-source LIMS package [redacted] Specific Private Vendor the Clinical Pathology Laboratory. If the system works well for this group, it will be extended to other [redacted] allows laboratory technicians to efficiently manage samples, storage space, experiments, inventory materials, equipment usage, analytical results, and user access. Minor enhancement or customization will be needed, and the IT staff will work with other institutes who are using [redacted] to make the necessary adaptations. Adopting open-source software tool reduces the cost of ownership and increases opportunities for sharing.

[redacted] Specific Private Vendor provides an open architecture that can be readily integrated with other applications under use. Work orders for testing will be distributed to the corresponding Service Cores through the portal applications. Data [redacted] Service Cores managed in [redacted] will be integrated at the application layer using an integrator [redacted] Specific Private Vendor tion, or at the web interface level using the web portal framework. Line items from the Service Cores can be generated and merged with those from other sources for a final billing invoice for research projects. Core Scientists and research staff will be able to login to the portal and view data as soon as the analysis is complete.

The internal web site functions as the information hub for Core Scientists and staff to identify available resources within the CNPRC. However, the web pages managed using the [redacted] content management system now only provide static information. The IT team will develop web applications to provide dynamic or automated business services online, such as telephone number searches, visitor approval forms, and forms for travel requests. This will save paper and improve business efficiency, enabling service groups to function more efficiently.

The external website for the CNPRC is also undergoing redesign and enhancement. IT staff are assisting the Public Information Officer on the server and technical aspects of the site. Applications that provide dynamic content and interactive services to external users will be developed to provide better information and online services to external researchers who wish to explore the resources and services available.

In addition to resource management and data access, process automation and prompt communication significantly affect the efficiency and quality of services. The IT team will develop applications on the portal framework to accept work orders online, distribute to corresponding service entities, record the status or outcome, and communicate to requesters. The goal is to enable the system to drive the process and communications after initiation by filling out online forms. Billing processes will be simplified as the work is tracked in the system. Line items along with up-to-date rates will be generated automatically. These line items can be reviewed and entered into the UC Davis Kuali financial system. Core and Affiliate Scientists will be able to look up the status and examine the data from the investigator portal. Applications will be developed on the portal to integrate this process and communicate with other systems, such as the animal record system, LIMS, and the electronic mail server. Providing effective information tools and automation of business processes will improve services and ultimately support state-of-the-art research.

Specific Aim 3. Aid in the training of the next generation of investigators with nonhuman primate expertise.

Biomedical research has evolved to large-scale data production using high throughput technology. A new generation needs to be trained to understand and use advanced technology, which involves biomedical informatics tools and methodology. The IT team will hold user-training sessions for new investigators to familiarize themselves with the informatics system and computational tools [redacted] will continue to work with [redacted] Excluded by Requester faculty to provide guidance for new investigators including graduate students and postdoctoral fellows in bioinformatics analysis.

Biomedical scientists and IT professionals often have difficulty understanding each other's respective terminologies. Training new investigators to understand informatics and computing aspects of biomedical research is important to be able to bring different cultures together and to work effectively with informaticians in

Excluded by Requester

their future career development. Both [redacted] the Project Manager, have a solid background in both biological science and IT, and they can provide translation between biomedical science and computing.

The CTSC Biomedical Informatics Program provides informatics training sessions and collaborates with the institutionally supported Health Informatics Graduate Group. This is a multidisciplinary group of approximately 30 faculty members from the Schools of Medicine and Veterinary Medicine, the College of Engineering (including the Departments of Computer Science and Mechanical and Aerospace Engineering), and the Betty Irene Moore School of Nursing, which offers a research-focused Master's degree, intended primarily for students that already hold degrees in either healthcare or IT. The program offers a comprehensive online Certificate Program for working professionals as well as a PhD program.

Specific Aim 4. Support nonhuman primate colony management and animal care.

ARMS will be critical for the daily management of the colony, care of the animals, and conformation to standard protocols. The current animal record system at the CNPRC needs to be enhanced with a full-featured electronic health record function. After evaluating available solutions for animal records management, the CNPRC partnered with the Washington and Yerkes NPRCs to enhance ARMS. This will help to achieve the goal using limited funding. With joint sponsoring, ARMS has been enhanced with billing, mobile functions, and functions to manage Institutional Animal Care and Use Committee (IACUC) activities. The IT team collaborates closely with IT groups in the Washington and Yerkes NPRCs. Weekly, monthly, and ad hoc conferences, electronic mail, and teleconferences have been conducted to share ideas, best practices, and potential solutions.

Steady progress has been made within the CNPRC. A prototype has been installed in ARMS and populated with CNPRC animal data on servers acquired by the CNPRC. The IT team is working with the end users to identify desirable functions and features for further enhancement of the application. The IT Project Manager is gathering requirements and analyzing workflow from the groups involved in colony management and animal care. A gap analysis has been performed, and detailed requirements for enhancement have been gathered from the **Primate Services** end users. Documents are shared among partners and with the [redacted]

Specific Private Vendor

the contractor that developed ARMS, to enhance ARMS in order to ensure that it captures medical efficiently and facilitates daily animal care and communications.

The custom-built pathology database has been used to record pathology data and generate pathology reports. The application needs to be enhanced to incorporate workflow. Web applications implementing pathology workflow will be developed on the portal framework and integrated with other animal records in order for users to access pathology findings along with other related information on individual animals.

Behavior data is collected using a mobile application [redacted] and uploaded to an Access Database. The IT team will work with **Behavior Management Services** to import and synchronize the data every night with

Specific Private Vendor

trial [redacted] and where other animal records are stored. Data integration, in this case, occurs at database level.

To provide easy access to data, web applications will be developed on a [redacted] to present data from different sources to the users based on their roles. These functions include animal breeding, behavioral observations, enrichment, pathology records, work orders, facility management, grants and contracts management, billing, personnel training, and security monitoring. Well-formatted reports will be developed on the SAP Business Objects platform for regulatory and other needs that do not require real-time data. End users will be able to revise and generate their own reports on this platform without the assistance of an IT programmer.

Specific Private Vendor

Streamlined access to all data about an animal at the same time is critical in many situations. Veterinarians need to view an animal's laboratory data, pathology report, and past treatment history together to evaluate health and develop treatment plans. An investigator should be able to see all project-related data from the animal's record, medical history, Service Core analyses, billing, genomic sequences, and related data from the public domain with minimal effort. Integrating data from different sources can be achieved at the web interface layer on the web portal platform (Figure 4). This allows the subsystems, such as an animal record system and the LIMS, to work independently.

Similarly, integration of processes is critical for the efficiency and quality of colony management, animal care, as well as research. Many daily routines involve multiple groups in **Primate Services**. Web applications will be the [redacted] to track requests, triage requests to different groups through the corresponding [redacted] tions such as ARMS and LIMS, trigger notifications and alerts, and generate line items for billing purposes. Electronic mail communications will be triggered through the system via event handling. Users can check on the status of a request or process on the web pages and communicate changes to the performing services and groups.

Specific Private
Vendor

Overall, the IT team will continue to work closely with end users and colleagues at other NPRCs to implement solutions to support the daily operations and research at the CNPRC. The main focus is on data, process, and research support. Data activities include data capture, integration, management, presentation and reporting, sharing, and analysis. Process will be automated by modeling the real-world workflows, and communications through the process will be facilitated by the software system. Efficient and adaptable research support is the ultimate goal. Progress will be reviewed with the management team and the Research Advisory Committee, and revisions addressing changing needs will be implemented. The goals in the next five-year period are to provide users with an effective information system, excellent services, and robust biomedical informatics support for research projects. Progress and milestones will be reviewed with the senior management team and the Research Advisory Committee regularly. Specific decisions will be made based on changing priorities, progress, hurdles, resources, and technology available.

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

ADMINISTRATIVE SERVICES: INFORMATION TECHNOLOGY SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Mrs. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Facilities Improvement

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename FIAbstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	FI_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	FIFacilitiesandOtherResources.pdf
11. Equipment	FIEquipment.pdf

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

ABSTRACT

Facilities Improvement includes overall infrastructure improvements that support the research enterprise. These funds are used to upgrade the facility and to replace obsolete equipment to ensure sustainability and the overall mission of the California National Primate Research Center (CNPRC). Facilities Improvement funds are permitted up to a maximum of \$600,000 annually per the funding opportunity announcement (FOA). The proposed use of these funds include addressing facility and equipment needs integral to colony management (e.g., replacement of cages, cage repairs), to replace outdated or nonfunctional equipment necessary to provide uninterrupted services to NIH-funded investigators in Primate Services and Service Cores (e.g., anesthesia machines, cryostat, centrifuges), and to improve Information Technology systems such as those critical to maintain the colony database. The Specific Aims for Facilities Improvement include: (1) Identify and prioritize requests for the improvement and modernization of the CNPRC, and (2) Ensure timely implementation of approved facilities improvement requests. The CNPRC Research Advisory Committee continuously evaluates and assesses needs to ensure optimal operation of the CNPRC. The Research Advisory Committee regularly identifies the most pressing needs, develops a foundation for proposed improvements, and provides a proactive approach to ensure that standards of excellence are maintained. The CNPRC interacts with UC Davis campus administration for the timely resolution of infrastructure and equipment needs based on best practices through standing committees with key UC Davis administrative personnel, and by expeditious integration of campus facilities staff with on-site CNPRC staff.

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: Not applicable

Office: Not applicable

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. The maintenance shop is central to the animal areas and includes shop equipment and supplies needed to maintain facilities, repair caging, and provide investigator support.

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

EQUIPMENT

A machine shop is located on-site and includes standard equipment items such as welders, plasma cutter, table saw, lathe, drill press, and band saws.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					0.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
					Total Salary, Wages and Fringe Benefits (A+B)		0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
1. Windows Domain Controller (2@\$5,117)	10,234.00
2. X-Ray Repository and Database	11,967.00
3. File Server	8,492.00
4. Motorized Wheelbarrows (2@\$5,568)	11,136.00
5. Cage Replacement (10@\$12,445)	124,450.00
6. Mule Vehicle Replacement	12,930.00
7. Dental System (2@\$12,950)	25,900.00
8. Dental X-Ray	44,033.00
9. MacroView D Mobile Digital Imaging System	48,600.00
10. Rainin Liquidator 96	14,575.00
11. Isotemp Freezer	5,928.00
12. MagNA Pure LC 2.0	33,210.00
13. GE PACS System for PET/CT	49,086.00
14. Metamorph Microscope Control Software	12,865.00
15. Leica RM2255 Microtome	24,507.00
16. Olympus Silicone Oil Immersion Objective Lenses: 40x and 60x	24,701.00
17. Sutter Instruments Lambda VF-5 Tunable Filter Changer	15,012.00
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	477,626.00
Additional Equipment: File Name:	

D. Travel**Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	121,800.00
Total Other Direct Costs	121,800.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	599,426.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	599,426.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: FIBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months Effort	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary		0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
					Total Salary, Wages and Fringe Benefits (A+B)		0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
1. IT Rack Replacement	12,539.00
2. Motorized Wheelbarrows (4@\$5,568)	22,272.00
3. Cage Replacement (10@\$12,445)	124,450.00
4. Replacement Steam Cleaners for Outdoors	12,617.00
5. Manufactured Tent Tarps for Corrals (3)	81,504.00
6. Electrocautery (2@\$6,151)	12,302.00
7. Tobii TX300 Eye Tracker	56,938.00
8. Real-time PCR Thermocycler	21,384.00
9. Luminex Reader	68,908.00
10. Leica CM1950 Cryostat	53,204.00
11. Prior Proscan III Microscope Stage Controller	11,848.00
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	477,966.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	121,800.00
Total Other Direct Costs	121,800.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	599,766.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	599,766.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: FIBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					0.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
1. Production Printer Replacement	7,721.00
2. Motorized Wheelbarrows (4@\$5,568)	22,272.00
3. Cage Replacement/Repair (10@\$12,445)	124,450.00
4. Mule Vehicle Replacement	12,930.00
5. Manufactured Tent Tarps for Corrals (3)	81,504.00
6. Anesthesia Machine: GE Aespire 7900 with Cardiocap/5 (2@\$40,293)	80,586.00
7. Bronchoscope	109,259.00
8. Olympus BX46 Microscope/camera with Cellsense Software	36,598.00
9. Nor-Lake Incubator	5,243.00
10. Tabletop Centrifuge-Sorvall Legend Series	10,658.00
11. Tecan Sunrise Microplate Reader	7,955.00
12. Tissue Homogenizer	17,010.00
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	516,186.00

Additional Equipment: File Name:

D. Travel

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	81,200.00
Total Other Direct Costs	81,200.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	597,386.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	597,386.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: FIBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
						Total Salary, Wages and Fringe Benefits (A+B)	0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
1. Firewall Server	13,270.00
2. Backup System Components	21,574.00
3. Motorized Wheelbarrows (3@\$5,568)	16,704.00
4. Cage Replacement (10@\$12,445)	124,450.00
5. Manufactured Tent Tarps for Corrals (3)	81,504.00
6. Radiographic Table	17,280.00
7. Anesthesia Machine: GE Aespire 7900 with Cardiocap/5	40,293.00
8. X-Ray Machine TRUDR eSeries 1717G radiology unit	62,575.00
9. Surgical drill: (2) Anspach Sythes small battery drive	55,016.00
10. Sorvall Legend XTR Refrigerated Centrifuge with Rotor	11,215.00
11. Liquid Scintillator Counter	33,463.00
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	477,344.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	121,800.00
Total Other Direct Costs	121,800.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	599,144.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	599,144.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: FIBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
					Total Salary, Wages and Fringe Benefits (A+B)		0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
1. Motorized Wheelbarrows (3@\$5,568)	16,704.00
2. Cage Replacement (10@\$12,450)	124,500.00
3. Replacement Steam Cleaner for Outdoors	12,617.00
4. Manufactured Tent Tarps for Corrals (3)	81,504.00
5. Video Gastroscope	103,273.00
6. Wizard2 Gamma Counter	44,852.00
7. Chambers for Inhalation Exposure (2@47,358)	94,716.00
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	478,166.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	121,800.00
Total Other Direct Costs	121,800.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	599,966.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	0.00	0.00
Total Indirect Costs			0.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	599,966.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: FIBudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**BUDGET JUSTIFICATION****PERSONNEL**

All effort for management of Facilities Improvement will be committed through Administration and Operations Services; therefore effort listed in this component for the Interim Associate Director for Administration and Operations does not fully demonstrate the level of commitment to these activities.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Interim Associate Director for Administration and Operations	% Effort			

The Interim Associate Director for Administration and Operations Services is the Lead

Excluded by Requester component EFFORT months served as Vice Chancellor for Administration for UC from 2003-2010, and served in other leadership positions in the Office of Administration since 1992.

Notably, he served as Executive Director of Facilities and Land Management at UC Davis during which time he was responsible for the maintenance of campus facilities, including oversight of the Animal Care Program as

Excluded by Requester Davis Institutional Official. In this capacity, instituted the Animal Care Leadership Team, with the Institutional Animal Care and Use Committee (IACUC) and campus researchers, the animal

facility managers, as well as federal and accrediting agencies to ensure a supportive environment for research while meeting the regulatory requirements for the use of animals in research and teaching.

EQUIPMENT

See attached quotes by Year for all equipment noted below. *Quotation totals may vary slightly from budgeted amounts due to anticipated university discounts and/or inflationary estimations.*

YEAR 1 (Year 54): TOTAL \$599,426**Equipment (\$477,626)****Information Technology Services**

Windows Domain Controller (\$4,738 + tax \$379 = \$5,117 x 2 = \$10,234)

Domain controllers are servers used to respond to security authentication requests, such as login and checking permissions, within the server domains. Two current domain controllers are, or will be soon, out of warranty – Apollo (2007) and Starbuck (2010). Dell typical 'end-of-life' warranty calls for a depreciation schedule of 5 years. Each of the CNPRC current Domain Controllers exceed this age and are no longer under warranty and are subject to natural hardware failure.

X-Ray Repository and Database (\$11,330 + tax \$637 = \$11,967)

The CNPRC currently has two systems that house radiology data – Xray1 (purchased in 2007) and a desktop-workstation class 'server' that was a part of X-ray hardware purchased that is not enterprise-class. The systems have both passed the period of support and run a high risk of failure. The aging system (Xray1) needs to be replaced with a new system in order to migrate data and service as soon as possible.

File Server (\$7,933 + tax \$559 = \$8,492)

This system is crucial for Information Technology staff projects, files, miscellaneous backup, and reference for internal data collaboration. The current system (purchased in 2009) is outside of warranty support because of end-of-life. The current disk utilization is over 70% of its capacity.

Primate Services**Colony Management and Research Services**

Motorized Wheelbarrows (\$4,853 + shipping \$352 + tax \$363 = \$5,568 x 2 = \$11,136)

The use of motorized wheelbarrows for cleaning and movement of soiled gravel has been assessed over the last 2 years on a trial basis through the UC Davis "Be Smart About Safety Program". The improvement for employees in terms of back safety has been notable, and the objective is to use motorized wheelbarrows for all

colony needs in the outdoor areas. Wheelbarrows will be provided to the North Colony to increase the number available for staff.

Cage Replacement/Repair (\$116,500 + tax \$7,950 = \$124,450)

Funds are requested to purchase rolling rack nonhuman primate caging. The current need is for male extra-large (XL) cages that are required by USDA for animals that are over 15 kg. Currently many rhesus males housed indoors for breeding and projects are over 15 kg and require the XL caging. The request for 10 racks/4 cages per rack will provide 40 new cages that can be used in all indoor areas and meet caging requirements.

Mule Vehicle Replacement (\$12,014 + tax \$916 = \$12,930)

Mules are used throughout the animal colony to transport personnel, animals, feed, and supplies to outlying areas. Funds are requested to replace worn and aged equipment. This replacement will be used by the Primate Medicine crew for round-up support and for daily treatments required around the colony.

Primate Medicine Services

Dental System (\$11,991 + tax \$959 = \$12,950 x 2 = \$25,900)

Funds are requested for the replacement of outdated equipment that cannot be serviced, does not meet the current clinical needs, and does not support clinical research programs evaluating new dental procedures to be used. The CNPRC dentistry program is an expanding area of interaction with the School of Veterinary Medicine Dentistry Service. The collaboration with the School of Veterinary Medicine has facilitated the expansion of the dentistry program to include endodontic and other advanced dental procedures that require replacement of outdated equipment.

VetPro Dental X-Ray (\$40,771 + tax \$3,262 = \$44,033)

The current dental X-ray equipment is outdated and does not provide the quality of images necessary for the advanced clinical dental procedures that have been incorporated into the CNPRC dental program. The new unit is necessary to fully support the continued growth and advancement of Primate Medicine dentistry.

Anatomic and Clinical Pathology Services

MacroView D Mobile Digital Imaging System (\$45,000 + tax \$3,600 = \$48,600)

Upgrade of the current digital imaging system in a primary necropsy room is a high priority. Currently Pathology Services uses a Nikon D70 that is more than 10-years-old, and an antiquated camera stand and lighting to take photographs of tissues. Images have become an increasingly important part of a well-documented necropsy report and the camera equipment is used several times a week to document lesions. The current set up is outdated and difficult to use in order to produce consistent results. The new imaging system has been selected because it is easy to clean, easy to operate by many different users, and produces consistent, good quality images that can be uploaded into the Primate Pathology Image Database.

Service Cores

Endocrine Core

Rainin Liquidator 96 (\$13,496 + tax \$1,079 = \$14,575)

These funds will provide for the replacement of outdated equipment purchased in 1988 that can no longer be serviced.

Isotemp Freezer (\$5,489 + tax \$439 = \$5,928)

These funds will provide for the replacement of a freezer purchased in 1998 that can no longer be used because it is not reliable and can no longer be serviced.

Immunology and Pathogen Detection Resources Core

MagNA Pure LC 2.0 (Nucleic Acid Purification System) (\$30,750 + tax \$2,460 = \$33,210)

The MagNA Pure LC 2.0 is used to process blood and tissue samples to extract and purify nucleic acids. The current, older generation instrument (M48) is no longer supported by the manufacturer thus is not covered by a service contract. All samples received for PCR (>3,000/year) are processed on this instrument. Manual methods are more labor intensive and have been documented to be less reproducible.

*Multimodal Imaging Core*GE PACS System for PET/CT (\$46,384 + taxable items \$2,702 = \$49,086)

The GE PET/CT was obtained through an NIH S10 High-End Instrumentation Grant. A PACS system is required in order to back-up, organize, and store the images obtained from the system, as well as provide a means for investigators to query, access, and view their imaging data, and other data related to each study.

Metamorph Microscope Control Software (\$11,967 + tax \$898 = \$12,865)

Currently, the Core has one research microscope that is used as a workhorse machine for virtually all client needs. It is 12-years-old and in recent years has had repairs for worn out parts. Repairs must be made through Olympus America in Pennsylvania, which generally takes about 1-2 months. Fortunately, the Olympus representative has had loaner parts but this is a finite resource as Olympus parts evolve for the newer model microscopes as parts for the older models disappear from inventory. Purchasing a copy of Metamorph software would allow use of a second virtually identical microscope as a backup system in the event of a repair on the first system. Without a backup microscope, clients could be without a workhorse microscope for the duration of the repairs. Currently, the second microscope runs with the aid of an outdated copy of Slidebook software that is not suited for general use by clients of the Core. Additionally, with this software, the second microscope could be made available during very busy periods when the first microscope is heavily used.

Leica RM2255 Microtome (\$22,509 + shipping \$197 + tax \$1,801 = \$24,507)

The Core currently has two Microm microtomes for cutting paraffin embedded tissue, one that is 22-years-old and the other is 18-years-old. Both have had significant repairs in the last few years and the service company has informed the Core that parts for both microtomes are very difficult to obtain. Some parts are only available from other microtomes that have been taken out of service – the parts are therefore used and also prone to failure. At least one of these microtomes must be replaced in the next year so that the Core can guarantee continuity of service.

Olympus Silicone Oil Immersion Objective Lenses (40 x and 60x) (\$22,978 + tax \$1,723 = \$24,701)

The Core has two research microscopes that are heavily used for fluorescent microscopy with a set of either water (R.I. 1.33) or oil (R.I. 1.52) immersion lenses. However, most fluorescent microscopy is performed with specimens mounted in media with refractive indexes (R.I.) of 1.40-1.46. The R.I. mismatch between lens immersion fluid and specimen mounting medium creates unnecessary optical aberrations in the specimen that degrade the image. The silicone oil immersion objectives improve imaging by using immersion oil with an R.I. of 1.41. The result is a brighter image with improved resolution.

Sutter Instruments Lambda VF-5 Tunable Filter Changer (\$13,900 + tax \$1,112 = \$15,012)

The Core has two research microscopes that are heavily used for fluorescent microscopy and each uses conventional filter cubes that consist of static filter combinations tuned for specific fluorochromes. Although they meet the general requirements for imaging a broad range of fluorochromes, they cannot be adjusted for special situations such as specimens that contain significant amounts of autofluorescence. The Sutter Instruments Lambda VF-5 system allows filter tuning in 1 nm increments over a very wide range of wavelengths for both excitation and emission. The bandwidth ranges from 12-16 nm, which allows very specific excitation and emission control. These filters would be very useful for isolating and reducing autofluorescence in a variety of specimens. Additionally, applications are being developed for hyperspectral imaging that will help to pinpoint the identity of fluorescent signals and discriminate fluorophore signals from autofluorescence.

Alterations and Renovations (\$121,800)Corn Crib Replacement (3 x \$40,600 = \$121,800)

Funds are requested for corn cribs in order to replace aged units that are ≥30 years. In 2013, a prototype was constructed and evaluated that was shown to meet all the needs of the animals, and will allow for efficient cleaning and maintenance. The new caging will provide enhanced areas for the animals to move and explore. This will allow replacement of South Colony Row 100.

YEAR 2 (Year 55): TOTAL \$599,766**Equipment (\$477,966)**

Information Technology Services

Rack Replacement (\$11,601 + tax \$938 = \$12,539)

Information Technology Services currently maintains servers on four Dell racks. Three of the server racks are beyond the warranty period, ranging from 7 to ≥11 years. The CNPRC has had a number of hardware failures on the power-module and network switch, with replacements on an immediate/as-needed basis. It has been calculated that one rack will need to be replaced every five years at a minimum, for proactive maintenance.

Primate Services

Colony Management and Research Services

Motorized Wheelbarrows (\$4,853 + shipping \$352 + tax \$363 = \$5,568 x 4 = \$22,272)

See above. Four wheelbarrows will be added to the North Colony to increase the number available to staff.

Cage Replacement/Repair (10 x \$12,445=\$124,450)

See above. The request for 10 racks/4 cages per rack will provide 40 new cages that can be used in all indoor areas and meet caging requirements.

Replacement Steam Cleaner for Outdoor Areas (\$11,391 + shipping \$400 + tax \$826 = \$12,617)

Funds are requested to purchase replacement steam pressure washers. The outdoor colony steam pressure washers are used to sanitize perch bars, A-frames, feed pads, play structures, and empty cages. They are typically used 5 days per week, and are rotated between cages. Replacement equipment is requested to maximize sanitation schedules.

Manufactured Tent Tarps for Field Corrals (\$24,500 + shipping \$800 + tax \$1,868 = \$27,168 x 3 = \$81,504)

Funds are requested to purchase and install overhead canopies for the one-half acre field corrals. The proposed 60 ft. x 100 ft. shade structures provide protection from the rain, wind, and sun as well as a dry area for feeding. The tarps also provide protection for veterinary and technical staff during round-up procedures in the field corrals that are conducted throughout the year. Several of the existing canopies are ≥10 years and are worn from sun and weather exposure.

Primate Medicine Services

Electrocautery (\$5,650 + shipping \$45 + tax \$456 = \$6,151 x 2 = \$12,302)

The current electrocautery units are old and heavily used. They do not function consistently and may create unnecessary research variables for surgical procedures. New electrocautery units are required to support the heavy surgery schedule particularly in areas of complex neurosurgical and spinal procedures.

Service Cores

Behavior Research Services Core

Tobii TX300 Eye Tracker (\$52,720 + taxable items \$4,218 = \$56,938)

Funds are requested to purchase the Tobii TX300 eye-tracking package of monitor, eye tracker, and software. Noninvasive eye tracking systems are commonly used in humans and are being rapidly adapted for nonhuman primate research. The Tobii system has recently been optimized for use specifically in the infant macaque model, with higher temporal resolution enabling more robust capture of primate eye movements with minimal restraint. The system includes a camera and microphone, and is compatible with The Observer software, a behavioral coding program, which allows for integrating eye tracking and behavioral data. This highly technical system has high precision and accuracy, robust eye tracking/high sampling rate, and compensation for large head movements. Eye tracking enables assessment of cognitive function, attention, and social/emotional responsiveness through detailed measurement of looking durations, frequencies, and patterns to various visual stimuli. It is used in human research focused on autism, schizophrenia, developmental disability, and aging.

Immunology and Pathogen Detection Resources Core

Real-Time PCR Thermocycler (\$19,800 + tax 1,584 = \$21,384)

The Core has one newer-generation instrument and two older units for which the CNPRC has been informed service support will be discontinued. The older units use XP software therefore they cannot be run on the CNPRC network. The CNPRC recently purchased one newer-generation instrument (with 3 years' service) for less than the cost of a 2-year service contract on one existing machine. Multiple instruments and service contracts are necessary to meet the workload and turn-around time of clients.

Luminex Reader (BioPlex) (\$63,804 + tax \$5,104 = \$68,908)

This item is a Luminex reader for multiplex immunoassays (>5,000/year). Software on the current, 12-year-old system cannot run on Windows 7, which is required for network use. Thus, the CNPRC is no longer able to upload data generated by the reader to the network. Furthermore, this replacement is less costly than a service contract (or backup instrument), which is necessary to fulfill turn-around time requirements of clients.

*Multimodal Imaging Core*Leica CM1950 Cryostat (\$48,695 + shipping \$614 + tax \$3,895 = \$53,204)

The current cryostat in the Core is 12-years-old, has had a number of repairs in the last 2-3 years, and is deteriorating with age. It is the only cryostat at the CNPRC that is available for cutting tissue that is not experimentally infected with agents such as SIV. A replacement is needed to meet the demands in the Core.

Prior Proscan III Microscope Stage Controller (\$10,970 + tax \$878 = \$11,848)

The Core has two research microscopes with computer-controlled stages that are used for moving microscope slides under the lens. There is no option for manually moving the slides on these two microscopes. The current stage controllers are 11-years-old and will become obsolete in the next 2-3 years. The software used to control the microscopes and stages is evolving and will no longer support the old controllers in the near future. The controllers need to be replaced before software updates prevent use of the stages.

Alterations and Renovations (\$121,800)Corn Crib Replacement (3 x \$40,600 = \$121,800)

See above. These funds will allow for replacement of South Colony Row 200.

YEAR 3 (Year 56): TOTAL \$597,386**Equipment (\$516,186)***Information Technology Services*Production Printer Replacement (\$6,950 + lease cost \$232 + tax \$539 = \$7,721)

The current production printer is 10-years-old and is the primary volume printer for Information Technology staff and bulk printing for billing reports, serves as backup for work order printing, and general black and white bulk printing for the Administration building as needed. Replacement for these printing needs is requested.

*Primate Services**Colony Management and Research Services*Motorized Wheelbarrows (\$4,853 + \$352 shipping + tax \$363 = \$5,568 x 4 = \$22,272)

See above. Four additional wheelbarrows will be provided to the North Colony to increase the number available for staff.

Cage Replacement/Repair (\$116,500 + tax \$7,950 = \$124,450)

See above. Ten rolling racks will hold a total of 40 animals and provide caging for a single breeding room in either infectious or non-infectious housing.

Mule Vehicle Replacement (\$12,014 + tax \$916 = \$12,930)

See above. Funds are requested for the replacement of an aging vehicle that will no longer be able to be maintained in good working order.

Manufactured Tent Tarps for Field Corrals (\$24,500 + shipping \$800 + tax \$1,868 = \$27,168 x 3 = \$81,504)

See above. Several of the existing canopies are over 10-years-old and are worn from sun and weather exposure and in need of replacement.

*Primate Medicine Services*Anesthesia Machine (\$37,286 + tax 3,007 = \$40,293 x 2 = \$80,586)

The current anesthesia units are heavily used in supporting both the clinical services as well as research needs in areas of experimental surgery, imaging procedures (e.g., microPET), and EMG recording. Some procedures are of extended duration resulting in extensive wear on the equipment. The case load dictates that the CNPRC have multiple machines available at all times therefore some of the anesthesia machines must be

replaced on a rotating schedule to ensure that there is routine access to up-to-date and properly functioning equipment.

Bronchoscope (\$101,166 + tax \$8,093 = \$109,259)

The current equipment is old and has decreased functionality due to broken optic fibers and impaired manipulation. New units are necessary to maintain service capability both clinically and for pulmonary studies.

Anatomic and Clinical Pathology Services

Olympus BX46 Microscope/camera with Cellsense Software (\$33,887 + tax \$2,711 = \$36,598)

The pathology residents are currently using an old Olympus BH2 microscope without a camera. This system needs to be updated to provide a system compatible to that used by the pathology residents in the School of Veterinary Medicine, and to allow them to capture images from the microscope. The Cellsense software is required to operate the camera.

Service Cores

Endocrine Core

Nor-Lake Incubator (\$4,855 + tax \$388 = \$5,243)

These funds provide for the replacement of a low temperature incubator purchased in 2002 that can no longer be serviced.

Immunology and Pathogen Detection Resources Core

Tabletop Centrifuge-Sorvall Legend Series (\$9,869 + tax 789 = \$10,658)

This purchase is a planned replacement of older equipment. Buying new-generation equipment covered by warranty is more cost effective than maintaining service contracts on older equipment.

Tecan Sunrise Microplate Reader for ELISAs (\$7,955)

The manufacturer will no longer support the current unit due to age. The cost of a service contract for 5 years is more than the cost of a new instrument. Purchasing a new reader and using the older microplate reader as backup (in lieu of a service contract) is the most cost effective way to meet user needs.

Tissue Homogenizer (\$15,750 + tax 1,260 = \$17,010)

Isolation of immune cells and nucleic acids from tissue samples requires a tissue homogenizer. The Core routinely (weekly to semiweekly) processes samples from ileum, colon, and lung tissue for various clients. The Core currently has a tissue homogenizer but it is nearing the end of expected lifetime.

Alterations and Renovations (\$81,200)

Corn Crib Replacement (2 x \$40,600 = \$81,200)

See above. These funds will provide new caging for South Colony Row 300.

YEAR 4 (Year 57): TOTAL \$599,144

Equipment (\$477,344)

Information Technology Services

Firewall Server (\$12,287 + tax \$983 = \$13,270)

The CNPRC is currently contracting with the UC Davis campus Information Technology services for turnkey service/maintenance for the border firewall. The currently supplied hardware is approximately 5-years-old and is in need of replacement. The newer hardware will serve as a firewall and a localized wireless infrastructure to implement SSL VPN locally.

Backup System Components (\$20,069 + tax \$1,505 = \$21,574)

The backup system components are localized hard drives for faster and immediate storage and retrieval to augment the LTO5 tape-based backup (tapes are sent out monthly to Iron Mountain). The current 20 TB localized hard drive backup space built-in to the backup server fills up very quickly with incremental backups. More backup storage will be needed as more data are backed up.

Primate Services*Colony Management and Research Services*

Motorized Wheelbarrows (\$4,853 + \$352 shipping + tax \$363 = \$5,568 x 3 = \$16,704)

See above. Three additional wheelbarrows will be provided to the North and South Colony to increase the number available for staff.

Cage Replacement/Repair (10 x \$12,450=\$124,450)

See above. Ten rolling racks will hold a total of 40 animals and provide caging for a single breeding room, or for either infectious or non-infectious housing.

Manufactured Tent Tarps for Field Corrals (\$24,500 + shipping \$800 + tax \$1,868 = \$27,168 x 3 = \$81,504)

See above. Several of the existing canopies are over 10-years-old and are worn from sun and weather exposure and in need of replacement.

Primate Medicine Services

Radiographic Table (\$16,000 + \$1,280 = \$17,280)

A new radiology table is needed to fully support the digital radiology equipment used by Primate Medicine Services. The current table is over 30-years-old and was part of the original film radiology equipment.

Anesthesia Machine (\$37,286 + tax \$3,007 = \$40,293)

The current anesthesia units are heavily used in supporting both the clinical services as well as research needs as noted. The case load dictates that the CNPRC have multiple machines available at all times therefore some of the anesthesia machines must be replaced on a rotating schedule to ensure routine access to up-to-date and properly functioning equipment.

X-Ray machine TRUDR eSeries 1717G Radiology Unit (\$57,940 + tax \$4,635 = \$62,575)

This additional radiology unit is needed to support both clinical radiology needs as well as to provide greater flexibility for services to investigators that are in need of radiographic images for their studies. The rapid advancements in imaging technologies demands that equipment is replaced with some frequency to ensure capabilities are maximized.

Surgical Drill, ANspach Synthes (small battery drive with accessories) (\$25,470 + tax \$2,038 = \$27,508 x 2 = \$55,016)

Replacement surgical drills are needed to support the extensive surgical demands from Primate Medicine Services for research support. The surgical drills are extensively used in craniotomies and laminectomies that are performed as part of spinal surgical procedures.

Service Cores*Endocrine Core*

Sorvall Legend XTR Refrigerated Centrifuge with Rotor (\$10,385 + tax \$830 = \$11,215)

These funds will provide for the replacement of a centrifuge purchased in 2000 that is no longer serviceable.

Liquid Scintillation Counter (\$30,984 + tax \$2,479 = \$33,463)

These funds will provide for the replacement of a Beckman LS1701 purchased for shared use in 1987 that is no longer serviceable.

Alterations and Renovations (\$121,800)

Corn Crib Replacement (3 x \$40,600 = \$121,800)

See above. These funds will allow replacement of the remainder of South Colony Row 300.

YEAR 5 (Year 58): TOTAL \$599,966

Equipment (\$478,166)

Primate Services*Colony Management and Research Services*

Motorized Wheelbarrows (\$4,853 + \$352 shipping + tax \$363 = \$5,568 x 3 = \$16,704)

See above.

Cage Replacement/Repair (10 x \$12,450 = \$124,500)

See above.

Replacement Steam Cleaner for Outdoor Areas (\$11,391 + shipping \$400 + tax \$826 = \$12,617)

See above.

Manufactured Tent Tarps for Field Corrals (\$24,500 + shipping \$800 + tax \$1,868 = \$27,168 x 3 = \$81,504)

See above.

Primate Medicine Services

Video Gastroscope with Processor, Monitor, and Cart (\$95,623 + tax \$7,650 = \$103,273)

A new video gastroscope is required for both clinical cases and research procedures involving collections of gastric biopsies and visualization of gastric mucosa. The current equipment has limited flexibility and is unable to capture images which impacts research publications and clinical monitoring.

Service Cores

Endocrine Core

Gamma Counter (\$41,529 + tax \$3,323 = \$44,852)

These funds will provide for the replacement for an instrument purchased in 2001 that will not be able to be serviced in the near future.

Inhalation Exposure Core

Inhalation Chambers (\$43,850 + tax \$3,508 = \$47,358 x 2 = \$94,716)

These funds will add the necessary chambers for the Inhalation Exposure facility. The new facility has space for 12 exposure chambers but the new building project only had the funds available for 8. This will allow an increase in the capacity of animals for studies that can be conducted simultaneously, which was the original goal when designing the facility.

Alterations and Renovations (\$121,800)

Corn Crib Replacement (3 x \$40,600 = \$121,800)

These funds will allow for the replacement of South Colony Row 400.

TRAVEL

Not applicable

SUPPLIES

None

OTHER EXPENSES

None

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**YEAR 1 (Year 54)**

Year	Component	Description (includes tax)	Total (with tax)
54	Information Technology Services	Windows Domain Controller (2 x \$5,117)	\$10,234
		X-ray Repository and Database	\$11,967
		File Server	\$8,492
	Colony Management and Research Services	Motorized Wheelbarrows (2 x \$5,568)	\$11,136
		Cage Replacement/Repair (10 x \$12,445)	\$124,450
		Mule Vehicle Replacement	\$12,930
		Corn Crib Replacement*	\$121,800
	Primate Medicine Services	Dental system (2 x \$12,950)	\$25,900
		Dental X-ray	\$44,033
	Pathology Services	MacroView D Mobile Digital Imaging System	\$48,600
	Endocrine Core	Rainin Liquidator 96	\$14,575
		Isotemp Freezer	\$5,928
	Immunology and Pathogen Detection Resources Core	MagNA Pure LC 2.0	\$33,210
	Multimodal Imaging Core	GE PACS System for PET/CT	\$49,086
		Metamorph Microscope Control Software	\$12,865
		Leica RM2255 Microtome	\$24,507
		Olympus Silicone Oil Immersion Objective Lenses: 40x and 60x	\$24,701
		Sutter Instruments Lambda VF-5 Tunable Filter Changer	\$15,012
			\$599,426

*Alterations and Renovations (quote after equipment)

Excluded by Requestor –Vendor Quotes

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ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**YEAR 2 (Year 55)**

Year	Component	Description (includes tax)	Total (with tax)
55	Information Technology Services	Rack Replacement	\$12,539
	Colony Management and Research Services	Motorized Wheelbarrows (4 x \$5,568)	\$22,272
		Cage Replacement/Repair (10 x \$12,445)	\$124,450
		Replacement Steam Cleaners for Outdoors	\$12,617
		Manufactured Tent Tarps for Corrals (3)	\$81,504
		Corn Crib Replacement*	\$121,800
	Primate Medicine Services	Electrocautery (2 x \$6,151)	\$12,302
	Behavior Research Services Core	Tobii TX300 Eye Tracker	\$56,938
	Immunology and Pathogen Detection Resources Core	Real-time PCR Thermocycler	\$21,384
		Luminex Reader	\$68,908
	Multimodal Imaging Core	Leica CM1950 Cryostat	\$53,204
Prior Proscan III Microscope Stage Controller		\$11,848	
			\$599,766

*Alterations and Renovations (quote after equipment)

Excluded by Requestor –Vendor Quotes

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ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**YEAR 3 (Year 56)**

Year	Component	Description (includes tax)	Total (with tax)
56	Information Technology Services	Production Printer Replacement	\$7,721
	Colony Management and Research Services	Motorized Wheelbarrows (4 x \$5,568)	\$22,272
		Cage Replacement/Repair (10 x \$12,445)	\$124,450
		Mule Vehicle Replacement	\$12,930
		Manufactured Tent Tarps for Corrals (3)	\$81,504
		Corn Crib Replacement*	\$81,200
	Primate Medicine Services	Anesthesia machine: GE Aespire 7900 with Cardiocap/5 (replacement) (2 x \$40,293)	\$80,586
		Bronchoscope	\$109,259
	Pathology Services	Olympus BX46 Microscope/camera with Cellsense software	\$36,598
	Endocrine Core	Nor-Lake Incubator	\$5,243
	Immunology and Pathogen Detection Resources Core	Tabletop Centrifuge-Sorvall Legend Series	\$10,658
		Tecan Sunrise Microplate Reader	\$7,955
Tissue Homogenizer		\$17,010	
			\$597,386

*Alterations and Renovations (quote after equipment)

Excluded by Requestor –Vendor Quotes

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ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**YEAR 4 (Year 57)**

Year	Component	Description (includes tax)	Total (with tax)
57	Information Technology Services	Firewall Server	\$13,270
		Backup System Components	\$21,574
	Colony Management and Research Services	Motorized Wheelbarrows (3 x \$5,568)	\$16,704
		Cage Replacement/Repair (10 x \$12,445)	\$124,450
		Manufactured Tent Tarps for Corrals (3)	\$81,504
		Corn Crib Replacement*	\$121,800
	Primate Medicine Services	Radiographic Table	\$17,280
		Anesthesia Machine: GE Aespire 7900 with Cardiocap/5 (replacement)	\$40,293
		X-ray machine TRUDR eSeries 1717G radiology unit (replacement)	\$62,575
		Surgical drill: Anspach Synthes small battery drive with accessories (2 x \$27,508)	\$55,016
	Endocrine Core	Sorvall Legend XTR Refrigerated Centrifuge with Rotor	\$11,215
Liquid Scintillator Counter		\$33,463	
			\$599,144
*Alterations and Renovations (quote after equipment)			

*Alterations and Renovations (quote after equipment)

Excluded by Requestor –Vendor Quotes

p. 607-641

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**YEAR 5 (Year 58)**

Year	Component	Description (includes tax)	Total (with tax)
58	Colony Management and Research Services	Motorized Wheelbarrows (3 x \$5,568)	\$16,704
		Cage Replacement/Repair (10 x \$12,450)	\$124,500
		Replacement Steam Cleaner for Outdoors	\$12,617
		Manufactured Tent Tarps for Corrals (3)	\$81,504
		Corn Crib Replacement*	\$121,800
	Primate Medicine Services	Video Gastroscope	\$103,273
	Endocrine Core	Wizard2 Gamma Counter	\$44,852
	Inhalation Exposure Core	Chambers for Inhalation Exposure (2 x \$47,358)	\$94,716
			\$599,966

*Alterations and Renovations (quote after equipment)

Excluded by Requestor –Vendor Quotes

p. 643-559

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		0.00
Section B, Other Personnel		0.00
Total Number Other Personnel	0	
Total Salary, Wages and Fringe Benefits (A+B)		0.00
Section C, Equipment		2,427,288.00
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		568,400.00
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	568,400.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		2,995,688.00
Section H, Indirect Costs		0.00
Section I, Total Direct and Indirect Costs (G + H)		2,995,688.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

FISpecificAims.pdf

3. Research Strategy*

FIResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

Resource_Sharing_Plan.pdf

Appendix (if applicable)**14. Appendix**

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

SPECIFIC AIMS

Facilities improvement funds are essential to ensure that the California National Primate Research Center (CNPRC) is able to provide optimal animal care and research support. Facilities Improvement funds are permitted up to a maximum of \$600,000 annually per the funding opportunity announcement (FOA PAR-14-226). The proposed use of these funds includes addressing facility and equipment needs integral to colony management (e.g., replacement of corn cribs, cage repairs, replacement of tarps for the field corrals), to replace outdated or nonfunctional equipment necessary to provide uninterrupted services to NIH-funded investigators (e.g., anesthesia machines, cryostat, centrifuges), and to improve Information Technology systems such as those critical to maintain the colony database.

Specific Aim 1. Identify and prioritize requests for the improvement and modernization of the CNPRC.

Plan. The Research Advisory Committee continuously evaluates and assesses needs to ensure optimal operation of the CNPRC. The Committee regularly identifies the most pressing needs, develops a foundation for proposed improvements, and provides a proactive approach and optimized efficiency for use of these funds.

Specific Aim 2. Ensure timely implementation of approved facilities improvement requests.

Plan. The CNPRC interacts with UC Davis campus administration to ensure the timely resolution of infrastructure and equipment needs based on best practices, through standing meetings with key UC Davis administrative personnel and officials, and by expeditious integration of campus facilities staff with on-site CNPRC staff. This collaborative approach will facilitate an efficient and synergistic partnership that benefits the CNPRC.

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT**RESEARCH STRATEGY****INTRODUCTION**

Facilities Improvement funds are critical for the sustainability of the California National Primate Research Center (CNPRC) mission, and the conduct of nonhuman primate research at the highest quality level. The sources of support for the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 1.

Table 1. Support for Facilities Improvement

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$572,654	\$599,426
Program Income from P51	\$0	\$0
Other Sources	\$828,535	\$522,121
TOTAL	\$1,401,189	\$1,121,547

Response to Summary Statement

reviewers' comments

reviewers' comments

SIGNIFICANCE

Facilities Improvement activity has primarily focused on the care and maintenance of nonhuman primates and ensuring regulatory requirements are met. The replacement of key equipment to sustain the mission of the CNPRC has also been a priority. The UC Davis campus supports CNPRC facility services, although there is a distinction between routine maintenance and the needs specific to the CNPRC infrastructure. For example, servicing of buildings for maintenance purposes, replacement of fixed equipment due to wear, and resolution of building systems and fixed equipment failure are generally provided through UC Davis campus-wide resources (see **Administration Overview**). The UC Davis campus also addresses the CNPRC infrastructure needs, such as electrical, gas, and water services, and works with the CNPRC administration to maintain and modernize specific areas of maintenance and improvements comparable to activities conducted for the entire UC Davis campus. Based on the priority of needs and the availability of funds, the UC Davis campus and the CNPRC work together to improve the infrastructure overall. Standard operating procedures and committees are in place to support this collaborative decision-making process and to ensure timely repairs and maintenance (Table 2).

An example of this shared effort is the recent upgrade to a modular building, sited specifically to house critical $\leq -80^{\circ}\text{C}$ freezers that maintain irreplaceable nonhuman primate specimens for research. The HVAC system was determined to be inadequate to prevent a temperature rise during the very hot summer months. To ensure that these crucial samples would not be compromised, the CNPRC and campus administration partnered to support the cost of a proactive upgrade of the HVAC system, completed in 2013 (see Table 3, below).

The CNPRC undergoes regular review from campus Facilities and Building Maintenance Services, including electrical, plumbing, HVAC and refrigeration, communications, and security services. Each of these services provides input and feedback to the CNPRC and the UC Davis campus leadership on a routine basis regarding the need for proactive upgrades. Examples in 2013 include the modular building HVAC upgrade noted above; the need for infrastructure improvements for electrical, plumbing, and gas services in the South Colony; as well as updating the control system in the Quarantine Facility. This comprehensive approach allows the funds

provided by the P51 base grant to be appropriately prioritized and addressed, with rapid response to any regulatory requirements that may arise for which funds are needed.

Table 2. Facilities and Improvement Committees

Committee	Members	Frequency and Function
Project Advisory Committee	Excluded by Requester	<ul style="list-style-type: none"> • Monthly • Address major capital projects (>\$750,000) • Comprehensive representation of campus entities that facilitate discussion of issues related to CNPRC facilities and infrastructure • Consults with the following as needed: <div>Excluded by Requester</div>
Facilities Update Committee		<ul style="list-style-type: none"> • Monthly • Reviews all minor capital construction projects (\$35,000-\$750,000)
Research Advisory Committee		<ul style="list-style-type: none"> • Biweekly • Address research needs and overall CNPRC function and infrastructure • Review proposed research projects in terms of scientific merit, resources available, animal availability, meeting the NPRC mission, applicability, and NIH priority

Progress and Major Accomplishments: Contributions to the CNPRC Mission

During the current funding period, the vast majority of funds have been used to support colony management. The current funding period has shown significant success in obtaining NIH C06 and G20 grants for construction and renovations totaling \$21,167,901 that substantially improved and expanded CNPRC capacity. In addition, successful collaboration with the UC Davis campus provided \$9,537,888 in support of the renovation and expansion of the CNPRC infrastructure. Overall, through application of P51 base grant Facilities Improvement funds, supplements, campus investment, grant support, program income, and non-federal funding sources, funds were provided to support colony management and improve the CNPRC infrastructure. The CNPRC has managed approximately \$37 million in facility improvements; institutional investments as noted above substantially supplemented these activities (Table 3). Projects completed or in progress are noted.

Table 3. Facility Improvements (May 1, 2010 to April 30, 2014)

Improvement	P51 (\$)	Campus (\$)	Other (\$)	Total Cost (\$)	Status
Back-up Generator (<i>Carryforward funds</i>)	303,373	0	Program income: 6,705	310,078	Completed
Cage Washer	0	801,086	NIH G20: 498,644 Non-federal: 193,917	1,493,647	Planning
Clean cage Storage	0	0	NIH C06: 596,404	596,404	Planning
Corn Crib Prototype (<i>Carryforward funds</i>)	49,000	0	Non-federal: 13,242	62,242	Completed
Corn Crib Replacement (<i>Carryforward funds</i>)	147,000	0	0	147,000	Planning
Field Corral Shade Structures (12)	915,201	0	Program income: 183,749 Non-federal: 120,000	1,218,950	Completed (8)
	0	0	NIH C06: 895,675	895,675	Planning (4)
HVAC for Freezer Building	92,549	25,000	0	117,549	Completed
Modular Animal Buildings (2)	960,620	0	0	960,620	Completed
Natural Gas to Field Corrals	0	0	NIH G20: 494,980	494,980	Completed
Perimeter Fence Cameras	0	0	NIH G20: 654,000	654,000	Completed
New ½ Acre Field Corrals (3)	997,000	0	0	997,000	Completed
Renovation of Capture Chutes (3 Field Corrals)	21,270	0	0	21,270	Completed
Renovation of Enrichment Preparation Area	53,370	0	0	53,370	Completed
Renovation of Field Corral	0	0	NIH SPF grant: 470,000	470,000	Completed
Renovation of PET/CT Imaging Facility (P51 Supplement)	491,196	0	0	491,196	Completed
Renovation of South Colony Kitchen (Food Prep)	93,370	0	0	93,370	Completed
Respiratory Diseases Center Building	0	3,999,802	NIH ARRA C06: 14,228,198	18,228,000	Completed
Sewer Line Extension (P51 Supplement)	51,773		0	51,773	Completed
Shop Facility (<i>Carryforward funds</i>)	423,758	0	0	423,758	Completed
Upgrade 6 Perimeter Cameras (to pan-tilt zoom)	0	28,000	0	28,000	Completed
Upgrade to Perimeter Fence Alarm System	0	0	Program income: 256,716	256,716	Completed
Virology and Immunology Building	0	4,684,000	NIH C06: 3,800,000 Non-federal: 200,000	8,684,000	Completed
Wireless Network	180,678	0	0	180,678	In Progress
TOTALS	\$4,780,158	\$9,537,888	\$22,612,230	\$36,930,276	

Total by Funding Category	
P51 Base Grant	\$4,780,158
Program Income	447,170
UC Davis	9,537,888
NIH C06	19,520,277
NIH G20	1,647,624
NIH SPF Grant	470,000
Non-federal	<u>527,159</u>
TOTAL	\$36,930,276

Total expenditures during the current funding period from the P51 base grant for equipment and renovations are summarized in Table 4, and equipment purchased with P51 supplemental funds is shown in Table 5.

Table 4. Equipment and Renovations Supported by the P51 Base Grant (Years 49-52)

Table 4: Equipment and Renovations Supported by the F-31 Base Grant (Years 49-52)				
Year	Dates	Category	Description	Cost (\$)
49	05/01/10 to 04/30/11	Equipment	Replacement Storage Container for Scratch/Feed	9,660
			Kawasaki Mules (3)	24,587*
		Renovation	Field Corral Shade Structures (4)	465,864
			Renovation of South Colony Kitchen (Food Prep)	93,370
		TOTAL		
50	05/01/11 to 04/30/12	Equipment	Steam/Pressure Washer	24,052
			Controlled Drugs Dispensing Cabinet	65,031
			Storage Server	38,803
		Renovation	Field Corral Shade Structures (4)	449,337
			Renovation of Capture Chutes (3 Field Corrals)	21,270
TOTAL				\$598,493
51	05/01/12 to 04/30/13	Equipment	Modular Animal Buildings (2)	598,620
TOTAL				\$598,620
52	05/01/13 to 04/30/14	Equipment	Dell Servers (3)	16,899
			Microscope	27,702
			Light Cycler 96 Instrument	21,285
			Modular Animal Building (see Year 51)	362,000
		Renovation	Freezer Building HVAC System	92,549
			Renovation of Enrichment Preparation Area	53,370
			Wireless Network**	25,678
TOTAL				\$599,483

*\$12,293 paid by P51 Supplement as shown in Table 5; total cost of \$36,880

**Total costs \$180,678; balance was covered by carryforward funds of \$155,000

Table 5. Equipment Purchased with P51 Supplemental Funds (Years 49-52)

Year	Dates	Item	Cost (\$)
49	05/01/10 to 04/30/11	Kawasaki Mules (3)	12,293*
		Robotic Workstation	18,731
		Forklift	32,475
		Advia Centaur	92,013
		Gastrosopes (3)	90,102
		Specific Private Vendor System	68,013
		Real-time PCR instrumentation	140,089
		Liquid Handler for Blood DNA Extraction	121,184
		Fluorochem System	13,408
		Hematology Unit	11,987
		TOTAL	\$600,295
50	05/01/11 to 04/30/12	Autoclave Bioseal Gasket	129,850
		Dell Servers (4)	47,810
		Videoconferencing System	21,002
		Whole Slide Scanner Accessory	48,777
		TOTAL	\$247,439
51	05/01/12 to 04/30/13	Primate Racks and Cages	136,652
		TOTAL	\$136,652
52	05/01/13 to 04/30/14	Laparoscopy	33,886
		TOTAL	\$33,886

*\$24,587 paid by P51 base grant as shown in Table 4; total cost of \$36,880

INNOVATION

While employees of the CNPRC on-site shop are not permitted to perform electrical repairs or installations due to campus policy, they do provide in a cost-efficient manner many timely and innovative solutions necessary to address a host of daily issues that arise. Due to the on-site location the staff (supported by program income) is able to immediately respond to requests for repair of any caging needs, and they are often first to respond when there is an HVAC issue to determine if the problem can be quickly addressed. This provides a clear advantage with regard to safety. They also weld repairs on indoor racks and cages and fabricate many devices for investigators on a recharge basis. The staff maintains all outdoor field corrals and corn cribs, including repairs to the roof and tarps, and they service all of the equipment including the mules, heaters, steam cleaners, lawn mowers, and weed eaters to ensure longevity. A recent example that emphasizes the innovation of the on-site staff is the development of a one-handed method to lock cage squeeze mechanisms.

APPROACH

Plans for the Next Funding Period

Funds requested for the P51 renewal as shown in Table 6 with details in Table 7 and the Budget Justification.

Table 6. Facilities and Improvements Proposed for Next Funding Period (CNPRC Base Grant Years 54-58)

Year	Information Technology Services (\$)	Primate Services* (\$)	Core Services (\$)	Total (\$)
1 (54)	30,693	388,849	179,884	599,426
2 (55)	12,539	374,945	212,282	599,766
3 (56)	7,721	548,799	40,866	597,386
4 (57)	34,844	519,622	44,678	599,144
5 (58)	0	460,398	139,568	599,966
TOTAL	\$85,797	\$2,292,613	\$617,278	\$2,995,688

*Animal Resources

Specific Aim 1. Identify and prioritize requests for the improvement and modernization of the CNPRC.

Each major infrastructure area identifies equipment and alteration/renovation needs. For example, Primate Services evaluates the needs for the care and support of the nonhuman primate colonies. The managers, veterinarians, and related staff provide information to the Assistant Director for Colony Management and Research Services and the Associate Director for Primate Services with a justification of the need. Items requested are prioritized and reviewed with the Associate Director for Administration and Operations, then brought to the Research Advisory Committee for evaluation and prioritization. The same process is used for Core Services and Information Technology Services, or any other needs that might arise. Each area is responsible for obtaining quotes for proposed equipment purchases from university-approved vendors. The UC Davis campus provides estimates for alterations and renovations. The amounts shown are based on current estimates or the price quotes currently available. During the process of review and prioritization, there may be other items that at the time are determined to be of greatest priority based on need. If more items are requested then can be accommodated for, a master list is maintained by the Director and other funding sources are pursued (e.g., equipment grants, non-federal sources). UC Davis has a process through which funds can be requested for CNPRC operations. These requests are considered by the Vice Chancellor for Research when submitted, and for funding in the following fiscal year.

Table 7. Facilities and Improvements Proposed for the Next Funding Period (CNPRC Base Grant Years 54-58)

Year	Component	Description	Amount (\$)	Quantity	Total (\$)
54	Information Technology Services	Windows Domain Controller	5,117	2	10,234
		X-Ray Repository and Database	11,967	1	11,967
		File Server	8,492	1	8,492
	Colony Management and Research Services	Motorized Wheelbarrows	5,568	2	11,136
		Cage Replacement/Repair	12,445	10	124,450
		Mule Vehicle Replacement	12,930	1	12,930
		Corn Crib Replacement*	40,600	3	121,800
	Primate Medicine Services	Dental system	12,950	2	25,900
		Dental X-Ray	44,033	1	44,033
	Pathology Services	MacroView D Mobile Digital Imaging System	48,600	1	48,600
	Endocrine Core	Rainin Liquidator 96	14,575	1	14,575
		Isotemp Freezer	5,928	1	5,928

	Immunology and Pathogen Detection Resources Core	MagNA Pure LC 2.0	33,210	1	33,210
	Multimodal Imaging Core	GE PACS System for PET/CT	49,086	1	49,086
		Metamorph Microscope Control Software	12,865	1	12,865
		Leica RM2255 Microtome	24,507	1	24,507
		Olympus Silicone Oil Immersion Objective Lenses: 40x and 60x	24,701	1	24,701
		Sutter Instruments Lambda VF-5 Tunable Filter Changer	15,012	1	15,012
				Total Y54	599,426
55	Information Technology Services	Rack Replacement	12,539	1	12,539
	Colony Management and Research Services	Motorized Wheelbarrows	5,568	4	22,272
		Cage Replacement/Repair	12,445	10	124,450
		Replacement Steam Cleaners for Outdoors	12,617	1	12,617
		Manufactured Tent Tarps for Corrals	27,168	3	81,504
		Corn Crib Replacement*	40,600	3	121,800
	Primate Medicine Services	Electrocautery	6,151	2	12,302
	Behavior Research Services Core	Tobii TX300 Eye Tracker	56,938	1	56,938
	Immunology and Pathogen Detection Resources Core	Real-time PCR Thermocycler	21,384	1	21,384
		Luminex Reader	68,908	1	68,908
	Multimodal Imaging Core	Leica CM1950 Cryostat	53,204	1	53,204
		Prior Proscan III Microscope Stage Controller	5,924	2	11,848
					Total Y55
56	Information Technology Services	Production Printer Replacement	7,721	1	7,721
	Colony Management and Research Services	Motorized Wheelbarrows	5,568	4	22,272
		Cage Replacement/Repair	12,445	10	124,450
		Mule Vehicle Replacement	12,930	1	12,930
		Manufactured Tent Tarps for Corrals	27,168	3	81,504
		Corn Crib Replacement*	40,600	2	81,200
	Primate Medicine Services	Anesthesia machine: GE Aespire 7900 with Cardiocap/5 (replacement)	40,293	2	80,586
		Bronchoscope	109,259	1	109,259
	Pathology Services	Olympus BX46 Microscope/Camera with Cellsense software	36,598	1	36,598
	Endocrine Core	Nor-Lake Incubator	5,243	1	5,243
	Immunology and Pathogen Detection Resources Core	Tabletop Centrifuge-Sorvall Legend Series	10,658	1	10,658
		Tecan Sunrise Microplate Reader	7,955	1	7,955
		Tissue Homogenizer	17,010	1	17,010
				Total Y56	597,386
57	Information Technology Services	Firewall Server	13,270	1	13,270
		Backup System Components	21,574	1	21,574
	Colony Management and Research Services	Motorized Wheelbarrows	5,568	3	16,704
		Cage Replacement/Repair	12,445	10	124,450
		Manufactured Tent Tarps for Corrals	27,168	3	81,504
		Corn Crib Replacement*	40,600	3	121,800
	Primate Medicine Services	Radiology Table	17,280	1	17,280
		Anesthesia machine: GE Aespire 7900 with Cardiocap/5 (replacement)	40,293	1	40,293
		X-ray machine TRUDR eSeries 1717G Radiology Unit (replacement)	62,575	1	62,575
		Surgical drill, Anspach Synthes	27,508	2	55,016

	Endocrine Core	Sorvall Legend XTR Refrigerated Centrifuge with Rotor	11,215	1	11,215
		Liquid Scintillator Counter	33,463	1	33,463
				Total Y57	599,144
58	Colony Management and Research Services	Motorized Wheelbarrows	5,568	3	16,704
		Cage Replacement/Repair	12,450	10	124,500
		Replacement Steam Cleaner	12,617	1	12,617
		Manufactured Tent Tarps for Corrals	27,168	3	81,504
		Corn Crib Replacement*	40,600	3	121,800
	Primate Medicine Services	Video Gastroscope	103,273	1	103,273
	Endocrine Core	Wizard2 Gamma Counter	44,852	1	44,852
	Inhalation Exposure Core	Chambers	47,358	2	94,716
				Total Y58	599,966
*Alterations and Renovations; based on prototype (noted in Table 3)				TOTAL	2,995,688

*Alterations and Renovations; based on prototype (noted in Table 3)

Specific Aim 2. Ensure timely implementation of approved facilities improvement requests.

The timely implementation of Facilities Improvement is critical for an efficient and effective program. The CNPRC has a flexible approach to address unexpected challenges that may arise that necessitate modifications of prior plans. An example is provided by the proactive recognition of a need for additional animal space, which required the purchase of two animal modular buildings. Although not originally planned in the prior renewal application, purchase of these modular buildings for placement on an existing cement pad provided the most effective use of Facilities Improvement funds. This change in request was submitted with the annual NIH budget report and subsequently approved. The new space allowed for needed warranty repairs in the animal building that could not have taken place without this additional housing. Thus, by a flexible approach, the CNPRC was able to continue ongoing research projects while providing the necessary upgrades and improvements. This is an example of needs that arise in a dynamic environment that must be met. Expertise in architectural and project management services is provided by the UC Davis campus and, combined with the expertise of staff at the CNPRC ensures the timely accomplishment of facility improvements.

The overall facility consists of 175,409 sq. ft., which includes research laboratories, an inhalation exposure facility, indoor animal housing, a Quarantine Facility, animal support areas, and administrative space (Table 8, see Figure 1). The field corrals and corn cribs (outdoor housing) encompasses [redacted] Cons [redacted] Specific Animal Location was also recently completed for the Respiratory Disease Center building, which has increased laboratory, and inhalation exposure space by 19,000 sq. ft. Included on the Primate Center grounds is the Center for Comparative Medicine that provides laboratory and office space for Core Scientists in the Infectious Diseases Research Unit. The UC Davis Translational Human Stem Cell Shared Research Facility, also located on-site, is a campus-wide facility dedicated to stem cell research and training, and a component of the UC Davis Stem Cell Program (see Reproductive Sciences and Regenerative Medicine Research Unit). The CNPRC currently employs over 300 individuals (academics, administrative, information technology, research support, animal care), and provides training and mentoring opportunities for students at all career stages (see other sections of this application).

Table 8. CNPRC Administration, Laboratory, Animal Housing, and Support Space

Category	Name	Square Footage	Use
Administration	Primate Center Administration	10,010	Administration
	Primate Security Kiosk	144	Admin/Security
	Total Administration	10,154	
Laboratory	Specific Animal Location		Laboratory
			Laboratory
			Laboratory
			Laboratory
			Laboratory
			Exposure Facility
			PET/CT Facility
			Laboratory Support Office/Laboratory
	Total Laboratory	63,114	
Animal Housing and Support	Specific Animal Location		Animal Housing
			Animal Housing
			Animal Housing
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			Animal Housing
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
			Animal Support
	Total Animal Housing and Support	102,141	
OVERALL TOTAL		175, 409 sq. ft.	

Figure 1. Sitemap of the CNPRC grounds. CCM=Center for Comparative Medicine

Specific Animal Location



ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

ADMINISTRATIVE SERVICES: FACILITIES IMPROVEMENT

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Colony Management and Research Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename CM_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	CM_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	CM_FacilitiesandOtherResources.pdf
11. Equipment	CM_Equipment_.pdf

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

ABSTRACT

The primary goal of Primate Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. The **Colony Management and Research Services** component addresses animal care and research service including environmental enrichment, staff training, and quality assurance to meet the needs of colony animals and investigators. The Colony Management and Research Services team aids in providing oversight for the animals at the CNPRC, which includes three species: rhesus macaques (*Macaca mulatta*), a small colony of long-tailed macaques (*Macaca fascicularis*), and titi monkeys (*Callicebus cupreus*). These nonhuman primate colonies and the support provided by the Colony Management and Research Services team ensure that a wealth of opportunities are available to meet the needs of investigators locally, regionally, and nationally for studies across the lifespan, and through the following Specific Aims: (1) Provide outstanding colony management and infrastructure support to maintain and utilize a national resource of nonhuman primates for translational research, (2) Ensure high quality training in all areas of animal care and colony management, and (3) Promote and support responsible conduct of research and animal care.

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: A 450 sq. ft. laboratory in the animal quarters is used for project support activities (e.g., drug preparation, sample processing and packaging, reagent preparation, diet preparation, shipments). This space is also used to provide day use laboratory space for visiting scientists, and includes a centrifuge, scale, a refrigerator, and $\leq -20^{\circ}\text{C}$ and $\leq -80^{\circ}\text{C}$ freezers.

Clinical: See **Primate Medicine Services**.

Animal: Indoor housing includes Specific Animal Location indoor cages in BSL2+ housing, 64 cages in quarantine, 40 cages for new world social housing, and several nurseries. Outdoor housing includes Specific Animal Location half-acre field corrals, Specific Animal Location corn crib units, Specific Animal Location pads for animal holding.

Computer: Twenty-seven computer workstations are available for staff use and are equipped with networked systems (10 workstations). Workstations are also available in the Animal Care Breakroom for general use. Three laser printers are available.

Office: Shared office space is provided for staff and for animal records use, meeting and training space, and lunch rooms and break areas. Office space and administrative support is provided for Colony Management and Research Services technicians, Enrichment Staff, Operations Manager, Quality Assurance Coordinator, Data Entry Staff, and the Assistant Director for Colony Management and Research Services (10 offices including 1,200 sq. ft.). A staging room for procedures and recordkeeping is maintained in the animal quarters. The Animal Care office and locker rooms house the supervisors and staff in one central location (1,400 sq ft. of office, meeting, and training space as well as locker room and breakroom space).

Other: The CNPRC is a part of the UC Davis AAALAC-accredited program.

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

EQUIPMENT

Tractors for the outdoor colony (2), Kawasaki mules for delivery of supplies and animals (8), full size cage washers (2), large portable steamers on trailers for outdoor cage sanitation (2), motorized wheelbarrows (4), 20 digital scales for animal weights, a tabletop centrifuge, and $\leq -80^{\circ}\text{C}$ and $\leq -20^{\circ}\text{C}$ freezers.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	.	0.0	27,225.00	10,858.00	38,083.00
2.					Core Scientist			0.0	0.0	9,075.00	3,036.00	12,111.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	50,194.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Assist Dir for Colony Management and Research Services	EFFORT			80,343.00	32,043.00	112,386.00
1	Affiliate Scientist	Excluded by Requester			14,756.00	5,885.00	20,641.00
1	Quality Assurance Specialist	Excluded by Requester			17,684.00	9,355.00	27,039.00
1	Facilities Manager	Excluded by Requester			18,327.00	9,695.00	28,022.00
1	Colony and Research Services Manager	Excluded by Requester			43,752.00	23,145.00	66,897.00
1	Training Manager	Excluded by Requester			22,681.00	11,998.00	34,679.00
6	Total Number Other Personnel					Total Other Personnel	289,664.00
Total Salary, Wages and Fringe Benefits (A+B)							339,858.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,000.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,000.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,594,605.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping Costs	1,500.00
9. SPF Testing- Immunology and Pathogen and Pedigree analysis- Vet Diagnostics Lab	116,000.00
10. AALAS Test fees	4,175.00
Total Other Direct Costs	3,716,280.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	4,062,138.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	4,062,138.00	922,105.00
Total Indirect Costs			922,105.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	4,984,243.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: CM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	11,489.00	38,714.00
2.					Core Scientist			0.0	0.0	9,075.00	3,196.00	12,271.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						50,985.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Assist Dir for Colony Management and Research Services	EFFORT			83,505.00	35,239.00	118,744.00
1	Affiliate Scientist	Excluded by Requester			15,347.00	6,476.00	21,823.00
1	Quality Assurance Specialist	Excluded by Requester			18,392.00	10,174.00	28,566.00
1	Facilities Manager	Excluded by Requester			19,060.00	10,543.00	29,603.00
1	Colony and Research Services Manager	Excluded by Requester			45,502.00	25,170.00	70,672.00
1	Training Manager	Excluded by Requester			23,589.00	13,049.00	36,638.00
6	Total Number Other Personnel					Total Other Personnel	306,046.00
Total Salary, Wages and Fringe Benefits (A+B)							357,031.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,180.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,180.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,702,294.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping Costs	1,545.00
9. SPF Testing- Immunology and Pathogen and Pedigree analysis- Vet Diagnostics Lab	119,480.00
10. AALAS Test fees	4,300.00
Total Other Direct Costs	3,827,619.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	4,190,830.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	4,190,830.00	951,318.00
Total Indirect Costs			951,318.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	5,142,148.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: CM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	11,893.00	39,118.00
2.					Core Scientist			0.0	0.0	9,075.00	3,305.00	12,380.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						51,498.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Assist Dir for Colony Management and Research Services	Excluded by Requester	EFFORT		86,899.00	37,960.00	124,859.00
1	Affiliate Scientist	Excluded by Requester			15,961.00	6,972.00	22,933.00
1	Quality Assurance Specialist	Excluded by Requester			19,127.00	10,925.00	30,052.00
1	Facilities Manager	Excluded by Requester			19,822.00	11,322.00	31,144.00
1	Colony and Research Services Manager	Excluded by Requester			47,322.00	27,029.00	74,351.00
1	Training Manager	Excluded by Requester			24,532.00	14,012.00	38,544.00
6	Total Number Other Personnel				Total Other Personnel		321,883.00
Total Salary, Wages and Fringe Benefits (A+B)							373,381.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,365.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,365.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,815,365.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping Costs	1,591.00
9. SPF Testing- Immunology and Pathogen and Pedigree analysis- Vet Diagnostics Lab	123,064.00
10. AALAS Test fees	4,429.00
Total Other Direct Costs	3,944,449.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	4,324,195.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	4,324,195.00	981,592.00
Total Indirect Costs			981,592.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	5,305,787.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: CM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester					Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	12,247.00	39,472.00
2.						Core Scientist			0.0	0.0	9,075.00	3,405.00	12,480.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						51,952.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Assist Dir for Colony Management and Research Services	EFFORT			87,768.00	39,481.00	127,249.00
1	Affiliate Scientist	Excluded by Requester			16,204.00	7,289.00	23,493.00
1	Quality Assurance Specialist	Excluded by Requester			19,701.00	11,587.00	31,288.00
1	Facilities Manager	Excluded by Requester			20,615.00	12,125.00	32,740.00
1	Colony and Research Services Manager	Excluded by Requester			49,215.00	28,947.00	78,162.00
1	Training Manager	Excluded by Requester			25,513.00	15,007.00	40,520.00
6	Total Number Other Personnel					Total Other Personnel	333,452.00
Total Salary, Wages and Fringe Benefits (A+B)							385,404.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,556.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,556.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,928,391.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping Costs	1,639.00
9. SPF Testing- Immunology and Pathogen and Pedigree analysis- Vet Diagnostics Lab	126,756.00
10. AALAS Test fees	4,562.00
Total Other Direct Costs	4,061,348.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	4,453,308.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	4,453,308.00	1,010,901.00
		Total Indirect Costs	1,010,901.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	5,464,209.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: CM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	.	0.0	27,225.00	12,623.00	39,848.00	
2.					Core Scientist			0.0	0.0	9,075.00	3,504.00	12,579.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person		52,427.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Assist Dir for Colony Management and Research Services	EFFORT			88,646.00	41,102.00	129,748.00
1	Affiliate Scientist	Excluded by Requester			16,281.00	7,549.00	23,830.00
1	Quality Assurance Specialist	Excluded by Requester			19,512.00	11,824.00	31,336.00
1	Facilities Manager	Excluded by Requester			20,326.00	12,318.00	32,644.00
1	Colony and Research Services Manager	Excluded by Requester			49,708.00	30,123.00	79,831.00
1	Training Manager	Excluded by Requester			25,769.00	15,616.00	41,385.00
6	Total Number Other Personnel					Total Other Personnel	338,774.00
Total Salary, Wages and Fringe Benefits (A+B)							391,201.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,753.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,753.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	4,045,652.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping Costs	1,688.00
9. SPF Testing- Immunology and Pathogen and Pedigree analysis- Vet Diagnostics Lab	130,558.00
10. AALAS Test fees	4,699.00
Total Other Direct Costs	4,182,597.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	4,580,551.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	4,580,551.00	1,039,785.00
Total Indirect Costs			1,039,785.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	5,620,336.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: CM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Associate Director for Primate Services	% Effort			
	Assistant Director for Colony Management and Research Services				
	Affiliate Scientist				
	Quality Assurance Specialist				
	Colony Operations Manager				
	Colony and Research Services Manager				
	Training Manager				
	Core Scientist				
<i>Technical Support (95)</i>	<i>Technicians</i>	0	100	0	100
<i>Shop Staff (6)</i>	<i>Mechanicians</i>	0	100	0	100
Excluded by Requester	<i>Administrative Assistant</i>	% Effort			

Individuals shown in italics are not supported by the P51 base grant; their salary support is provided by Program Income

Excluded by Requester **DVM, DACLAM, Associate Director for Primate Services** EFFORT months % Effort

Excluded by is Associate Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine, the Associate Director for Primate Services, and Chief Veterinarian. He has responsibilities for all aspects of the nonhuman primate colonies and related services provided through Colony Management and Research Services.

Excluded by Requester **Assistant Director for Colony Management and Research Services** EFFORT months
% Effort Excluded by Requester reports directly to the Associate Director for Primate Services. is responsible for the overall management of the nonhuman primate colonies including daily operations, management production and research colonies, supervision of all staff, budget expenditures, training, long range planning for the colony, and management of animal resources including the selection and assignment of animals. Monthly recharge billing is monitored, as well as rate development for recharge procedures. Excluded by Requester responsible for project budgeting, assisting investigators with budgets for grant and contract submission animal sales.

Excluded by Requester **DVM MPH, PhD, Affiliate Scientist** EFFORT months % Effort Excluded by Requester has been working with Excluded by and the veterinary staff on the study of idiopathic chronic diarrhea (see Primate Medicine Services). Excluded by developed a standardized template for these studies to ensure that result-focused trials are performed consistently with limited confounding variables, permitting comparisons between studies and identification of potentially useful interventions. Excluded by Requester will focus on the impact of idiopathic chronic diarrhea and related subjects on colony animals.

Excluded by Requester **Quality Assurance Specialist** EFFORT months % Effort Excluded by Requester provides quality assurance/quality control (QA/QC) services for all aspects of colony management, and for the conduct of Good Laboratory Practice (GLP) studies performed according the requirements for the Food and Drug Administration (FDA). From a colony management perspective, areas of QA/QC include water quality assessment, chow analysis, environmental monitoring, equipment calibration, microbiological testing, and controlled drug administration. Excluded by Requester is also responsible for maintaining all standard operating procedures (SOPs) and ensuring they are updated on a regular basis.

Excluded by Requester

Colony Operations Manager

EFFORT

months

% Effort

Excluded by Requester

is responsible for coordinating the CNPRC shop for day-to-day facility operations, and managing all aspects of facility needs including security. He is the point-of-contact for facility and environmental monitoring needs, the scheduling and daily assessments of facility repair and maintenance, minor renovations for upgrade animal facility, and coordination with UC Davis campus groups responsible for facilities maintenance and repair.

Excluded by Requester

Excluded by Requester

Colony and Research Services Manager

EFFORT

months

% Effort

Excluded by Requester

supervises centralized staff that provide technical support to investigators as requested, and all related activities. She assists the Assistant Director for Colony Management and Research Services with monthly recharge billing, management of the colonies, budget expenditures, and developing project budgets for grant and contract submissions. She also coordinates activities between the different Primate Services components for colony and research needs, and provides oversight for indoor enrichment and pairing activities according to the Primate Well-Being Plan.

Excluded by Requester

Training Manager

EFFORT

months

% Effort

Excluded by Requester

has developed and implemented a state-of-the-art training program for all areas related to animal care, colony management, and research. S is responsible for one-on-one training for new employees and group training for annual re- or existing work groups, students, and visiting investigators and trainees regularly and updates current areas of instruction. He also leads the training classes required for American Association for Laboratory Animal Science (AALAS) certification at all levels.

Excluded by Requester

Excluded by Requester

Excluded by Requester

Core Scientist

EFFORT

months

% Effort

Excluded by Requester

is Professor-in-Residence, Department of Obstetrics and Gynecology, School of Medicine, and a Core Scientist in the Reproductive Sciences and Regenerative Medicine Research Unit. She has extensive expertise in gamete biology and cryopreservation techniques, and over 20 years experience working with nonhuman primates on assisted reproductive techniques including artificial insemination protocols. She will be responsible for the collection and cryopreservation of rhesus monkey sperm.

A total of 95 technical staff members (e.g., Animal Resource Supervisors, Animal Care Technicians, Project Technicians, Enrichment Technicians) address all aspects of Colony Management and Research Services as described in the Research Strategy section. In addition, a staff of 6 mechanics provide support on-site for facilities (see Administration and Operations Services) and investigator needs (e.g., installing equipment, fabrication of testing equipment). Along with Administrative Assistant Maureen Touchstone (primary responsibility for entry of all animal colony demographic data updated every 24 hours, work order processing, billing), these staff members are supported by Program Income.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are listed in the **Facilities Improvement** section.

TRAVEL

\$6,000 is requested (4 x \$1,500) for Excluded by Requester to attend the Annual AALAS National Meeting, Excluded by Requester to attend the National Quality Assurance Meeting, and for Excluded by Requester to travel to another National Research Center to share training strategies.

Excluded by Requester

Excluded by Requester

SUPPLIES

\$3,541,605 is requested for per diem for 1,707 animals supported by the P51 base grant including the long-term production colonies, indoor colonies, and animals in the research project pool in between project assignments. The number of animals is based upon annualized animal days. This includes rhesus monkeys and titi monkeys; the long-tailed macaques are supported by research projects. Daily per diem includes feeding, cleaning, sanitation, environmental enrichment, preventive health care, and veterinary care. The rate,

consistent with the rate charged to research projects, is developed in compliance with the NIH Cost Analysis and Rate Setting Manual and updated annually.

\$50,000 is requested for short-term workup of animals and to support colony-related findings identified by research and professional staff that will contribute to improvement of animal resources, and/or improved husbandry and management practices.

\$3,000 is requested for sperm cryopreservation supplies including extender and media components, cryoprotectants, straws, liquid nitrogen, pipettes, and other laboratory supplies used for sperm cryobanking.

OTHER EXPENSES

\$86,000 is requested for Specific Pathogen Free (SPF) testing in the Immunology and Pathogen Detection Resources Core (see Core). The SPF animals are tested from 1 to 4 times annually based on age and SPF status. Included is testing for Herpes B-virus, simian retrovirus (SRV), simian T-cell leukemia virus (STLV), and simian immunodeficiency virus (SIV).

\$30,000 is requested for pedigree analysis in the UC Davis Veterinary Genetics Laboratory. Blood samples are collected from all newborns in the field corrals for this analysis.

\$1,000 is requested for overnight shipping costs of specimens in required shipping containers from any animals involved in a human exposure. Samples are collected for shipment to the National Herpes B Laboratory to determine B-virus status at the time of the potential human exposure to B-virus seropositive animals.

\$4,175 is requested for testing fees for employees to complete the AALAS technical certifications.

\$500 is requested for sperm cryopreservation shipping costs.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		257,056.00
Section B, Other Personnel		1,589,819.00
Total Number Other Personnel	30	
Total Salary, Wages and Fringe Benefits (A+B)		1,846,875.00
Section C, Equipment		0.00
Section D, Travel		31,854.00
1. Domestic	31,854.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		19,732,293.00
1. Materials and Supplies	19,086,307.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	7,963.00	
9. Other 2	615,858.00	
10. Other 3	22,165.00	
Section G, Direct Costs (A thru F)		21,611,022.00
Section H, Indirect Costs		4,905,701.00
Section I, Total Direct and Indirect Costs (G + H)		26,516,723.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	6,678,300.00	Animal Sales and Services; Per Diem
2	7,045,607.00	Animal Sales and Services; Per Diem
3	7,433,115.00	Animal Sales and Services; Per Diem
4	7,841,936.00	Animal Sales and Services; Per Diem
5	8,273,242.00	Animal Sales and Services; Per Diem

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

CM_SpecificAims.pdf

3. Research Strategy*

CM_ReserachStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

CM_Vertebrate_Animals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

Resource_Sharing_Plan.pdf

Appendix (if applicable)**14. Appendix**

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

SPECIFIC AIMS

The Colony Management and Research Services team provides support for all indoor and outdoor-housed monkeys with a current census of approximately 5,000 animals. The rhesus macaque (*Macaca mulatta*) is the primary species housed at the California National Primate Research Center (CNPRC), with subsets of animals defined by age and viral status. There are also two small colonies of long-tailed macaques (*Macaca fascicularis*) and titi monkeys (*Callicebus cupreus*) that are used for specialized research projects. The experienced Colony Management and Research Services team manages this large and complex colony providing continuous care, 24 hours a day, 7 days a week, as well as a range of research support capabilities to meet investigator needs.

Specific Aim 1. Provide outstanding colony management and infrastructure support to maintain and utilize a national resource of nonhuman primates for translational research.

Plan. The overriding goal is to provide a well-managed colony and well-trained workforce to support all Colony Management and Research Services operations. The efficient management of the animal colonies is essential to ensure a readily available source of healthy animals and associated resources to maximize research opportunities for investigators. This service function closely integrates with all Primate Services components as well as the National Primate Research Center (NPRC) Consortium where best practices are shared for continued improvements and refinements. Staff respond to the dynamic research environment, and provide a central hub for the flow of information to all Primate Services entities to ensure that overall goals in colony management and research support are achieved.

Specific Aim 2. Ensure high quality training in all areas of animal care and colony management.

Plan. An essential effort is focused on the training of staff in daily husbandry, care, and management to meet regulatory requirements and ensure expectations are achieved. Working knowledge of daily husbandry and animal needs, appropriate animal handling techniques, the importance of infectious disease control, safe practices training, and refined technical procedures that are targeted to the species is critical to the CNPRC mission. One-on-one training, group training, and on-the-job training provided by dedicated training specialists ensure that the knowledge and skillset required are achieved and sustained. The training program is focused on all aspects of job performance, with an emphasis on consistency, safe practices, and compliance. Training is also provided for all levels of the American Association for Laboratory Animal Science Technician Certification Program, and staff members are encouraged to participate in and meet the qualifications for certified animal care technicians.

Specific Aim 3. Promote and support responsible conduct of research and animal care.

Plan. A central focus is to ensure the highest quality standards of animal care and research conduct for the well-being of the animals, and to meet the CNPRC scientific mission. The goal is to continue to evaluate and review established guidelines, standard operating procedures, and practices to ensure that standards of excellence are consistently maintained.

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

RESEARCH STRATEGY

INTRODUCTION

A primary goal of Colony Management and Research Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. The CNPRC vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards for animal research at UC Davis and the CNPRC. At UC Davis, a **single Institutional Animal Care and Use Committee (IACUC)** oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met.

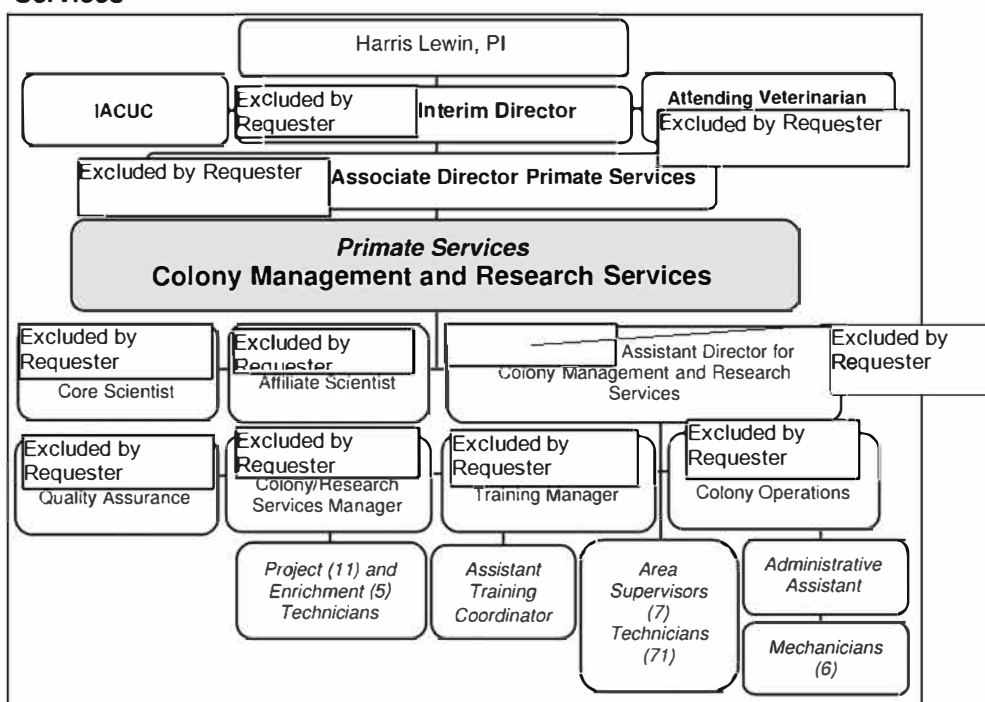
The CNPRC leadership, Core Scientists, and staff work together as an integrated team with the IACUC and the overall UC Davis Animal Care Program infrastructure to ensure that investigators nationwide can access the unique resources and capabilities available. This is accomplished by:

- State-of-the-art husbandry for ~5,000 nonhuman primates in a variety of housing conditions. Efficient management of the animal colony is essential to facilitate research utilization.
- Specific management programs for different animal colonies within the CNPRC including various levels of Specific Pathogen Free (SPF) rhesus monkeys from infants to aged individuals, and a unique colony of titi monkeys.
- A team of highly trained research technicians with expertise in working with the nonhuman primate model to support colony management needs and provide research support to individual investigators as requested.
- Manage 24 outdoor field corrals for animal production and to serve as a dynamic laboratory for investigators conducting research at the CNPRC. Many of the field corrals have been managed as stable breeding populations for over 30 years. These multigenerational, complex social communities provide a unique resource to study health across the lifespan.

As one of seven National Primate Research Centers (NPRCs), the CNPRC has a significant responsibility to investigators, the NIH, the public, and the animals under our care. Over the past 53 years of operation the CNPRC has continuously strived to improve and refine the management of nonhuman primates. Through Primate Services, the CNPRC has been a leader in the development of outdoor breeding corrals, colony pedigrees, providing for the enrichment of the captive environment, and establishing SPF populations of rhesus macaques. The CNPRC is working with the six other NPRCs through the **NPRC Consortium** to continually improve and maintain the high quality of the research primate and best practices for colony management and care. Primate Services is also committed to meeting the research needs of investigators at the CNPRC. This mission requires careful balancing of these needs with the regulatory requirements to ensure optimal outcomes and successful projects.

Members of the Colony Management and Research Services team are shown in Figure 1 and Table 1.

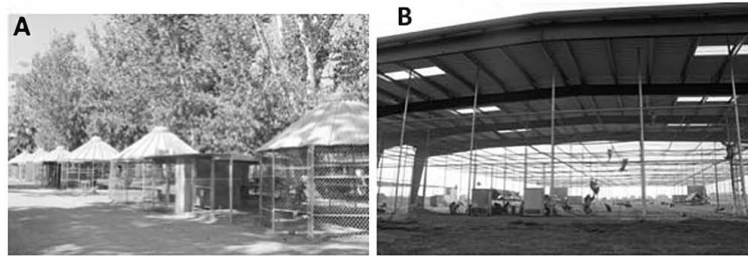
Figure 1. Organizational Chart: Colony Management and Research Services



stages of life. Each of these groups is utilized in NIH-supported research at the CNPRC. During the current funding period, the long-tailed macaque colony was dispersed to other NPRCs with a small group of 12 animals maintained. The Chinese SPF colony, consisting of 125 animals, was relocated to the Oregon NPRC in 2013 when the supporting NIH grant ended.

Outdoor Housing and Production. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, group housing in corn cribs (which can accommodate approximately 12-20 individuals), and half-acre outdoor field corrals each of which can house up to approximately 150 animals (Figure 2). The advantage of this colony is that it can cost effectively provide

Figure 2. Rhesus monkeys are housed as follows: indoor paired housing, corn cribs (A), or half-acre field corrals (B).



sufficient numbers of healthy animals for research with known life histories and demographic profiles. The long-term production colony is housed in the field corrals with a current population of 2,800. These animals provide infants, juveniles, adults, and aged animals. This housing also provides a very valuable opportunity for the investigation of social behavior. As the population of the field corrals has grown, the CNPRC has split these cages in an effort to decrease the density, and to populate new

production corrals. Input from **Behavior Management Services** and **Genetics Management Services** aids in implementing these events. The live birth rate remains constant (approximately 80%), resulting in an average of 600 live births in the outdoor housing areas annually (Table 3). The field corrals continue to be the primary breeding source for the CNPRC. This colony provides high quality rhesus macaques that are available for research or sale to other NPRCs and approved institutions. In the current funding period, there has been an increasing use of the field corrals in observational research using animals in a natural social environment.

Table 3. Field Corral Production (May 1, 2010 to April 30, 2014)

Grant Year	Females (N)	Conceptions	Live Births (N)	Live Birth Rate (%)	Birth Rate/Conceptions (%)
2010 - 2011	759	675	582	76.7	86.2
2011 - 2012	816	689	628	77.0	91.2
2012 - 2013	773	671	621	80.3	92.6
2013 - 2014*	652	590	528	80.9	90.4
TOTALS	3,000	2,625	2,359	78.6	87.5

*Estimated

Each year animals are harvested from the field corrals as needed for research projects. They are also removed from the field corrals on occasion for behavior management reasons, and may be relocated to another housing area or assigned to a project (Table 4).

Table 4. Field Corral Harvests (May 1, 2010 to April 30, 2014)

Grant Year	Sex	Infants (N)	Juveniles (N)	Adults (N)	Total
2010 - 2011	Male	53	129	119	301
	Female	45	101	172	318
2011 - 2012	Male	50	245	119	414
	Female	68	149	249	466
2012 - 2013	Male	32	73	126	231
	Female	45	106	155	306
2013 - 2014	Male	47	112	127	286
	Female	54	82	109	245
TOTALS	Male	181	559	491	1,227
	Female	213	438	685	1,334

Approximately 700 rhesus monkeys are housed outdoors in corn cribs, which provide options for caging in smaller social groups. Included in this population are young rhesus monkeys in peer housing with an adult, as well as harem breeding groups consisting of one adult male and multiple cycling females of reproductive age.

Typically, these females would have a first birth in this outdoor setting. The corn cribs are also an excellent housing option for vaccine studies and for investigators in need of social housing to monitor behavior.

Indoor Housing and Monitoring. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and Animal Welfare Act. Typical nonhuman primate rooms provide 10-15 air changes per hour and are negatively pressurized relative to anterooms/corridors and the outside. Lighting is provided by fluorescent lights which are controlled by timers (12 hours on/12 hours off), and room temperature is maintained between 68°F and 80°F, depending on the species and age of the animals in the room. Emergency generator power is provided for all animal rooms. Power failures, major temperature fluctuations, and other environmental disturbances are alarmed directly to Campus Physical Plant Services and are monitored by CNPRC personnel on a daily basis. The Colony Operations Supervisor and the Maintenance Shop Supervisor carry pagers 24 hours/day and are alerted to any environmental monitoring alarms and rooms that may be out of the acceptable temperature and humidity range.

The indoor colony is housed in caging with partitions to allow daily socialization of compatible pairs. The indoor population also includes animals housed in nurseries, weanling groups, and the aged colony (see **National Institute on Aging Colony**). The indoor time-mate colony provides investigators with pregnancies of known gestational age that are monitored closely during pregnancy. The time-mate colony population is approximately 300 animals (males and females). Females are evaluated annually for continued inclusion in the time-mate program. Screening for simian immunodeficiency virus (SIV), simian retrovirus (SRV), and simian T-cell leukemia virus (STLV) is conducted annually with these evaluations. Based on menstrual cycles, mating typically begins in October and continues through May, with the majority of conceptions in November and December. Females are time-mated based on cycle length for two days (Table 5).

Table 5. Time-Mate Production Colony (May 1, 2010 to April 30, 2014)

Grant Year	Females Bred (N)	Conception Rate	Project Use
2010 - 2011	276	76%	89%
2011 - 2012	306	75%	70%
2012 - 2013	238	73%	76%
2013 - 2014	227	72%	77%
TOTALS	1,047	74%	78%

Pregnancies are detected by ultrasound in early gestation using established protocols developed by Dr. Tarantal (**Reproductive Sciences and Regenerative Medicine Research Unit**; also see **Multimodal Imaging Core**), and are assigned to IACUC-approved projects on a rotational basis, and based on animal history. Once assigned, ultrasound evaluations are dictated by study needs.

Computerized reproductive histories are maintained for all breeding females in the WebVitals program, which is maintained by the CNPRC **Information Technology Services** team (see below). All animals are monitored throughout the breeding season, and an annual evaluation is conducted during the non-breeding summer months with Excluded by Requester (Senior Veterinary Manager, **Primate Medicine Services**). Animals with marginal reproductive histories are removed from the breeding colony and assigned to other uses.

Aged Rhesus Colony. The aged rhesus colony at the CNPRC provides a unique opportunity to support and maintain aged animals for research with known life histories. The CNPRC's aged rhesus colony (≥ 19 years of age) currently consists of 104 animals, of which 42 are supported by the National Institute on Aging. Currently, 41 of the 42 animals are assigned to projects. These animals are managed as one colony and participate in a semi-annual geriatric veterinary work-up and routine evaluations (see **National Institute on Aging Colony**).

SPF Colonies. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony consists of ~1,500 animals ranging in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus (RhCMV). All viral screening is performed in the **Immunology and Pathogen Detection Resources Core**. This SPF Level 2 colony currently totals 234 animals and is supported by a NIH grant (#U42-OD010990); animals are provided to AIDS-related investigators. SPF Level 1 animals

are made available to investigators upon request, and are harvested from the breeding colony specifically for projects (Table 6). Surplus animals may be sold and shipped to approved research facilities and other NPRCs.

Table 6. SPF Animals Provided to Investigators (Internal and External) (May 1, 2010 to April 30, 2014)

SPF Level	May 2010 - April 2011	May 2011 - April 2012	May 2012 - April 2013	May 2013 - April 2014
1	90	80	42	93
2	42	66	61	35

With the establishment of several productive SPF breeding corrals, nursery rearing was eliminated in 2010.

Long-Tailed Macaques and Titi Monkeys. The CNPRC supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) is generally housed in family groups and used by Core and Affiliate Scientists in the **Brain, Mind, and Behavior Research Unit** (see Unit description). This unique resource is the only captive colony of titi monkeys in the world; these animals are used in NIH-supported studies focused on the neurobiology and physiology of social bonds. All titi monkeys are housed indoors in dedicated space according to the Primate Well-Being Plan requirements.

Animal Health Program. A health check is performed each morning by the animal care staff. Each animal has a location and animal identification barcode that is scanned, and an animal technician records physical signs listed on a menu using a portable barcode reader. After completion of the health check, the information is downloaded, and a morning health report is generated directly to the veterinary staff. Primate Medicine Veterinarians or Animal Health Technicians perform a visual examination of each animal on health report. Results of the health check and assessment by the veterinarian are recorded in the animal's record. For animals on study, a computerized report is also sent daily to the investigator by electronic mail. Animals in the outdoor colony are checked twice each day, once each in the morning and afternoon. Identification of animals in the field corrals is performed by unique individual dye markings. Technicians check each cage for any animals that require medical attention. The majority of animals used in research projects at the CNPRC are from the production colony. Any animals brought into the CNPRC from off-site facilities complete a 90-day period in the CNPRC Quarantine Facility and undergo a complete physical examination with complete blood counts (CBCs), blood and fecal parasitology, and rectal culture. Five tuberculin tests are completed and animals are screened for simian retroviruses (see **Vertebrate Animals** section).

Colony Management and Research Services Staff. Colony Management and Research Services is the largest of the Primate Services components and include approximately 125 CNPRC employees. All of the staff report to the Assistant Director for Colony Management and Research Services. Excluded by Requester Each of the staff provides critical functions within the CNPRC infrastructure, and they work cohesively as a team to ensure all colony and research needs are met. **Colony Management staff** maintain the colonies through an established **Animal Care Resource Supervisor** structure defined by area and function, and consisting of approximately 90 animal care technicians. These individuals provide 24-hour care for the entire colony including indoor breeding and specialized research space, as well as the outdoor field corrals. Each of the seven Animal Care Resource Supervisors is responsible for staffing, scheduling, and related animal and research support for their assigned area. Each Animal Care Resource Supervisor has extensive experience in nonhuman primate care and management, and has been extensively trained in all aspects of primate husbandry, handling, safe practices, and technical support. Supervisors are cross-trained and are able to step in and assist in other areas as needed. These seven areas and general functions include:

- **Indoor Colony** (e.g., husbandry, morning health, preventive health procedures under the direction of Primate Medicine)
- **Indoor Cage Crew** (e.g., remove and replace cages, cage washing and facilities)
- **Infectious Housing and Quarantine** (e.g., husbandry, morning health; all handling of BSL2+ animals is performed under chemical immobilization)
- **Nursery Care** (e.g., husbandry, morning health, specialized care under the direction of Primate Medicine)
- **Outdoor Colonies** (e.g., husbandry for North and South Colonies, morning and afternoon health checks)
- **Technical Support** (e.g., animal relocations, sedation and delivery to procedure rooms, blood collection, weights, time-mating procedures in coordination with scheduling by Research Services staff; chair and transfer box training; positive reinforcement training; pairing animals; investigator assistance as requested)
- **Environmental Enrichment** (e.g., daily colony enrichment activities; see below)

Environmental enrichment activities are an integral component of indoor colony management. Because enrichment and pairing can have a significant impact on research protocols, Colony Management and

Research Services staff members work closely with investigators to implement customized plans to address both experimental and behavioral requirements. Technical staff is responsible for indoor social pairing (e.g., new pair formations; pairing data management including compliance and deferrals; current success rate 68-75%); indoor environmental enrichment implementation (e.g., rotational enrichment, supplemental enrichment); and indoor behavior management (e.g., evaluation and monitoring of potential for injurious self-directed behavior with Primate Medicine veterinarians; case-by-case targeted behavioral assessments/reports). They also provide support for experimental projects as requested through animal and pairing selections, modifications to pairing and/or enrichment according to IACUC-approved protocols, and animal relocations. While every animal in the colony is viewed by at least one staff member during morning health rounds, **Behavior Management Services** assess all indoor animals monthly to identify any abnormal behaviors and ensure they receive daily enrichment targeting the specific behavior by working closely with the enrichment staff. These animals receive a detailed behavioral assessment monthly to monitor their status.

Research Services staff work very closely with Colony Management staff and serve as the hub for ensuring communications between all Primate Services components, and on subjects that directly impact colony management and research projects. They also provide a spectrum of research support services (see examples, below, and in the **National Institute on Aging Colony** section), and step in as needed to aid investigators when additional short-term technical support is needed. Their primary functions include:

- **Coordination of Colony Management Procedures** (e.g., routine weights, tuberculin tests, and physical examinations; monitoring menstrual cycles and scheduling time-mating; SPF colonies; round-up)
- **Centralized Communications** (e.g., work orders, billing, scheduling procedures with Primate Medicine and Anatomic and Clinical Pathology staff)
- **Technical Support to Facilitate Investigator Needs** (e.g., protocol-specific technical procedures including sample collections, immunizations, inoculations, sample processing; animal support for procedures such as pulmonary function testing; see examples below)
- **Assist Other Primate Services Components** (e.g., animal training; physical therapy; Primate Medicine support of animals post-operatively)

Research Services staff coordinate all colony management activities and aid with environmental enrichment; provide centralized management of work orders and billing; collate general colony demographics; assist investigators with hands-on technical support; provide budgetary information for grant and contract submissions; and work with all Primate Services components to coordinate work flow and project information. Depending on the investigator, a range of services is made available upon request, from basic procedures, such as animal selection to project management. This may include activities for which Research Services staff have extensive training or may require special training from the PI and project research team. Specific examples highlight the range of options depending on the investigator and research program. In the **National Institute on Aging Colony** section the research programs of [Excluded by Requester] (University of Arizona) and [Excluded by Requester] (Mt. Sinai School of Medicine) are highlighted, and the services provided described. Another [Excluded by Requester] (UC

[Excluded by Requester] (ego). As an off-site investigator, [Excluded by Requester] visits the CNPRC to perform the surgical procedures [Excluded by Requester] associated with his projects. He has a project manager and research staff on-site that oversee and coordinate

all aspects of his studies, and monitor the animals daily. [Excluded by Requester] project manager utilizes [Excluded by Requester] Management and Research Services to assist with study needs in the following ways:

- Identify and screen animals for study assignment.
- Husbandry needs including specialized bedding and animal care and maintenance.
- Work orders for coordination of research activities such as scheduled surgeries with Primate Medicine.
- Updated budgetary information, as requested.
- Assist with IACUC protocol submissions and amendments, as needed.
- Train new staff and surgery participants in order to meet the CNPRC entry requirements.
- Assist Primate Medicine with daily drug administration through percutaneous endoscopic gastrotomy tubes.
- Assist with training on a specialized treadmill.

Complex projects such as these require many members of the Primate Services team to share the activities, and to work with the investigator and staff to ensure success of the project and optimal animal care. Animals may also require imaging off-site for diagnostic and related purposes, which involves the support of both Colony Management and Research Services and Primate Medicine Services (e.g., transport, anesthesia, stereotaxic placement, procedure recovery). Recharge activity for such services is shown in Table 7.

Table 7. Colony Management and Research Services Research Support Recharge (May 1, 2010 to April 30, 2014)

Grant Year	Service Type	# Users	Investigators (N)	Service Cost (\$)	Total Cost (\$)
2010 - 2011	Colony Management Research Support	91	Core Scientists (14) UC Davis (26) External (51)	281,523 165,976 126,513	574,012
	Research Services Research Support	104	Core Scientists (14) UC Davis (23) External (67)	209,637 165,673 255,618	630,927
2011 - 2012	Colony Management Research Support	69	Core Scientists (13) UC Davis (19) External (37)	108,469 74,671 119,917	303,057
	Research Services Research Support	72	Core Scientists (12) UC Davis (20) External (40)	77,609 154,376 215,080	447,065
2012 - 2013	Colony Management Research Support	70	Core Scientists (12) UC Davis (24) External (34)	114,642 116,059 124,041	354,743
	Research Services Research Support	91	Core Scientists (12) UC Davis (26) External (53)	84,181 182,716 213,893	480,790
2013 - 2014	Colony Management Research Support	68	Core Scientists (14) UC Davis (20) External (34)	87,219 100,743 94,981	282,943
	Research Services Research Support	80	Core Scientists (13) UC Davis (19) External (48)	89,593 174,657 254,439	518,689
TOTAL					\$3,592,226

Information Technology (IT) and WebVitals.

WebVitals is widely used by Core Scientists and staff to obtain information regarding animals in the colonies. After an animal identification number is entered, the Animal Summary page presents demographics, project assignment and other information about an individual animal (Figure 3). The Assignment page shows the history of assignment to research projects, and other links to the conception history, enrichment information, diarrhea incidence, fostering, immunization, morning health observations, pairing, pedigree, relocation history, reproductive records (daily menses reports), serum banked samples, SNOMED, virology testing, weights, and tuberculin test dates and outcomes. Data entry includes colony related information generated by daily activities including surgeries.

Figure 3. Screen view of the WebVitals database.

The screenshot displays the CNPRC WebVitals database interface. At the top, there is a search bar and a 'Submit' button. Below the search bar, a navigation menu includes links for Home, Animal Selection, MH Files, and Exit. The main content area is titled 'Animal Summary' and shows details for a 'SHIPPED' animal. The summary includes fields for Sex (Male), Generation (05), Birth (01/15/2014), Birth Con No (001-0007), Dam ID (001), Sire ID (001), Acquisition (01/15/2014), Previous ID (001), and Departure (01/15/2014). The animal's location is 'SHIPPED' and its weight is '12.630 Kg'. The summary also lists various tests and procedures, including TB Test, Serum Bank, Harvest, SPF Status, Colony, Breeding Group, and Purification. At the bottom, there is a section for 'Last Project(s)' and 'Canvas Flags'.

Staff Training. The training program within Colony Management and Research Services includes two full-time training coordinators. Training is viewed as an initial step at hire but also as an ongoing process through in-house classes and support to attend relevant training programs, meetings, and conferences. Training and campus compliance activities that are required of all employees at UC Davis are described in the **Administration Services** section in the **Director's Office** (e.g., Injury/Illness Prevention Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management). The cornerstone of the program are standard operating procedures (SOPs) and a set of "Attention to Detail" documents that describe how each task or skill conducted is properly performed. Based on the *Attention to Detail* documents, training sessions are provided and address the following:

- All aspects of animal care from fan raking in a field corral to hosing an indoor animal room to performing the daily health check of animals in each of the different housing areas.
- Clinical procedures conducted by members of the Primate Medicine staff.

- Technical procedures conducted by research staff.
- Zoonoses awareness and infection control measures.
- Overview of occupational health risks and worker protection and safety.
- Overview of regulatory agencies and programs that impact research and facility operations.

The CNPRC training team has expanded from basic procedures to more complex procedures and cross-training (see below) including for Animal Health Technicians in Primate Medicine on subjects such as gas anesthesia monitoring, endotracheal intubation, stereotaxic placement, bandaging, and catheterization to ensure consistency to meet investigator needs. All staff training is entered in the Staff Training Database, with updates and annual re-training scheduled through the area supervisors.

For the American Association for Laboratory Animal Science (AALAS) preparatory class sessions, 75 sessions are conducted annually. Many of the training procedures are performed on animals scheduled for euthanasia (~70 sessions per year; IACUC approved). Approximately 500 sessions are provided for one-on-one or small group training sessions, in addition to approximately 30 training sessions that include the entire crew in a particular area. During the current funding period, training sessions have expanded to include health assessment training for the afternoon health checks outdoors, and new staff performing morning health checks in the indoor housing areas. To date, 63 staff have successfully completed the Assistant Laboratory Animal Technician requirements, 12 have completed the Laboratory Animal Technician requirements, and 5 the Laboratory Animal Technologist requirements. Overall, 63% of the Colony Management and Primate Medicine staff members are AALAS certified. New employees are encouraged to enroll in AALAS classes within the first few months of employment. The historic averages demonstrate that 95% of those individuals that participate in these classes pass and achieve certification the first time.

SOPs and Quality Assurance (QA). In addition to the above training, an extensive library of 185 SOPs in a standardized format provide details on all operational procedures including husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by staff and undergo full review and revision every three years. SOPs are available online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC and can be listed by SOP number in IACUC protocol submissions. The CNPRC also has the expertise to provide the QA requirements for Good Laboratory Practice (GLP) studies. The relationship with the FDA since this program was initiated in 1985 has been favorable, and inspections have consistently resulted in “no action indicated” documentation. QA staff provides the requisite services for GLP studies, as well as generalized QA services for day-to-day animal care activities. These include SOP program management and review; implementation and refinement of the controlled drug tracking program; to serve as administrator for the MedDispense controlled drugs system; administrator for the environmental and microbiological monitoring program (e.g., cage washer, pH monitoring, animal feed and water analysis); and maintain facility records (e.g., inspections, electronic scale maintenance). A complete instruction manual has also been developed to complete CITES permits for shipping nonhuman primate specimens.

Providing Animals for Research. The high level of production from the rhesus colony is needed to meet the age range requirements of investigators. Using harvest strategies from all areas, the CNPRC has been able to

meet these requests. The CNPRC also remains a national resource for the breeding and sale of high quality nonhuman primates. Other NPRCs as well as recognized research institutions purchase animals of all ages based on research needs. Figure 4 shows the range of locations nationwide where animals have been purchased from the CNPRC. Table 8 shows animal sales during the current funding period.

Figure 4. Examples of animal sales nationwide.



Table 8. Animal Sales (May 1, 2010 to April 30, 2014)

Grant Year	# Users	Investigators (N)	Cost (\$)	Total Cost (\$)
2010 - 2011	80	Core Scientists (12)	907,740	2,926,370
		UC Davis (14)	203,010	
		External (54)	1,815,620	
2011 - 2012	66	Core Scientists (10)	564,870	3,195,645
		UC Davis (14)	892,925	
		External (42)	1,737,850	
2012 - 2013	64	Core Scientists (11)	528,465	2,785,935
		UC Davis (17)	781,235	
		External (36)	1,476,235	
2013 - 2014	55	Core Scientists (11)	456,230	2,317,343
		UC Davis (14)	350,773	
		External (30)	1,510,340	
TOTAL				\$11,225,293

During the current funding period, the greatest demand has been for newborns harvested on the day of birth (Table 9), females of prime reproductive age, and aged rhesus females.

Table 9. Nursery Reared Infants for Research Projects (May 1, 2010 to April 30, 2014)

Mav 2010 - April 2011	Mav 2011 - April 2012	Mav 2012 - April 2013	Mav 2013 - April 2014
170	210	194	99

The CNPRC currently maintains approximately 5 project nurseries to support research in areas such as infectious disease, immunology, nutrition, and regenerative medicine/gene therapy. Project nurseries include highly trained staff that provides continuous care 24 hours a day, 7 days a week.

INNOVATION

At one time, a rhesus monkey was a basic animal for research use where the quantity of cohorts within a defined age or gender was the primary need. The research enterprise has significantly changed with the increase in high-throughput technologies and defined models. With refinement of the nonhuman primate model, the management and use have evolved to address, for example, subdivisions of breeding populations based on SPF status. The evolution of AIDS research includes technologic advances focused on pedigrees and genotypes desirable for AIDS-related studies. This refinement of the nonhuman primate model has continued during the current funding period with the expansion of SPF populations and the development of complete pedigrees for all of the breeding colonies (see **Genetics Management Services**). In addition, the Biobehavioral Assessment (BBA) Program (see **Brain, Mind, and Behavior Research Unit**) has developed behavioral profiles for over 3,000 infants born in the outdoor field corrals. The colony database on individual animals (see Figure 3) is expanding from basic census information such as weight, viral status, number of offspring, and age to incorporate information such as behavioral reactivity, pedigree, and defined alleles such as MamuA*01. This information greatly increases the value of the colony, but simultaneously increases the complexity of colony management and the need for a well-trained staff.

The Core Scientists provide a unique intellectual resource that closely integrates with Colony Management and Research Services, and emphasizes innovation in management practices and research support. For example, the **Brain, Mind, and Behavior Research Unit** provides scientific direction for the Animal Well-Being Plan (see **Behavior Management Services**). The **Infectious Diseases Research Unit** was the genesis for the SPF program and continues to provide essential insights and contributions on the immunology of colony animals and endemic microbial populations in the colony. The **Reproductive Sciences and Regenerative Medicine Research Unit** developed the reproductive monitoring program (ultrasound-based and endocrinology), and provides essential insights on reproductive endocrinology and development including the maternal/fetal interface, novel research paradigms, and model development. The **Respiratory Diseases Research Unit** provides critical information for understanding the respiratory physiology of animals, particularly in the outdoor field corrals. This depth of scientific knowledge and primate expertise provides an important and unique basis to support cutting-edge NIH supported research with nonhuman primates. It is a particular strength of the CNPRC that Core Scientists and staff are engaged and integrated within Primate Services.

Efficient management of nonhuman primate colonies requires methods to predict the detailed structure of populations in terms of age, sex, and life stage distribution as this can greatly improve resource management,

animal housing plans, and personnel needs. Because of the limitations of current mathematical models that have traditionally been used in studies of free-ranging nonhuman primates to predict future population size, the CNPRC modified two mathematical models to allow for projections of age, life stage, and gender, as well as simulations of the effect on population structure of various demographic and management parameters. With this model, the CNPRC reviews predictions for 10 years of the future population in the field corrals, and can graph the population trajectory for age, life stage, and gender as well as the population as a whole. Further, using a mathematical rather than a statistical model, this method can be used for newly established colonies with a small initial population. This modeling program is utilized to predict the impact of particular harvest strategies on individual cage production as the model takes into account the actual demographics of a cage including sex and age make-up of the current population. In addition, vital events such as conception rates, live birth rates, mortality rates, and harvests can be added, and the annual production for up to 10 years can be estimated. This approach can also address the longevity and productivity of a cage over time. For example, this approach is used when considering requests from investigators for SPF Level 2 animals that are housed in two field corrals. If an investigator is interested in conducting a study that requires the removal of 20 juveniles between 2 and 4 years of age, the model is used to determine how removing this quantity of a particular age group will impact production in two years versus 5 years. Similarly, if 25 prime reproductive age females are requested, the mathematical model can determine the long-term impact and the sustainability of the field corral based on harvesting this quantity of breeding females.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Provide outstanding colony management and infrastructure support to maintain and utilize a national resource of nonhuman primates for translational research.

A long-term CNPRC plan is conversion of the conventional breeding colony to SPF status Level 1. Achieving this goal serves both personnel safety and research by greatly reducing the occupational health risks associated with potential exposure to Herpes B-virus and other nonhuman primate pathogens. This approach also eliminates persistent infections representing potential confounding variables for research. In addition, total colony conversion to SPF status would greatly reduce the costs associated with maintaining two separate colonies (conventional and SPF).

Colony Conversion. Over the next funding period, the CNPRC plans to slowly decrease the conventional colony in the field corrals, while replacing these cages with SPF Level 1 animals. The overall number of breeding corrals will remain constant. The CNPRC will reduce the size and production of the conventional colony in proportion to the projected increase in the SPF Level 1 colony. We expect to reduce the conventional colony by approximately 1 field corral per year, and replace with an SPF Level 1 colony by approximately 1 corral per year over the next 5 years. Long term, some conventional colony production will be needed in order to continue to provide animals for ongoing research projects that do not require SPF animals, and for which the change in the status of the animals mid-project would present a confounding variable. Of the conventional corrals, those that house hybrid rhesus where males have been vasectomized to reduce overall production will be selected first. These animals can be harvested and used to meet current research needs. This will allow for slow expansion of SPF Level 1 full Indian rhesus corrals, which are currently the most desirable and are in high demand from external investigators. New corrals will be populated from existing social groups of juveniles currently in corn cribs and intact social groups in current SPF Level 1 field corrals.

- **SPF Level 1** – Expansion of field corrals to allow steady repopulation of up to 15 field corrals beyond the 9 currently in production. Based on production numbers in existing cages, it is projected that the ability to populate one additional field corral with SPF Level 1 animals can occur in each of the next 5 years.
- **SPF Level 2/Indian** – No expansion of the SPF Level 2 Indian colony is planned. Based on current utilization of SPF Level 2 animals, two production cages should provide sufficient numbers of animals to meet projected research demands. This group is maintained to support Office of AIDS Research grants. Support for the SPF Level 2 colony is currently through a U42 grant as noted. It is anticipated that this colony will be maintained through competing renewals and program income from animal sales.

Colony Size. A goal for the overall production colony includes ongoing assessments of colony size and a planned reduction of approximately 500 animals over the next 1-2 years. This reduction will allow for alignment with needs of the CNPRC overall, and the demands of current research. Currently, the request for “hybrid rhesus macaques” has declined, and the anticipation is that this trend will continue. In the outdoor breeding colony, there are 5 field corrals composed of between 90-130 animals in each corral. In each of these corrals

the adult males have been vasectomized during the last 3 years in order to limit production and growth. Animals from these field corrals will be harvested for research use as noted, as well as advertised for sale in a systematic process with the goal of reducing the population of hybrid rhesus, and disbanding the cages. Other NPRC's will be consulted, and these animals will be made available through the NPRC Consortium "Animal Locator" website (see **NPRC Consortium**). Utilizing this system, the CNPRC will have the capability to routinely list animals available for sale. This information is updated every 24 hours, and a recent addition to the website has added the capability for an NPRC to post a call for animals. Adjustments in colony size are made thoughtfully utilizing the mathematical model described above, which allows careful planning and adjustments based on national needs.

NPRC Consortium. The CNPRC plays a leadership role in coordinating two high priority initiatives in the NPRC Consortium. The *Virology Testing Quality Improvement Initiative* is led by staff in the CNPRC **Immunology and Pathogen Detection Resources Core** and is focused on assessing whether resource laboratories are within acceptable limits for virology testing. Results from this Initiative are being incorporated into a white paper on virus testing standards commissioned by the Division of Comparative Medicine and the SPF Directors. Similarly, the multi-center *Measles Vaccination Safety and Efficacy Study* is currently testing an alternative measles vaccine candidate. NPRC breeding colonies are at risk for a measles epizootic since vaccination programs for measles have lapsed with the discontinuation of domestic monovalent measles vaccines. This project has been ongoing since 2011, and Excluded by Requester **Primate Medicine**) and Affiliate Scientist Excluded by Requester **Infectious Diseases Research Unit**) provided the scientific leadership and expertise in designing this study.

The value of nonhuman primate models is in their genetic diversity, behavioral complexity, and anatomy, immunology, and physiology. The scientific resources that have been developed in genetics and genomics provide a means to better define individual rhesus monkeys over a lifespan, and to identify models of human disease. The **NPRC Consortium** has initiated an "Extreme Phenotype" survey, and plans are underway for a white paper on a program using targeted and state-of-the-art genomics to discover genotype-phenotype relationships related to human disease. The proposal primary goals are to identify common genetic variations across the NPRCs, develop an online searchable database as a resource to the research community, and establish a genome sequencing service that will generate whole genome or whole exome sequences for specific animals with significant phenotypes. As an active member of the NPRC Consortium, the CNPRC will participate in these efforts (see Primate Medicine Services).

Specific Aim 2. Ensure high quality training in all areas of animal care and colony management.

A cornerstone in the sustainability of high quality animal care is the training of staff in daily husbandry, management, and safety practices. Working knowledge of daily husbandry needs, appropriate animal handling techniques, the importance of infection control, and technical procedures that are focused on the species is critical to the mission of the CNPRC. The current CNPRC Training Program is comprehensive and effective.

Cross-Training and Training in Safe Practices. During the proposed funding period, the cross-training program between areas and specialties will be expanded in order to increase efficiencies in the utilization of staff. A more diversified staff will improve efficiency, safe practices, and also maintain a motivated workforce. In conjunction with these efforts, the Training Program staff will complete and/or update the *Attention to Detail* documents for every activity conducted at the CNPRC. This includes procedures performed in Primate Medicine, technical procedures performed by research staff, and tasks performed in animal care. The specific methods by which tasks are performed may change over time therefore *Attention to Detail* documents will require updates to maintain accuracy. Through the staff's comprehensive training program an emphasis on safety and safe practices is regularly reinforced.

AALAS Certification. Beginning in January 2014, a new approach was initiated to encourage individuals to pursue AALAS certification. This approach consists of an informational/training session that is held on a specific topic and at a related location each week. For example, anatomy will be addressed while trainees view a tissue harvest with the pathologists. Principles of sanitation and disinfection will be covered in the cage wash area, and husbandry will be addressed while visiting facilities housing for a particular species. The objective is to present the material in a manner that accommodates different learning styles, and which may not necessarily be achieved in a standard classroom setting. The goal is to engage staff and encourage their learning while building enthusiasm to successfully achieve AALAS technical certification.

Specific Aim 3. Promote and support responsible conduct of research and animal care.

The goal over the next funding period is to continue to evaluate and review established guidelines, SOPs, and practices, and to ensure that standards of excellence are maintained. Continued interactions with the IACUC and NPRC Consortium efforts will aid in this ongoing process and identifying best practices across the entire animal care operation.

UC Davis IACUC. At UC Davis, a single IACUC oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. The IACUC reviews all submitted protocols for compliance with the requirements of the Animal Welfare Act, the NIH *Guide for the Care and Use of Laboratory Animals*, the Public Health Service Policy on the Humane Care and Use of Laboratory Animals, and UC Davis Policies and Guidelines. The UC Davis IACUC is a faculty-based committee and inspects all animal facilities, evaluates all aspects of the institutional animal care program, establishes policy and procedure for the UC Davis campus, and coordinates training, compliance, and occupational health programs across UC Davis. The IACUC requires that every vivarium have an assigned Scientist-in-Charge (SIC) and Technician-in-Charge (TIC). This program delineates lines of authority and establishes the primary point-of-contact for each vivarium for regulatory and AAALAC-related purposes, and promotes general animal care program communication and education. The SIC is typically a UC Davis faculty member managing the vivarium and is experienced in animal research. The TIC is typically a staff member who has direct responsibility for the vivarium and serves as the point-of-contact for the Attending Veterinarian, [Excluded by Requester] and the IACUC in matters related to vivarium management, animal health concerns, compliance with IACUC protocols, and SOPs. At the CNPRC, [Excluded by Requester] serves as the SIC and [Excluded by Requester] serves as the TIC, and they participate in quarterly meetings with colleagues from other vivaria, the Attending Veterinarian, and the IACUC Administrator. These essential campus-wide activities will continue during the next funding period.

Emergency Response and Planning Options. Emergency planning has been a focus of the UC Davis campus. As part of the *UC Ready Plan*, CNPRC staff members attend several training sessions on a regular basis to review and evaluate needs of the CNPRC during natural disasters or failure of infrastructure resources. Contingency plans have been made for acquisition of supplemental water, back-up power with the use of on-site generators, and a 4-week supply of monkey chow. Inventories have been planned to assure an on-site backup of medical supplies as well as protective clothing. The CNPRC will continue to expand the scope of the plan to ensure that all emergency scenarios have been anticipated. The SIC/TIC participates in activities to address emergency and contingency planning, and training to provide for the humane handling, treatment, transportation, housing, and care of animals in the event of an emergency or disaster. These meetings present a situation followed by a discussion of actions based on the scenario including identifying the person(s) in charge, functions to be addressed, and contacts to be made.

Controlled Substance Program. The MedDispense controlled drug units and related training program was implemented during the prior funding period. Three units are available in the hospital and the research areas to provide the necessary access. The administrative duties for daily monitoring and reconciliation are shared between the QA Coordinator, Primate Medicine staff (overseen by a Senior Veterinarian), and trained members of the MedDispense team. This program has allowed for close monitoring, tracking, and reporting of controlled drug use at the CNPRC. A QA focus is to continue enhancements and refinements for the MedDispense Program. In working closely with the product vendor and **Information Technology Services** staff, upgrades that will expedite the addition of new animals to the system, removal of animals from the system, specialized codes that support many of the special CNPRC needs (e.g., emergency kits which include many drug combinations), and the need for additional units in other locations around the CNPRC, will improve accessibility and overall efficiencies.

Facility Needs. Enhancements to the animal care program and overall facility remain a major priority for the CNPRC. Upgrades to outdoor breeding areas will continue in order to improve the heating and shade to animals in an efficient and clean manner. With an increase in the microbiological monitoring of caging, water lines, and most animal testing rooms, the goal is to develop an online workflow system that will calendar, send reminders, report results, and track trends.

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian and the IACUC.

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of Specific Animal indoor animal space. The outdoor animal housing area includes Specific Animal field corrals and Specific Animal corn cribs. Specific Animal The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLTV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian). Excluded by Requester Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see **Primate Medicine Services**). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an

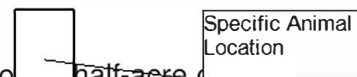
approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Housing and Environmental Monitoring. Animal rooms are maintained within the recommended guidelines established by the current edition of the *ILAR Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. Typical nonhuman primate rooms provide 10-15 air changes per hour and are negatively pressurized relative to anterooms/corridors and the outside. Lighting is provided by fluorescent lights, which are controlled by timers (12 hours on/12 hours off). Room temperature is maintained between 68°F and 80°F, depending on the species and age of the animals in the room, and are checked and recorded daily. Emergency generator power is provided for all animal rooms. Indoor animal housing is monitored on a daily basis for temperature, light, and humidity. Power failures, major temperature fluctuation, and other environmental disturbances are either alarmed directly to Campus Physical Plant Services or monitored by CNPRC personnel on a daily basis. The Colony Operations Supervisor and the Maintenance Shop Supervisor carry pagers 24 hours/day and are alerted to environmental monitoring alarms and rooms that are out of temperature and humidity range.

Caging Systems. Indoor cages are stainless steel construction and either wall or rolling rack mounted. Cages incorporate a squeeze mechanism to bring the animal to the front of the cage for manipulation. Cage sizes are determined by the USDA and NIH policies. Cage designs incorporate sliding partitions to allow socialization or pair housing.

Environmental Enrichment. The Environmental Enrichment program is part of the Colony Management and Research Services component of Primate Services, is integrated with **Behavior Management Services**, and includes all animals, with emphasis placed on indoor-housed animals on research projects. Indoor cages are outfitted with a variety of enrichment options including manipulation mirrors (allowing the animal to view adjacent animals), and cage toys. Perches are present in all indoor cages. Low caloric items, such as forage, are provided on forage boards located on each cage. Animals also receive fruit or vegetables twice weekly. Non-food enrichment is also emphasized. One example of such enrichment is the placement of televisions, which provide visual stimulus to colony animals. Socialization can provide substantial benefit to the animals and is generally accomplished within the limitations of research protocols and daily management practices. Cages have been retrofitted or purchased with sliding partitions to allow pairing. The current strategy is to pair animals during the day and separate them at night to facilitate the assessment of physical signs each morning. Animals are paired early in the morning when animal care staff begin daily activities, animals are then separated at night when there are limited personnel available to monitor for potential aggressive interactions. The ability to observe each animal's individual daily physical signs is essential to many research programs and overall clinical care. Behavior Management Services staff members view every animal in the colony during morning health rounds and ensure they receive daily enrichment items targeting their specific behavior aberration. All indoor animals are also assessed monthly to identify any abnormal behaviors; these animals receive a detailed behavioral assessment monthly to monitor their status and progress.

Surveillance. The majority of animals at the CNPRC are from the production colony of half-acre field corrals. Animals brought into the CNPRC from off-site facilities complete a 90-day quarantine at the CNPRC Quarantine Facility. During this time, animals undergo a complete physical examination with complete blood counts, blood and fecal parasitology, and rectal culture. Five tuberculin tests are completed, and animals are screened for simian retroviruses including Type D simian retrovirus (SRV), Simian Immunodeficiency Virus (SIV), and simian T-cell leukemia virus (STLV). Animals of foreign origin are treated for malaria and intestinal parasites. Animals with positive tuberculosis tests and SRV assays, or



demonstrating signs of clinical illness, are humanely euthanized and a complete necropsy performed.

Feeding. The animals are fed commercial monkey chow twice daily. Monkey Chow is pre-analyzed for content. The analysis of each lot of feed is reviewed by CNPRC Quality Assurance and a Senior Veterinarian. Animals are supplemented with fruit or vegetables twice weekly. Water is provided by automatic lixits, which are checked daily for proper operation. Portable caging with detachable waterlines is checked daily. The CNPRC potable water supply is obtained from wells operated by UC Davis. All UC Davis wells are monitored by the Office of Environmental Health and Safety quarterly. The water is tested for chloroforms, a variety of chemical markers including heavy metals and a variety of toxic minerals, pesticides, and chemical contaminants. Additionally, the CNPRC tests for general mineral, organic, and inorganic contamination annually.

Sanitation. Indoor cages are hosed daily with a quaternary ammonium detergent/disinfectant and are sanitized every 2 weeks in a mechanical cage-washer. A microbiological monitoring program is in place to ensure efficacy of sanitation practices. Each animal area is monitored twice per year. Microbiological monitoring results are reviewed and signed off by each area supervisor, a Senior Veterinarian, and the Assistant Director for Colony Management and Research Services. Monitoring of caging pH during cage washing is included in the cage sanitation surveillance program. In addition, water lines in both the indoor and outdoor colony are monitored with microbiological testing on a rotational basis in conjunction with cage change activities.

Record Keeping. Record keeping includes a written individual animal record and entry of specific information into a computerized Vitals database (see **Information Technology Services**). Maintenance of the animal colony database, including information on project history, reproductive history, clinical data, viral status, as well as genealogical data is included. Also included are the current location of the animals, weight history, date of last tuberculosis test, and the date of the last serum banking. These data are available to aid in project design and animal selection by investigators. This database has also been critical to several retrospective studies involving prenatal mortality, transmission of retroviral agents in colony management, effects of housing changes on health, and risk factors for spontaneous diseases such as endometriosis. Management of this informational database represents a valuable resource to the entire biomedical research community. Historical animal-related data are maintained on a yearly basis to reflect the production statistics of the colonies including: conception rates, live birth rates, pregnancy loss, and infant mortality.

Animal Health Program. A health check is performed each morning by the colony management staff. Each animal has a location and animal identification barcode that is scanned, and an animal technician records physical signs listed on a menu using a portable barcode reader. After completion of the health check, the information is downloaded onto the main computer, and a morning health report is generated directly to the veterinary staff. Veterinarians or Animal Health Technicians perform a visual examination of each animal on health report. Results of the health check and assessment by the veterinary clinician are then recorded in the animal's record. For animals on study, a report is generated to the investigator on a daily basis by electronic mail. Animals in the outdoor colony are also checked twice each day, once in the morning and afternoon. Identification of animals in the field corrals is performed by individual dye mark. Technicians check each cage closely for animals potentially requiring medical attention. The afternoon health check was added to the outdoor colony in 2012, and increased health surveillance is particularly important during the birth season.

Centralized Research Support. The various services represented in Primate Services work synergistically to provide high quality, technical research support to all investigators utilizing the CNPRC, as needed, whether located locally or at a distant site. Staff veterinarians also provide extensive clinical support to animals on long-term research protocols (see Primate Medicine Services).

Staff Training. The program emphasizes occupational safety, as well as increasing demands for technical expertise in the care and research support of nonhuman primates. Training is viewed not only as the initial step at hire, but as an ongoing process through in-house classes and support to attend relevant training programs, meetings, and conferences. A spectrum of training opportunities is available specific to the

CNPRC and to meet campus-wide training requirements. These include: UC Davis Primate Handling and Husbandry Training, Campus Laboratory Animal Care Classes (AAALAC preparation); Injury / Illness Prevention Plan; Infection Control Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management; Campus Back Safety Class; Campus Radiation Safety Class; Pesticide and Antimicrobial Safety; Training in Good Laboratory Practices; Supervisor Training with Job Skills Worksheet; and position specific training for all levels of husbandry, animal care, and technical skills. The training program also includes a series of "*Attention to Detail*" documents that provide very detailed information for each of the training and skill areas the staff is expected to meet including information to enhance understanding and the need to adhere to defined guidelines for critical procedures.

Standard Operating Procedures (SOPs). Primate Services has an extensive collection of 185 SOPs that provide detail on all operational procedures including: husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by all staff and undergo full review and revision every three years. SOPs are available in an electronic format online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC, and SOPs by number can be noted in IACUC protocol submissions.

- 4. Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
- 5. Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

PRIMATE SERVICES: COLONY MANAGEMENT AND RESEARCH SERVICES

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

ANIMAL RESOURCES: COLONY MANAGEMENT AND RESEARCH SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2:
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

National Institute of Aging Colony

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: — 1 — 2 — 3 — 4 — 5 — 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename NIA_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	NIA_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	NIAFacilitiesandOtherResources.pdf
11. Equipment	NIA_Equipment.pdf

PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY

ABSTRACT

The primary goal of Primate Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. The CNPRC manages a colony of geriatric rhesus macaques for use by investigators in aging research. The CNPRC aged rhesus monkey colony (≥ 19 years) includes animals that are supported by the **National Institute on Aging**, which promotes the support of colonies of aged animals necessary for research on aging processes and age-related diseases. The CNPRC has unique capabilities to support aging studies in nonhuman primates, representing a valuable resource at the national level for translational studies important to geriatric populations, the fastest rising age group in the U.S. today. The following Specific Aims are proposed: (1) Support and maintain National Institute on Aging rhesus monkeys for investigators nationwide that are conducting aging-related research, and (2) Provide high quality expertise and services to investigators at the local, regional, and national levels.

PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY

FACILITIES AND OTHER RESOURCES

Laboratories: See **Colony Management and Research Services**.

Clinical: Two clinical rooms totaling 446 sq. ft. are used for physical examinations, treatments, and minor surgical procedures. Intensive care support is also provided in a dedicated suite. Surgical preparation is carried out in an anteroom in each of the two surgical suites, which includes an autoclave for instrument sterilization. Diagnostic examination rooms include radiography, fluoroscopy, ultrasound, and DEXA bone density scanning. See **Primate Medicine Services**.

Animal: Indoor housing includes Specific Animal Location housing. Outdoor housing includes Specific Animal Location half-
Specific Animal Location old corrals Specific Animal Location corn crib units, and 3 hose down pads for animal holding. See **Colony Management and Research Services**.

Computer: Primate Medicine veterinarians and staff are equipped with networked computers including two computer workstations located in the clinical areas.

Office: Office space and administrative support is provided to the veterinarians including private and shared offices and a conference room for meetings.

Other: The CNPRC is a part of the UC Davis AAALAC-accredited program.

PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY EQUIPMENT

See **Colony Management and Research Services** and **Primate Medicine Services**.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	1,810.00	6,348.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						6,348.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							6,348.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	94,019.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	94,019.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	100,367.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	100,367.00	22,783.00
Total Indirect Costs			22,783.00
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	123,150.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: NIA_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*	
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Ease Salary	EFFORT	0.0	0.0	4,538.00	1,915.00	6,453.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	6,453.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							6,453.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description	
List items and dollar amount for each item exceeding \$5,000	
Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	96,840.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	96,840.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	103,293.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	103,293.00	23,448.00
Total Indirect Costs			23,448.00
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	126,741.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: NIA_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	1,982.00	6,520.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						6,520.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							6,520.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	99,745.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	99,745.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	106,265.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	106,265.00	24,122.00
Total Indirect Costs			24,122.00
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	130,387.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: NIA_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	2,041.00	6,579.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					6,579.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							6,579.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	102,737.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	102,737.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	109,316.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	109,316.00	24,815.00
Total Indirect Costs			24,815.00
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	134,131.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: NIA_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	2,104.00	6,642.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					6,642.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							6,642.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	105,819.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	105,819.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	112,461.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	109,316.00	25,529.00
Total Indirect Costs			25,529.00
Cognizant Federal Agency			
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	137,990.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: NIA_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Associate Director for Primate Services	% Effort			
Excluded by Requester	DVM, DACLAM, Associate Director for Primate Services	EFFORT months % Effort			

is Associate Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine, and Chief Veterinarian. He has responsibilities for all aspects of the nonhuman primate colonies and related services including the National Institute on Aging Colony.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None

TRAVEL

None

SUPPLIES

\$84,019 is requested to support 42 aged animals at the CNPRC, both males and females, that are in overall good health and the best candidates for assignment to projects focused on aging. These animals are maintained in the respective colony areas including indoor housing, corn cribs, and field corrals to maintain their social environment until needed. Daily per diem includes feeding, cleaning, sanitation, environmental enrichment, preventive health care, and veterinary care.

\$10,000 is requested for supplies required for the maintenance of the animals as described in the Research Strategy section.

OTHER EXPENSES

None

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		32,542.00
Section B, Other Personnel		0.00
Total Number Other Personnel	0	
Total Salary, Wages and Fringe Benefits (A+B)		32,542.00
Section C, Equipment		0.00
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		499,160.00
1. Materials and Supplies	499,160.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		531,702.00
Section H, Indirect Costs		120,697.00
Section I, Total Direct and Indirect Costs (G + H)		652,399.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

NIA_SpecificAims.pdf

3. Research Strategy*

NIA_ResearchStrategy.pdf

4. Progress Report Publication List

NIA_ProgressReport_Pubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

NIA_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

NIA_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY

SPECIFIC AIMS

The National Institute on Aging (NIA) supports research on aged rhesus monkeys at National Primate Research Centers including the California National Primate Research Center (CNPRC). The CNPRC **NIA Colony** of geriatric rhesus macaques (≥ 19 years) has a current census of 42 animals, and is managed and supported for use by investigators in aging research, an area of increasing prominence and importance. All aged monkeys at the CNPRC, including the NIA Colony, participate in semi-annual assessments by the veterinary staff (e.g., physical examination, clinical pathology) to ensure overall health and to monitor for potential age-related complications. The Colony Management and Research Services staff also tracks eligible animals at 19 years of age in the field corrals for potential use in the NIA Colony. The CNPRC breeding corrals represent an important resource for the recruitment of aged surgery-naïve animals. The history of individual animals (e.g., health history, vaccination records, virology status, housing history, body weights, behavior profile, and pedigree) is maintained in a complete colony database that includes every animal in the colony, supported by the CNPRC Information Technology Services staff. The overriding objective of the NIA Colony is to provide rhesus monkeys for aging research.

Specific Aim 1. Support and maintain NIA rhesus monkeys for investigators nationwide that are conducting aging-related research.

Plan. The goal is to proactively manage the NIA Colony in order to maximize the number of healthy, surgery-naïve geriatric rhesus monkeys for aging research. The Primate Services team work closely together with investigators to support translational rhesus monkey models of human aging.

Specific Aim 2. Provide high quality expertise and services to investigators at the local, regional, and national levels.

Plan. Through established protocols, guidelines, and expertise, the goal is to ensure investigators are provided sufficient healthy, well-characterized aged animals and correlative services and infrastructure to support aging and lifespan health research objectives.

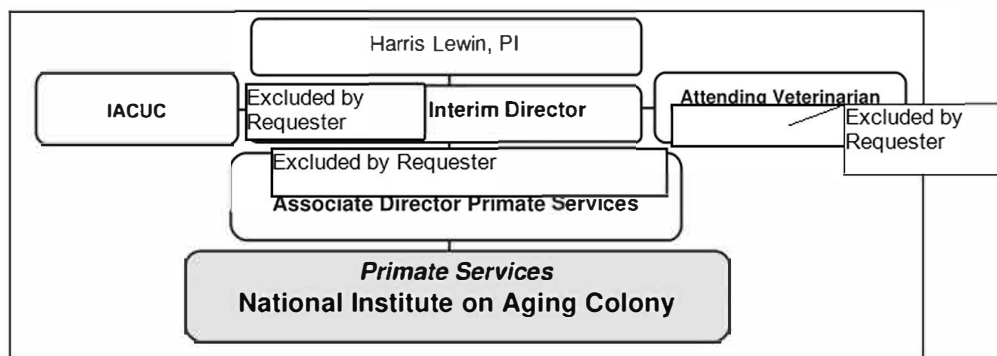
PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY

RESEARCH STRATEGY

INTRODUCTION

The National Institute on Aging (NIA) is at the forefront of research dedicated to understanding the nature of aging, and supporting research that focuses on the health and well-being of older humans and nonhuman primates. NIA maintains groups of nonhuman primates (*Macaca mulatta*) at National Primate Research Centers (NPRCs) for this purpose (Figure 1).

Figure 1. Organizational Chart: National Institute on Aging Colony



The NIA Colony at the California National Primate Research Center (CNPRC) encompasses a group of 42 animals (≥ 19 years of age). This colony is also a part of the NIA Biological Resources Branch that has a compendium of nonhuman primate resources available for aging research as noted on the NIA website.

Personnel are shown in Table 1, and the sources of support for the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 1. NIA Colony Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Excluded by Requester DVM, DACLAM	Department of Medicine and Epidemiology, School of Veterinary Medicine	Associate Director for Primate Services

Table 2. Support for the NIA Colony

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$95,616	\$100,367
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$95,616	\$100,367

Response to the Summary Statement.

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

The NIA document "*Living Long & Well in the 21st Century: Strategic Directions for Research on Aging*" includes research goals focused on improving understanding of healthy aging and disease among older adults, and an understanding of Alzheimer's disease and other dementias of aging and the aging brain. Goals are also focused on supporting infrastructure and resources to promote high quality research. This latter NIA goal emphasizes the support of colonies of aged animal models necessary for research on aging processes and specific age-related diseases. The NIA Colony at the CNPRC is maintained to meet this goal and objective and is reflected in the research grants and studies currently conducted at the CNPRC (Table 3).

Table 3. Examples of Research Supported by the NIA Colony (May 1, 2010 to April 30, 2014)

PI (Institution)	Grant Title (NIH Grant Number)	Animals (N)
Excluded by Requester	Neurobehavioral Relations in Senescent Hippocampus (#R01-AG003376)	5
	Novel Adjuvants for Influenza (#U01-AI074512)	9*
	Estrogen and the Aging Brain (#P01-AG016765)	11
	Cognitive Function in the Aged Monkey (#R01-AG010606)	15
	Cortical Correlates of Age-Related Hearing Deficits (#R01-AG034137)	4
	Gene Delivery and Environment in Primates (#P01-AG10435)	6

*Total N used for project is 26; balance provided by the CNPRC aged colony

Aging Research and Infrastructure Support. The research supported through the NIA colony as noted in

Table 3 includes studies performed by Excluded by Requester 2012; Excluded by Requester

Excluded by Requester 2011; 2012; Excluded by Requester 2012; Excluded by Requester 2011; Excluded by Requester 2012]. The objective of the Excluded by Requester

Excluded by Requester program is to understand the basis of memory impairments that result from normal aging. Over the past decades, Excluded by Requester has discovered links between spatial memory deficits and age-related changes in hippocampal connectivity and plasticity at the cellular and network levels. While the empirical focus on the hippocampus is justified, structures that play a critical role in memory, and the extent to which changes in upstream cortico-hippocampal inputs contribute to these age-related behavioral deficits, are unknown. Whether the perirhinal cortex transmits degraded information to the aged hippocampus, resulting in deficits in visual perception or stimulus associations is a major question addressed in the currently funded grant. A complementary question is whether the breakdown during aging in the connectivity and plasticity mechanisms of hippocampal circuits leads to defective associative binding among neocortical areas, and hence less robust stabilization of episodic memories. Understanding the bidirectional interactions between these structures and how alterations result from the aging process could provide insights into the neural mechanisms of memory at all ages.

This research program provides an excellent example of the importance of the NIA colony at the CNPRC and the integrated infrastructure that ensures the research needs of Excluded by Requester are met at the highest quality.

Excluded by Requester off-site Affiliate Scientist Excluded by Requester visits the CNPRC regularly for study-related activities. She Excluded by Requester al staff available on-site daily to oversee and participate in all aspects of these studies and to monitor Excluded by Requester animals. These technicians, supported by Excluded by Requester interact routinely with Primate Services staff Excluded by Requester in order to facilitate the needs of the study in the following ways:

- **Colony Management and Research Services.** Identify and screen animals for assignment to the study; special husbandry and enrichment needs; assist with centralized work orders for experimental procedures and colony-based requirements related to the study; provide budgetary information as requested; assist with

Institutional Animal Care and Use Committee (IACUC) amendments as needed; and training to meet the CNPRC requirements for facility entry and use.

- **Primate Medicine Services.** Surgical assistance; stereotaxic placement; procedure recovery; daily monitoring and support; veterinary consults for standard operating procedures (SOPs); and assist with IACUC protocols and amendments.
- **Anatomic and Clinical Pathology Services.** Clinical pathology services (e.g., complete blood counts-CBCs, chemistry panels, urinalysis) and anatomic support for brain perfusions and complex tissue collection protocols.
- **Behavior Management Services.** Assist with animal selection based on study needs; monitor animal well-being; and oversee and propose additional environmental enrichment needs.

Animals assigned to this study also undergo structural and functional magnetic resonance imaging (fMRI) scans in order to obtain information for placement of electrodes, to guide serial sectioning of the brain and histological reconstruction of individual electrode tracks, and for diagnostic purposes. Because the CNPRC does not currently have these imaging capabilities on-site (see **Multimodal Imaging Core**), transport of the animals to the Veterinary Medical Teaching Hospital is required to meet the study needs. This involves the support of both Primate Medicine Services and Colony Management and Research Services (e.g., transport, anesthesia, assist with stereotaxic placement, procedure recovery).

Another example is provided by the studies conducted by [Excluded by Requester] Mt. Sinai School of Medicine. Dr.

[Excluded by Requester] collaborates with Core Scientist [Excluded by Requester] **Reproductive Sciences and Regenerative Medicine Research Unit**) through an NIH program project grant, supported since 1999 (#P01-AG016765). Studies recently tested the hypothesis that the number and morphology of mitochondria in dorsolateral prefrontal cortex presynaptic boutons are altered with aging and menopause in rhesus monkeys. It was shown that these metrics correlate with delayed response accuracy, a well-characterized measure of dorsolateral prefrontal cortex-dependent working memory. Published outcomes have suggested that hormone replacement therapy, highly relevant to women's healthy aging, may benefit cognitive aging in part by promoting mitochondrial and synaptic health in the dorsolateral prefrontal cortex [Excluded by Requester] et al., 2014]. This long-standing program has benefited substantially from the expertise in reproductive endocrinology and groundbreaking research on the menopausal transition at the CNPRC by [Excluded by Requester] (Reproductive Sciences and Regenerative Medicine Research Unit). After decades of focusing only on ovarian function, a new understanding of the endocrine foundations has been uncovered through studies in nonhuman primates [Excluded by Requester] also has technical [Excluded by Requester] members supported through the program project grant on-site to oversee and coordinate all research activities. These individuals benefit from and take advantage of the many services available to facilitate their ongoing research including Colony Management and Research Services, Primate Medicine Services (e.g., ovariectomies, hormone replacement therapy), Anatomic and Clinical Pathology Services, Behavior Management Services, as well as the many services provided in the Endocrine Core led by [Excluded by Requester] (see **Endocrine Core**).

Other infrastructure services that are provided to investigators include:

- **Administrative Services.** Assistance with subcontracts for NIH grant submissions; human resources support for on-site technical staff; billing services; and special study needs that require assistance of the shop mechanics (e.g., specialized testing cages).
- **Core Science Services.** Access to services from Cores, such as the Endocrine Core (e.g., reproductive hormone and related assays), Immunology and Pathogen Detection Resources Core (e.g., screening of animals for pathogens prior to study assignment), and Multimodal Imaging Core (coordination, scheduling, and imaging services for research or diagnostic purposes; pursuit of an MR imaging system to be located on-site [see Core]).

By embedding the NIA Colony in the rich environment provided by the CNPRC, users of this colony can benefit from access to multiple services and the range of unique opportunities available.

Colony Management. The aged rhesus monkey colony supported by the NIA is maintained to provide animals for investigators in need of rhesus monkeys at the later stages of life (≥ 19 years of age). A high priority investigator request is for surgery-naïve aged females as noted above. These animals are critical for NIH-funded studies focused on the aging brain where surgical procedures may be required. Such requests can only be met by a proactive plan to identify and maintain suitable candidates in reserve as noted. To meet

investigator needs the CNPRC has initiated a proactive program to identify surgery-naïve animals between 16 and 19 years of age. These animals are maintained in the breeding colony and may be used in research studies until they are needed for aging research. When these animals reach the age of 19 years, they are assigned as needed to fill the NIA geriatric colony requirements in order to maintain the population at 42 animals (Table 4).

Table 4. Current NIA Colony Census

Age (Years)	Male (N)	Female (N)	Total (N)
19-21	3	7	10
22-24	13	5	18
≥25	8	6	14
TOTAL	24	18	42

Animals that have been added to the NIA colony during the current funding period are shown in Table 5. This emphasizes the importance of the P51 aging colony to ensure that the population of 42 animals is maintained to meet investigator needs.

Table 5. NIA Colony Transitions (May 1, 2010 to April 30, 2014)

05/01/10 – 04/30/11		05/01/11 – 04/30/12		05/01/12 – 04/30/13		05/01/13 – 04/30/14	
Removed*	Added	Removed	Added	Removed	Added	Removed	Added
14	15	18	13	26	20	21	9

*Removed from the colony due to medical issues or project endpoint

Currently, there are 13 males and 69 females between 16 and 19 years of age in the CNPRC colony that are under consideration for assignment to the NIA Colony. Of the 69 females identified 37, are surgery-naïve. As noted, these animals may be housed in outdoor field corrals, and those that are housed indoors participate in routine pair housing, rotational enrichment, and breeding protocols based on their reproductive status. They also serve as surrogate dams for infants and juveniles.

Management of the entire aged colony (supported by the NIA, P51 base grant, other funding sources) focuses on preventive health care measures by **Primate Medicine Services**. The maintenance of healthy geriatric subjects for long-term cognitive function testing that requires intracranial surgeries are a priority. Geriatric nonhuman primates have many of the same aging changes and challenges often seen in the human population and similarly may have multiple chronic health conditions simultaneously. In one example, an off-site Affiliate Scientist relied on the Primate Medicine staff to provide the necessary day-to-day support including guidelines and SOPs for the cleaning and maintenance of cranial implants as well as a proactive health care plan. Early identification of spontaneous age-associated health problems, such as diabetes, ileocolic adenocarcinoma, amyloidosis, or endometriosis that arise after an animal has been assigned to a study, are managed aggressively by the veterinary staff to maximize the research study needs. Treatment includes diabetes management, hormonal therapy, and surgical resection of tumors and endometriomas not responsive to clinical management. When warranted, animals are euthanized at the discretion of the veterinary staff in consultation with the investigators.

INNOVATION

To ensure optimal conditions and the highest possible quality of animals, the CNPRC incorporates all of the research infrastructure and services available to fully support the NIA Colony and investigators that use these animals in their research programs. This includes Core Scientists (PIs on subcontracts, collaborators, on-site scientific expertise and input), Primate Services, Core Services, and Administrative Services as noted.

APPROACH

Plans for the Next Funding Period

The overall goal is to continue the proactive management plan that has been successful in ensuring the NIA Colony has a sufficient quantity of healthy animals available for aging and lifespan health research. With the current national focus on lifespan health, and the many program announcements and requests for applications (RFAs) at the NIH level, it is anticipated the needs for this colony will grow. Investigators that require NIA Colony animals will have available to them all of the services within the CNPRC specialized infrastructure which is dedicated to high quality research focused on lifespan health and healthy aging.

Specific Aim 1. Support and maintain NIA rhesus monkeys for investigators nationwide that are conducting aging-related research.

The CNPRC will proactively manage the NIA colony in order to maximize the number of healthy, surgery-naïve geriatric rhesus monkeys for aging research. Core Scientists and the Primate Services team will work together to support translational rhesus monkey models of human aging and lifespan health, and to meet investigator needs.

Specific Aim 2. Provide high quality expertise and services to investigators at the local, regional, and national levels.

Through the continued refinement of protocols, guidelines, SOPs, and expertise, Core Scientists and Primate Services staff will ensure investigators are provided healthy, well-characterized aged animals to support aging and lifespan health research objectives, new tools and technologies to advance aging research, and assistance with any health-related problems that may arise.

PRIMATE SERVICES: NATIONAL INSTITUTE ON AGING COLONY

PUBLICATIONS (May 1, 2010 to April 30, 2014)

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VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, and the IACUC.

1. Proposed Use of Animals. The current CNPRC vivarium consists of [Specific Animal Location] of indoor animal space. [Specific Animal Location] outdoor animal housing area includes [Specific Animal Location] acre field corrals [Specific Animal Location] corn cribs [Specific Animal Location] indoor space is used primarily to support the long-term breeding program. The rhesus production provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with rhesus monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease associated with aging. The NIA Colony is primarily focused on rhesus monkeys because this is the species that investigators use in their NIH-funded research. Animal numbers selected for projects are typically determined by a power analysis as described in individual research project IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian), [Excluded by Requester] Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Housing and Environmental Monitoring. Animal rooms are maintained within the recommended guidelines established by the current edition of the *ILAR Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. Typical nonhuman primate rooms provide 10-15 air changes per hour and are negatively pressurized relative to anterooms/corridors and the outside. Lighting is provided by fluorescent lights, which are controlled by timers (12 hours on/12 hours off). Room temperature is maintained between 68°F and 80°F, depending on the species and age of the animals in the room, and are checked and recorded daily. Emergency generator power is provided for all animal rooms. Indoor animal housing is monitored on a daily basis for temperature, light, and humidity. Power failures, major temperature fluctuation, and other environmental disturbances are either alarmed directly to Campus Physical Plant Services or monitored by CNPRC personnel on a daily basis. The Colony Operations Supervisor and the Maintenance Shop Supervisor carry pagers 24 hours/day and are alerted to environmental monitoring alarms and rooms that are out of temperature and humidity range.

Caging Systems. Indoor cages are stainless steel construction and either wall or rolling rack mounted. Cages incorporate a squeeze mechanism to bring the animal to the front of the cage for manipulation. Cage sizes are determined by the USDA and NIH policies. Cage designs incorporate sliding partitions to allow socialization or pair housing.

Environmental Enrichment. The Environmental Enrichment program is part of the Colony Management and Research Services component of Primate Services, is integrated with Behavior Management Services, and includes all animals, with emphasis placed on indoor-housed animals on research projects. Indoor cages are outfitted with a variety of enrichment options including manipulation mirrors (allowing the animal to view adjacent animals), and cage toys. Perches are present in all indoor cages. Low caloric items, such as forage, are provided on forage boards located on each cage. Animals also receive fruit or vegetables twice weekly. Non-food enrichment is also emphasized. One example of such enrichment is the placement of televisions, which provide visual stimulus to colony animals. Socialization can provide substantial benefit to the animals and is generally accomplished within the limitations of research protocols and daily management practices. Cages have been retrofitted or purchased with sliding partitions to allow pairing. The current strategy is to pair animals during the day and separate them at night to facilitate the assessment of physical signs each morning. Animals are paired early in the morning when animal care staff members begin daily animal care activities, animals are then separated at night when there are limited personnel available to monitor for potential aggressive interactions. The ability to observe each animal's individual daily physical signs is essential to many research programs and overall clinical care. Behavior Management Services staff members view every animal in the colony during morning health rounds and ensure they receive daily enrichment items targeting their specific behavior aberration. All indoor animals are also assessed monthly to identify any abnormal behaviors; these animals receive a detailed behavioral assessment monthly to monitor their status and progress.

Surveillance. The majority of animals at the CNPRC are from the production colony half-acre outdoor field corrals. Animals brought into the CNPRC from off-site facilities complete a 90-day quarantine at the CNPRC Quarantine Facility. During this time, animals undergo a complete physical examination with complete blood counts, blood and fecal parasitology, and rectal culture. Five tuberculin tests are completed, and animals are screened for simian retroviruses including Type D simian retrovirus (SRV), Simian Immunodeficiency Virus (SIV), and simian T-cell leukemia virus (STLV). Animals of foreign origin are treated for malaria and intestinal parasites. Animals with positive tuberculosis tests and SRV assays, or demonstrating signs of clinical illness, are humanely euthanized and a complete necropsy performed.

Feeding. The animals are fed commercial monkey chow twice daily. Monkey Chow is pre-analyzed for content. The analysis of each lot of feed is reviewed by CNPRC Quality Assurance and a Senior Veterinarian. Animals are supplemented with fruit or vegetables twice weekly. Water is provided by automatic lixits, which are checked daily for proper operation. Portable caging with detachable waterlines is checked daily. The CNPRC potable water supply is obtained from wells operated by UC Davis. All UC Davis wells are monitored by the Office of Environmental Health and Safety quarterly. The water is tested for chloroforms, a variety of chemical markers including heavy metals and a variety of toxic minerals, pesticides, and chemical contaminants. Additionally, the CNPRC tests for general mineral, organic, and inorganic contamination annually.



Sanitation. Indoor cages are hosed daily with a quaternary ammonium detergent/disinfectant and are sanitized every 2 weeks in a mechanical cage-washer. A microbiological monitoring program is in place to ensure efficacy of sanitation practices. Each animal area is monitored twice per year. Microbiological monitoring results are reviewed and signed off by each area supervisor, a Senior Veterinarian, and the Assistant Director for Colony Management and Research Services. Monitoring of caging pH during cage washing is included in the cage sanitation surveillance program. In addition, water lines in both the indoor and outdoor colony are monitored with microbiological testing on a rotational basis in conjunction with cage change activities.

Record Keeping. Record keeping includes a written individual animal record and entry of specific information into a computerized Vitals database (see **Information Technology Services**). Maintenance of the animal colony database, including information on project history, reproductive history, clinical data, viral status, as well as genealogical data is included. Also included are the current location of the animals, weight history, date of last tuberculosis test, and the date of the last serum banking. These data are available to aid in project design and animal selection by investigators. This database has also been critical to several retrospective studies involving prenatal mortality, transmission of retroviral agents in colony management, effects of housing changes on health, and risk factors for spontaneous diseases such as endometriosis. Management of this informational database represents a valuable resource to the entire biomedical research community. Historical animal-related data are maintained on a yearly basis to reflect the production statistics of the colonies including: conception rates, live birth rates, pregnancy loss, and infant mortality.

Animal Health Program. A health check is performed each morning by the colony management staff. Each animal has a location and animal identification barcode that is scanned, and an animal technician records physical signs listed on a menu using a portable barcode reader. After completion of the health check, the information is downloaded onto the main computer, and a morning health report is generated directly to the veterinary staff. Veterinarians or Animal Health Technicians perform a visual examination of each animal on health report. Results of the health check and assessment by the veterinary clinician are then recorded in the animal's record. For animals on study, a report is generated to the investigator on a daily basis by electronic mail. Animals in the outdoor colony are also checked twice each day, once in the morning and afternoon. Identification of animals in the field corrals is performed by individual dye mark. Technicians check each cage closely for animals potentially requiring medical attention. The afternoon health check was added to the outdoor colony in 2012, and increased health surveillance is particularly important during the birth season.

Centralized Research Support. The various services represented in Primate Services work synergistically to provide high quality, technical research support to all investigators utilizing the CNPRC, as needed, whether located locally or at a distant site. Staff veterinarians also provide extensive clinical support to animals on long-term research protocols (see Primate Medicine Services).

Staff Training. The program emphasizes occupational safety, as well as increasing demands for technical expertise in the care and research support of nonhuman primates. Training is viewed not only as the initial step at hire, but as an ongoing process through in-house classes and support to attend relevant training programs, meetings, and conferences. A spectrum of training opportunities is available specific to the CNPRC and to meet campus-wide training requirements. These include: UC Davis Primate Handling and Husbandry Training, Campus Laboratory Animal Care Classes (AAALAC preparation); Injury / Illness Prevention Plan; Infection Control Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management; Campus Back Safety Class; Campus Radiation Safety Class; Pesticide and Antimicrobial Safety; Training in Good Laboratory Practices; Supervisor Training with Job Skills Worksheet; and position specific training for all levels of husbandry, animal care, and technical skills. The training program also includes a series of "*Attention to Detail*" documents that provide very detailed information for each of the training and skill areas the staff is expected to meet including information to enhance understanding and the need to adhere to defined guidelines for critical procedures.

Standard Operating Procedures (SOPs). Primate Services has an extensive collection of 185 SOPs that provide detail on all operational procedures including: husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by all staff and undergo full review and revision every three years. SOPs are available in an electronic format online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC, and SOPs by number can be noted in IACUC protocol submissions.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

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- Excluded by Requester [redacted] Age-associated deficits in pattern separation functions of the perirhinal cortex: A cross-species consensus. *Behav Neurosci* 125:836-847, 2011. PMCID: PMC3255096
- Excluded by Requester [redacted] Characterizing cognitive aging of associative memory in animal models. *Front Aging Neurosci* 4:10, 2012. PMCID: PMC3439635
- Excluded by Requester [redacted] Presynaptic mitochondrial morphology in monkey prefrontal cortex correlates with working memory and is improved with estrogen treatment. *Proc Natl Acad Sci U S A* 111:486-491, 2014. PMCID: PMC3890848
- Excluded by Requester [redacted] A pathophysiological framework of hippocampal dysfunction in ageing and disease. *Nat Rev Neurosci* 12:585-601, 2011. PMCID: PMC3312472
- Excluded by Requester [redacted] Age-related changes in the mesial temporal lobe: the parahippocampal white matter region. *Neurobiol Aging* 33:1168-1176, 2012. PMCID: PMC3158300

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RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

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 Division: Office of Research
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7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Primate Medicine Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
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Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename PM_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	PM_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	PM_FacilitiesOtherResources.pdf
11. Equipment	PM_Equipment.pdf

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

ABSTRACT

The primary goal of Primate Services is to ensure optimal animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. Animal care and research service is provided by a highly trained staff of veterinarians, Core Scientists, technicians, and administrators to meet the needs of the animals as well as the investigators using the CNPRC resource. **Primate Medicine Services** provides centralized clinical care, research support, training, and veterinary oversight to ensure compliance with the highest quality standards of research conduct and animal care. The Primate Medicine team is responsible for the clinical care of ~5,000 nonhuman primates which encompasses a range of health care needs across the lifespan, from neonatal to geriatric stages, and from preventive medicine to intensive care, and provides research project support to investigators. Primate Medicine veterinarians integrate with other CNPRC services, Core Scientists, the UC Davis Animal Care Program, the Institutional Animal Care and Use Committee (IACUC), and the Veterinary Medical Teaching Hospital to ensure optimal management practices, and to develop standard operating procedures as well as implement strategic plans. The Specific Aims for Primate Medicine Services are to: (1) Provide high quality care for nonhuman primates at the CNPRC to support research, (2) Provide expertise and research support to investigators locally, regionally, and nationally, (3) Mentor and train the next generation of veterinarians with nonhuman primate expertise, and (4) Ensure the highest standards of responsible conduct of research and animal care.

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: See **Colony Management and Research Services**.

Clinical: Three clinical rooms totaling 560 sq. ft. are used for physical examinations, treatments, and minor surgical procedures. Intensive care support is also provided in a dedicated suite. Surgical preparation is carried out in an anteroom (137 sq. ft.), two surgical operating rooms (582 sq. ft.), and a surgeon's prep and instrument sterilization area (168 sq. ft.). Diagnostic equipment rooms include radiography, fluoroscopy, ultrasound, and DEXA bone density scanning.

Animal: Animals from the outdoor rhesus monkey colony are hospitalized in a 310 sq. ft. hospital room, 96 sq. ft. of space is available for surgical recovery, and an infectious disease isolation area is available 36 sq. ft. Two separate SPF hospitals are maintained.

Computer: Primate Medicine veterinarians and staff are equipped with networked computers including 11 located in the clinic areas.

Office: Office space and administrative support is provided to the Staff Veterinarians and support staff in the Primate Medicine trailer which includes 7 private and shared offices and a conference room.

Other: The CNPRC is a part of the UC Davis AAALAC-accredited program.

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

EQUIPMENT

Major equipment includes a DEXA density scanner, ultrasound imaging system, Datex anesthetic monitors (4), gas anesthesia units (3), a digital radiology unit, bronchoscope tower, gastroscope tower, laparoscope tower, and MedDispense machines (3).

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	10,858.00	38,083.00
2.					Senior Veterinarian			0.0	0.0	14,977.00	5,973.00	20,950.00
3.					Senior Veterinarian			0.0	0.0	11,105.00	4,429.00	15,534.00
4.					Senior Veterinarian			0.0	0.0	10,997.00	4,386.00	15,383.00
5.					Senior Veterinarian			0.0	0.0	11,074.00	4,417.00	15,491.00
6.					Senior Veterinarian			0.0	0.0	11,105.00	4,429.00	15,534.00
7.					Associate Veterinarian			0.0	0.0	8,533.00	4,514.00	13,047.00
8.					Senior Veterinarian			0.0	0.0	10,106.00	4,031.00	14,137.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

148,159.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			4,567.00	2,416.00	6,983.00
2	Primate Medicine Residents				54,037.00	21,552.00	75,589.00
3	Total Number Other Personnel					Total Other Personnel	82,572.00
					Total Salary, Wages and Fringe Benefits (A+B)		230,731.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,500.00
2. Foreign Travel Costs	0.00
Total Travel Cost	10,500.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	23,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	24,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	265,231.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	265,231.00	60,207.00
		Total Indirect Costs	60,207.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	325,438.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	11,489.00	38,714.00
2.					Senior Veterinarian			0.0	0.0	15,576.00	6,573.00	22,149.00
3.					Senior Veterinarian			0.0	0.0	11,549.00	4,874.00	16,423.00
4.					Senior Veterinarian			0.0	0.0	11,437.00	4,826.00	16,263.00
5.					Senior Veterinarian			0.0	0.0	11,517.00	4,860.00	16,377.00
6.					Senior Veterinarian			0.0	0.0	11,549.00	4,874.00	16,423.00
7.					Associate Veterinarian			0.0	0.0	8,874.00	4,909.00	13,783.00
8.					Senior Veterinarian			0.0	0.0	10,510.00	4,435.00	14,945.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

155,077.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			4,704.00	2,602.00	7,306.00
2	Primate Medicine Residents				55,932.00	23,604.00	79,536.00
3	Total Number Other Personnel					Total Other Personnel	86,842.00
					Total Salary, Wages and Fringe Benefits (A+B)		241,919.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,815.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	10,815.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	23,690.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	24,720.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	277,454.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	277,454.00	62,982.00
Total Indirect Costs			62,982.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	340,436.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	11,893.00	39,118.00
2.					Senior Veterinarian			0.0	0.0	15,732.00	6,872.00	22,604.00
3.					Senior Veterinarian			0.0	0.0	11,665.00	5,096.00	16,761.00
4.					Senior Veterinarian			0.0	0.0	11,551.00	5,046.00	16,597.00
5.					Senior Veterinarian			0.0	0.0	11,632.00	5,081.00	16,713.00
6.					Senior Veterinarian			0.0	0.0	11,665.00	5,096.00	16,761.00
7.					Associate Veterinarian			0.0	0.0	8,963.00	5,119.00	14,082.00
8.					Senior Veterinarian			0.0	0.0	10,616.00	4,637.00	15,253.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

157,889.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			4,705.00	2,687.00	7,392.00
2	Primate Medicine Residents				56,224.00	24,561.00	80,785.00
3	Total Number Other Personnel					Total Other Personnel	88,177.00
					Total Salary, Wages and Fringe Benefits (A+B)		246,066.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	11,139.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	11,139.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	24,401.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	25,462.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	282,667.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	282,667.00	64,165.00
Total Indirect Costs			64,165.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	346,832.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	12,247.00	39,472.00
2.					Senior Veterinarian			0.0	0.0	16,361.00	7,360.00	23,721.00
3.					Senior Veterinarian			0.0	0.0	12,132.00	5,457.00	17,589.00
4.					Senior Veterinarian			0.0	0.0	12,013.00	5,404.00	17,417.00
5.					Senior Veterinarian			0.0	0.0	12,097.00	5,442.00	17,539.00
6.					Senior Veterinarian			0.0	0.0	12,132.00	5,457.00	17,589.00
7.					Associate Veterinarian			0.0	0.0	9,321.00	5,482.00	14,803.00
8.					Senior Veterinarian			0.0	0.0	11,040.00	4,966.00	16,006.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

164,136.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			4,847.00	2,851.00	7,698.00
2	Primate Medicine Residents				58,197.00	26,179.00	84,376.00
3	Total Number Other Personnel					Total Other Personnel	92,074.00
					Total Salary, Wages and Fringe Benefits (A+B)		256,210.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	11,473.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	11,473.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	25,133.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	26,226.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	293,909.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	293,909.00	66,717.00
Total Indirect Costs			66,717.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	360,626.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	27,225.00	12,623.00	39,848.00
2.					Senior Veterinarian			0.0	0.0	17,016.00	7,890.00	24,906.00
3.					Senior Veterinarian			0.0	0.0	12,616.00	5,850.00	18,466.00
4.					Senior Veterinarian			0.0	0.0	12,494.00	5,793.00	18,287.00
5.					Senior Veterinarian			0.0	0.0	12,581.00	5,833.00	18,414.00
6.					Senior Veterinarian			0.0	0.0	12,616.00	5,850.00	18,466.00
7.					Associate Veterinarian			0.0	0.0	9,694.00	5,875.00	15,569.00
8.					Senior Veterinarian			0.0	0.0	11,482.00	5,324.00	16,806.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

170,762.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			4,992.00	3,025.00	8,017.00
2	Primate Medicine Residents				60,240.00	27,932.00	88,172.00
3	Total Number Other Personnel				Total Other Personnel		96,189.00
Total Salary, Wages and Fringe Benefits (A+B)							266,951.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description	
List items and dollar amount for each item exceeding \$5,000	
Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	11,817.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	11,817.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	25,887.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	27,013.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	305,781.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	305,781.00	69,412.00
Total Indirect Costs			69,412.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	375,193.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Associate Director for Primate Services	EFFORT			
	Senior Veterinary Manager				
	Senior Veterinarian				
	Senior Veterinarian				
	Senior Veterinarian				
	Senior Veterinarian				
	Senior Veterinarian				
	Associate Veterinarian				
	Resident				
	Resident				
TBN	Resident				
Excluded by Requester	Administrative Assistant				
<i>Animal Health Technicians (16)</i>	<i>Animal Health Technicians</i>	0	100	0	100

Individuals shown in italics are not supported by the P51 base grant; their salary support is provided by Program Income

TBN=to-be-named

Excluded by Requester **DVM, DACLAM, Associate Director for Primate Services** EFFORT months % Effort

Excluded by Requester is Associate Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine, the Associate Director for Primate Services, and Chief Veterinarian. He has responsibilities for all aspects of the nonhuman primate colonies and related services provided through Primate Medicine Services. Excluded by Requester has been in the field of medical primatology for 30 years.

Excluded by Requester **DACLAM** EFFORT months % Effort Excluded by Requester is the Senior Veterinary Manager for Primate Medicine, and Adjunct Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine. She is also the Chief of Service for the Primate Medicine Clinical Rotation, and has over 10 years of experience in medical primatology. Excluded by Requester oversees the daily operation and management of Primate Medicine Services, and she provides didactic teaching and clinical mentoring for veterinary students, residents, and visiting veterinarians.

Excluded by Requester **DVM, DACLAM** EFFORT months % Effort Excluded by Requester is a Senior Veterinarian and skilled primate clinician with more than 13 years primate medicine experience. She provides clinical care for colony animals and veterinary support for research protocols.

Excluded by Requester **DVM, DACLAM** EFFORT months % Effort Excluded by Requester is a Senior Veterinarian with 10 years of experience in primate medicine and surgery, of which nine years was at another National Primate Research Center.

Excluded by Requester **DVM, DACLAM** EFFORT months % Effort Excluded by Requester is a Senior Veterinarian with 4 years of experience in medical primatology including experiences in large outdoor nonhuman primate housing facilities.

Excluded by Requester [REDACTED] EFFORT [REDACTED] months [REDACTED] % Effort [REDACTED] Excluded by Requester [REDACTED] is a Senior Veterinarian and skilled clinician and surgeon with more than 13 years of primate medicine experience. [REDACTED] Excluded by Requester [REDACTED] provides clinical care for colony animals and veterinary support for research protocols.

Excluded by Requester [REDACTED] DVM, DAACLAM [REDACTED] EFFORT [REDACTED] months [REDACTED] % Effort [REDACTED] Excluded by Requester [REDACTED] is a Senior Veterinarian with 5 years of experience in primate medicine and surgery. [REDACTED] Excluded by Requester [REDACTED] provides clinical care in the hospital service of Primate Medicine.

Excluded by Requester [REDACTED] DVM [REDACTED] EFFORT [REDACTED] months [REDACTED] % Effort [REDACTED] Excluded by Requester [REDACTED] is an Associate Veterinarian that recently joined the full-time veterinary staff at the CNPRC after completing his residency. He has 4 years experience in laboratory animals and primate medicine.

Veterinary Residents [REDACTED] EFFORT [REDACTED] months each [REDACTED] % Effort [REDACTED] One named [REDACTED] Excluded by Requester [REDACTED] and a to-be-named Veterinary Resident is included for the Laboratory Animal Medicine Residency Program. The residency has a focus on primate medicine.

Excluded by Requester [REDACTED] **Administrative Assistant** [REDACTED] EFFORT [REDACTED] months [REDACTED] % Effort [REDACTED] Excluded by Requester [REDACTED] is responsible for primary administrative support including scheduling of all medical and surgical procedures, controlled substances inventory, and she serves as a primary liaison between Primate Medicine and Anatomic and Clinical Pathology Services.

Animal Health Technicians (AHTs) (16) function similar to physician assistants, and assist the veterinarians in providing daily support for colony and experimental procedures. A high level Clinic Manager oversees the AHTs, and addresses the day-to-day workload and strives to optimize efficiencies, while the Primate Medicine Senior Veterinary Manager retains oversight.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are listed in the **Facilities Improvement** section.

TRAVEL

\$10,500 is requested (7 x \$1,500) for the veterinarians to attend annual meetings, such as the national meeting of the Association of Primate Veterinarians.

SUPPLIES

\$23,000 is requested for essential supplies for development of new therapeutic or surgical procedures.

OTHER EXPENSES

\$1,000 is requested for manuscript submission.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		796,023.00
Section B, Other Personnel		445,854.00
Total Number Other Personnel	15	
Total Salary, Wages and Fringe Benefits (A+B)		1,241,877.00
Section C, Equipment		0.00
Section D, Travel		55,744.00
1. Domestic	55,744.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		127,421.00
1. Materials and Supplies	122,111.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,425,042.00
Section H, Indirect Costs		323,483.00
Section I, Total Direct and Indirect Costs (G + H)		1,748,525.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	464,400.00	Services
2	489,942.00	Services
3	516,889.00	Services
4	545,318.00	Services
5	575,310.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?* ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

PM_SpecificAims.pdf

3. Research Strategy*

PM_ReserachStrategy.pdf

4. Progress Report Publication List

PM_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

PM_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

PM_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

SPECIFIC AIMS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards for animal care at UC Davis and the CNPRC. Primate Medicine provides high quality centralized clinical care, research support, training, and veterinary oversight to ensure compliance with optimized standards of research conduct and animal care. The Primate Medicine team is responsible for the clinical care of ~5,000 nonhuman primates and encompasses all health needs across the lifespan, from neonatal to geriatric stages, and from preventive medicine to intensive care. Primate Medicine Services also provides research project support to investigators. The range of opportunities and the quantity of animals across all age groups provides unique opportunities for Primate Medicine staff to educate and train veterinarians, residents, veterinary students, and other trainees from institutions worldwide. Primate Medicine veterinarians also integrate with other CNPRC services, Core Scientists, the UC Davis Animal Care Program, the Institutional Animal Care and Use Committee (IACUC), and the Veterinary Medical Teaching Hospital to ensure optimal management practices, develop guidelines, algorithms, and standard operating procedures (SOPs), as well as provide input on future plans.

Specific Aim 1. Provide high quality care for nonhuman primates at the CNPRC to support research.

Plan. Well-trained experienced veterinarians in medical primatology and Animal Health Technicians (AHTs) trained to the level of physician assistants provide preventive health care, medical care, and input into the CNPRC management programs. Preventive health includes a Center for Disease Control (CDC) approved quarantine program, biannual tuberculin (TB) testing, routine physical examinations, serum banking, and a vaccination program. Medical care addresses the spectrum of diagnostics to treatment in general medicine, dentistry, emergency medicine, intensive care, project-related clinical findings, and specialized surgical procedures.

Specific Aim 2. Provide expertise and research support to investigators locally, regionally, and nationally.

Plan. The veterinarian's role is to provide the necessary support and expertise to ensure successful project outcomes. The veterinarians work in a close partnership with Core and Affiliate Scientists and the entire Primate Services team that is built on mutual respect and a common vision focused on improving human health-related problems, while concurrently ensuring nonhuman primate well-being. As a part of the centralized services, the veterinary staff members keep pace with technology to support research and aid in refining research protocols.

Specific Aim 3. Mentor and train the next generation of veterinarians with nonhuman primate expertise.

Plan. Primate Medicine is committed to mentor and train the next generation of veterinarians in collaboration with Core Scientists. Primate Medicine provides a spectrum of learning opportunities for veterinarians (including the Mountain Gorilla Project), residents, veterinary students from institutions worldwide, animal technicians, and new investigators in order to support their career goals.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

Plan. CNPRC veterinarians have been trained in American College of Laboratory Animal Medicine (ACLAM) approved residency programs and are ACLAM boarded which adds significantly to the quality of animal care and research standards. Primate Medicine works with the Primate Services team and Core Scientists that have specialized expertise in infectious diseases, genetics, behavior, reproduction, respiratory illnesses, and pathology in order to provide optimal colony management and psychological well-being. Metrics obtained support policies, SOPs, guidelines, and strategic plans; these experiences are also shared with various oversight committees and regulatory agencies.

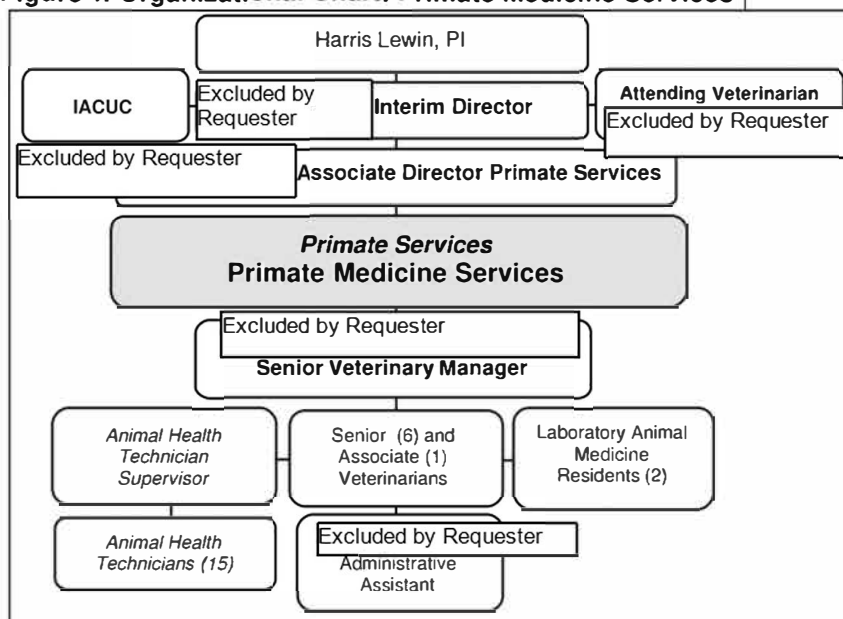
PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

RESEARCH STRATEGY

INTRODUCTION

The California National Primate Research Center (CNPRC) is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited Animal Care Program. The Associate Director for Primate Services, the Primate Medicine Senior Veterinary Manager, meet monthly with the UC Davis Attending Veterinarian, to ensure close integration of the CNPRC within the UC Davis Animal Care Program (Figure 1). The Attending Veterinarian reports to the UC Davis Institutional Official, who oversees all animal care of UC Davis campus. The veterinary staff affiliated with Primate Medicine Services is also integrated closely with the School of Veterinary Medicine. For example, Dr. [redacted] is an Associate Professor in the Department of Medicine and Epidemiology, (Pathology) both hold adjunct appointments in the School of Veterinary Medicine. Primate Medicine and Anatomic and Clinical Pathology Services work closely together and are actively involved in training veterinary students and externs from other institutions. Both Services are also extensively involved in Graduate Clinical education with residents in Laboratory Animal Medicine, Zoological Medicine, and Pathology. Primate Medicine staff members are shown in Table 1. The sources of

Figure 1. Organizational Chart: Primate Medicine Services



support for the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 1. Primate Medicine Services Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
[redacted]	Department of Medicine and Epidemiology, School of Veterinary Medicine	Associate Director for Primate Services
[redacted]	Department of Medicine and Epidemiology, School of Veterinary Medicine	Senior Veterinary Manager
[redacted]	CNPRC	Senior Veterinarian
[redacted]	CNPRC	Senior Veterinarian
[redacted]	CNPRC	Senior Veterinarian
[redacted]	CNPRC	Senior Veterinarian
[redacted]	CNPRC	Senior Veterinarian
[redacted]	CNPRC	Associate Veterinarian
[redacted]	CNPRC	Resident
TBN	CNPRC	Resident
[redacted]	CNPRC	Administrative Assistant
Animal Health Technicians (16)	CNPRC	Animal Health Technicians

TBN=to-be-named

Table 2. Support for Primate Medicine Services

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$259,685	\$265,231
Program Income from P51	\$440,680	\$464,400
Other Sources	\$0	\$0
TOTAL	\$700,365	\$729,631

Primate Medicine works in tandem with Core Scientists, Service Cores, and the Primate Services team to promote the advancement of nonhuman primate models for translational research at all life stages. Primate Medicine goals are to provide high quality clinical care, research support, mentoring, and training, and to ensure the highest standards of responsible research conduct and animal care. Preventive health is addressed both individually and from a “herd health” perspective including routine physical examinations, dental evaluations and cleaning, regular weights, serum banking, and a vaccination program. At an individual level, each animal receives personalized health care through diagnostic work-ups for any clinical problems that may arise to emergency medicine. The CNPRC colonies include animals at all life stages, which translates to evolving health status based on age; infants and geriatric animals require the most intensive oversight and care. The veterinary staff is proactive in diagnostics with the geriatric colony to ensure optimal maintenance of these valuable research animals (see **National Institute on Aging Colony**). Metrics for success include a significant reduction in dental issues through prophylactic dental care, and detection of amyloidosis or gastrointestinal (GI) adenocarcinomas at very early stages when treatment is still an option. Preventive health care at every stage across the lifespan ensures health and well-being, and avoids or delays the onset of disease while reducing healthcare costs.

Working with nonhuman primates requires specialized knowledge and expertise. The veterinary staff applies their training and vast experiences when working with investigators from project inception to study endpoints. Meeting research objectives and the needs specific to the species is a primary goal. Veterinarians share their knowledge of an animal's medical/health status with investigators and work together to plan next steps. Further, Primate Medicine strives to provide procedural support requested by investigators while integrating the vast expertise of the Core Scientists and Scientific Core Services to implement new capabilities and assist with the design and refinement of research protocols. Primate Medicine is also committed to providing a spectrum of learning opportunities for graduate veterinarians, residents, senior veterinary students from institutions worldwide, Animal Health Technicians (AHTs), animal care technicians, and new investigators. With the size of the nonhuman primate colony and the extensive caseload, Primate Medicine provides a wealth of learning opportunities within an environment of sharing and dissemination of knowledge.

One of the strengths of the CNPRC centralized Primate Services and Core Scientist infrastructure is the synergism that ensures integrated expertise for the highest standards of responsible conduct of research and animal care. It is within this collaborative infrastructure that problem solving and the exchange of new ideas flourish, which benefits investigators and the animals. This integrated approach includes the UC Davis IACUC, Veterinary Medical Teaching Hospital, faculty in the Schools of Medicine and Veterinary Medicine, the UC Davis Attending Veterinarian, and other UC Davis animal care service programs. Primate Medicine works together with Primate Services and Core Scientists to provide optimal colony management and psychological well-being. Metrics support policies, standard operating procedures (SOPs), guidelines, and strategic planning.

Response to Summary Statement.

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE**Progress and Major Accomplishments: Contributions to the CNPRC Mission**

During the current funding period, Primate Medicine Services implemented changes that have vastly improved function and productivity, as shown in the following examples.

The Director's Office supported the hire of [Excluded by Requester] DVM, MPH, PhD (under the mentorship of Dr. [Excluded by Requester] [Excluded by Requester] **Infectious Diseases Research Unit**) after completion of his graduate studies at UC Davis in order to facilitate investigation of idiopathic chronic diarrhea (ICD). [Excluded by Requester] developed a standard template for studies to ensure that result-focused trials were performed consistently with limited confounding variables, permitting comparisons between studies and identification of useful interventions. This plan was established with the clinical veterinarians, CNPRC Anatomic and Clinical Pathology Services, and [Excluded by Requester] a GI specialist in the School of Veterinary Medicine. Projects include the study of [Excluded by Requester] mentation, which suggested that inulin has the potential to improve ICD, and which may also be associated with an alteration of the GI microbiota. In collaboration with the **Multimodal Imaging Core**, a new method was developed to quantitatively assess microscopic colitis [Excluded by Requester] 2013]. A collaborative study with investigators at UC San Francisco also focused on therapeutic helminth treatment, which suggested amelioration of colitis by restoring mucosal barrier functions, and reducing overall bacterial attachment and communities of attached bacteria [Excluded by Requester] et al., 2012].

Primate Medicine hired a Clinic Manager to coordinate and manage the AHT staff. This position provides a considerable savings of valuable veterinary time needed to provide clinical care, research support, teaching, and management. The high level Clinic Manager addresses the day-to-day workload and strives to optimize efficiencies while the Primate Medicine Senior Veterinary Manager retains oversight.

The Senior Veterinary Manager is an Assistant Clinical Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine, and is integrated into departmental communications, meetings, and training which encourages collaborations with School of Veterinary Medicine faculty [Excluded by Requester] Chief of Primate Medicine Service at the Veterinary Medical Teaching Hospital, and attends a monthly [Excluded by Requester] Service meeting where all service chiefs discuss the residency programs, veterinary student rotations, and

[Excluded by Requester] issues. In addition [Excluded by Requester] is co-director of the UC Davis Laboratory Animal Medicine (LAM) [Excluded by Requester]ncy Program, and Director of the Northern California LAM Resident Training Day. Resident Training Day is an opportunity for all of the LAM residents in Northern California to visit different facilities and obtain training from experts at each of the sites. The residents develop camaraderie and learn from each other, and have established study groups [Excluded by Requester] is also an honorary Attending Veterinarian in California and attends the University of California Attending Veterinarian Meetings biannually to discuss facilities, research, training, animal care, and regulatory changes.

In recognition of the expertise and professional capabilities of the School of Veterinary Medicine faculty, Primate Medicine has reached out to a number of Veterinary Medical Teaching Hospital services for consults and currently collaborates with faculty in dentistry and ophthalmology. Both groups have facilitated outstanding training for CNPRC veterinary staff and residents. In addition, faculty from these departments have consulted and assisted with complex CNPRC cases. CNPRC Staff Veterinarians also work closely with the UC Davis

Attending Veterinarian Excluded by Requester and the IACUC to address complex research protocols and to communicate with and respond to regulatory agencies.

The Colony Management Advisory Committee consists of Core Scientists from all of the Scientific Research Units and includes Primate Services Veterinarians (see **Administration Services** section). Committee discussion topics range from vaccination protocols to enrichment and diet. A large number of colony management protocols and research project ideas have emerged from these topical discussions. Examples include measles vaccination trials and testing new treatments for ICD (Table 3).

Table 3. Examples of Colony Management Pilot Projects (May 1, 2010 to April 30, 2014)

Grant Year	Team	Project Title
2011 - 2012	Excluded by Requester	Assessment of Impact of Lysozyme Transgenic Goat's Milk in Nonhuman Primates with Acute Diarrhea
		Measles Vaccine Clinical Study
		Treatment of Idiopathic Chronic Diarrhea Animals with Serum-Derived Bovine Immunoglobulin
2012 - 2013		Treatment of Chronic Diarrhea in Macaques with Raw Bovine Colostrum
		Genetic Markers: Titi Monkey Colony
		Endometriosis Treatment Trial
2013 - 2014		Test Antibody Response to One-half Dose of Vanguard DM Measles
		Alternate Paleo diet
		Colonic Enteroendocrine Cells as a Marker of Idiopathic Chronic Diarrhea

*See Anatomic and Clinical Pathology Services

In addition, the Morbidity and Mortality Review Committee was established to integrate a team consisting of a Core Scientist and IACUC Co-Chair, Senior Veterinary Managers for Primate Medicine and Pathology, the UC Davis Attending Veterinarian, the Assistant Director for Colony Management and Research Services, and the Associate Director for Primate Services. This committee has provided an excellent forum to monitor and discuss monthly outcomes and any unanticipated findings, and determine next steps on etiologies or improvements. The first charge was to evaluate the CNPRC's outdoor infant mortality to better define the timing of increased risk and to determine possible interventional strategies. Dams with infants that did not thrive well the prior year were identified and positive reinforcement training was used (**Behavior Management Services**) to train the dams to allow closer newborn monitoring.

Primate Medicine improved management of the controlled substance inventory to ensure compliance with the UC Davis campus and the U.S. Drug Enforcement Agency. The CNPRC has a computerized MedDispense unit that is managed by administrators (see **Colony Management and Research Services**); the program is overseen by a Senior Veterinarian. These locked dispense units require individual identification and passwords to obtain access to controlled substances. They digitally record each transaction of controlled substance removal and thus the total inventory as well. Reports can also be run and compared with animal records to check accuracy and ensure regulatory compliance.

Primate Services has made several electronic improvements that have facilitated work efficiency. For example, the electronic formulary was enhanced to allow posting and sharing of information with Core Scientists. Primate Medicine also improved the Specific Private Vendor in collaboration with the **Information Technology Services** staff to make it easier to track treatments, implement changes in the treatment over the course of administration, and add comments on treatment administration.

One of the strengths of the centralized CNPRC services is that all of the individual Primate Services components work together to bring the appropriate expertise together to care for the animals, and to provide the necessary skills and support. It is these interactions that facilitate the distribution of work and increase problem-solving skills. Primate Medicine Services provides a range of research support services (see Tables 4 and 5 and Innovation, below).

Table 4. Examples of Primate Medicine Services Veterinary Research Support

Project Title (Funding Source)	Procedures
Primate Models of Social Behavior (NIH grant #R37-MH057502)	Infant lesion surgery, post-operative care, assistance with MRI
Neurobehavioral Relations in Senescent Hippocampus* (NIH grant #R01-AG003376)	Cranial implant surgery, post-operative care, assistance with MRI and microPET
Estrogen and the Aging Brain* (NIH grant #P01-AG016765)	Ovariectomy, assistance with MRI
The Impact of Tolerance in the Newborn of Lentiviral Infection (NIH grant #R01-AI090677)	Cesarean section, infant lymph node and colon biopsies
Fluoxetine: Sensitive Ages and Genotypes for Adverse Effects in Juvenile Monkeys (NIH grant #R01-HD065826)	Morphometric measurements, long bone X-ray, CSF samples
Use of GDNF-Releasing Nanofiber Nerve Guide Conduits for the Repair of Conus Medullaris/Cauda Equina Injury in the Nonhuman Primate* (DOD grant #SC090273)	EMG and urodynamics, neurotracer injections, post-operative care, assistance with MRI
Effects of Chronic Intranasal Oxytocin (NIH grant #R01-HD071998)	Titi monkey CSF samples, assistance with microPET and MRI
Lung Regeneration Following Partial Pneumonectomy in Macaques (P51 Pilot Project)	Pneumonectomy with assistance of UC Davis Medical Center surgeon, post-operative care
Effects of Pathogenic and Non Pathogenic Bacteria in the Context of SIV Infection (NIH grant #R01-AI043274)	Bowel loop surgery
Magnetic Anastomosis for Glycemic Insulin Control (MAGIC): A Pilot Study of Side-to-Side Duodeno-Distal Ileal Anastomosis in Diabetic Monkeys (Pilot Project funded by external source, UCSF)	GI anastomoses, post-operative care
Plasticity and Regeneration in the Primate Spinal Cord* (NIH grant #R01-NS042291) and Consortium Study (VA San Diego Healthcare System)	Bone marrow aspirates, skin biopsy, EMG recordings, hemisection and neurotracer surgeries, CSF samples, post-operative care
Maternal Temperament, Stress, and Inflammation in Preterm Birth* (NIH grant #R01-HD078127)	Skin biopsies, amniocentesis
A Human Fc Bifunctional Fusion Protein to Treat Severe Allergic Asthma (Pilot Project)	Bronchoalveolar lavage, assistance with pulmonary function tests

*Off-Site Affiliate Scientist. MRI=magnetic resonance imaging; CSF=cerebrospinal fluid

Table 5. Service Use: Primate Medicine (May 1, 2010 to April 30, 2014)

Grant Year	Service Type	# Users	Investigators (N)	Service Cost (\$)	Total Cost (\$)
2010 - 2011	Research Support	68	Core Scientists (13)	263,204	598,373
			UC Davis (21)	150,557	
			External (34)	184,612	
2011 - 2012	Research Support	57	Core Scientists (11)	114,689	480,601
			UC Davis (17)	110,026	
			External (29)	255,886	
2012 - 2013	Research Support	56	Core Scientists (12)	98,129	533,415
			UC Davis (21)	174,661	
			External (23)	260,625	
2013 - 2014	Research Support	56	Core Scientists (13)	90,967	408,284
			UC Davis (20)	133,767	
			External (23)	183,550	
TOTAL					\$2,020,673

INNOVATION

As a component of the CNPRC centralized service, the veterinary staff is regularly challenged to keep pace with new technology and methodologies to support research or new techniques. Some examples of innovative ways Primate Medicine has integrated with specific research programs are noted above (Table 4) and below.

At present, spinal cord injury models (hemisection or contusion) present one of the most challenging post-operative care protocols. Because one of the projects has a PI that is an off-site investigator, the Primate Medicine veterinary staff provides the day-to-day support for these animals pre- and post-hemisection/contusion. Prior to surgery, the animals learn to perform specific tasks prior to surgery (e.g., reaching, grasping, fine motor skills, arm chair training, treadmill walking), and Primate Medicine veterinarians and staff place percutaneous endoscopic gastrotomy (PEG) tubes in order to consistently administer immunosuppressive agents for a therapeutic stem cell treatment. Postoperatively, these animals require

extensive intensive care. Since they also present with a significant loss of limb performance, they require assistance with feeding and changes in body position. The animals are placed in specially constructed cages (provided through the on-site shop staff mechanics) that allow easy access to meet their needs. As these animals acquire more independent function, the intensive care needs gradually diminish. An algorithm was developed to address Brown-Sequard Syndrome that can occur, and new applications have been assessed in the use of Botox based on human clinical experiences for incision closure. Efforts are underway to continue to address efficiencies in patient care, such as remote visual monitoring and telemetry, as well as improved nutrition and fluids delivery systems. This complex project with very valuable animals requires all members of the research and Primate Services teams to work together to ensure success concurrently with the best animal care (see **Colony Management and Research Services**).

Since the CNPRC maintains a large breeding colony, Primate Medicine is able to support research projects across the lifespan – from neonatology to geriatrics. For example, a protocol was developed to support a project led by Core Scientist [Excluded by Requester] (**Brain, Mind, and Behavior Research Unit**) with lesioned infants requiring a neurosurgery with a prolonged surgical recovery. Infants were maintained in the surgical suite until full recovery was successfully managed by a veterinarian.

A similar example specific to the age group was shown in two NIH-funded projects that required colon biopsies in young monkeys. Rather than use the established Golytely protocol typically used in adult animals, a modified protocol was developed that focused on limiting the diet to only liquids 48 hours prior to the procedure, then offering Pedialyte in the last 24 hours. With this method of “bowel prep”, biopsies have been achievable with a more age-specific and refined approach.

Geriatric rhesus monkeys have many of the same aging changes and challenges often seen in the human population, including multiple chronic health concerns simultaneously. In one example, an off-site Affiliate Scientist relied on the Primate Medicine staff to provide the necessary day-to-day support for these animals. Guidelines and SOPs were developed for the cleaning and maintenance of cranial implants as well as a proactive health care plan.

The CNPRC vaccination program consists of measles and tetanus vaccination. Shortages of both human vaccines during the current funding period necessitated investigation into alternative vaccine sources. Through the National Primate Research Centers (NPRCs) Consortium, five of the NPRCs collaborated on a vaccine trial using a measles vaccine from India. This trial was led by [Excluded by Requester] and conducted using a standard template from a previous measles vaccine trial. Currently, a half-dose measles vaccine trial to determine efficacy is underway (see **NPRC Consortium**). Similarly, when there was a tetanus vaccine shortage, investigation identified an equine vaccine that had been previously tested in nonhuman primates, and a safety and efficacy trial was performed.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Provide high quality care for nonhuman primates at the CNPRC to support research.

One goal during the next funding period is to continue to refine clinical and research procedures in collaboration with CNPRC Core Scientists and Service Cores. While many procedures can be refined with small changes, two in particular, laparoscopy and imaging, will be emphasized. Laparoscopic procedures provide a means to transition from invasive surgical procedures to less invasive techniques that more closely parallel human care. *In vivo* imaging is a primary focus of the **Multimodal Imaging Core** (see Core description) and the veterinary staff. New techniques have been established in the Core, and others are under development that will provide new ways to incorporate imaging in research projects and across an animal's lifespan. Primate Medicine will continue to gain substantially from these advances, particularly for assistance with clinical cases and with new study design applications. The new on-site PET/CT scanner provides many opportunities to better assess both clinical and experimental cases. Recently, CT was used to diagnose an unusual extensive neoplasia that presented in facial subcutaneous tissues (see Multimodal Imaging Core). Ultimately, as stated in the Core, the goal is to obtain all imaging modalities on-site for experimental and clinical purposes. [Excluded by Requester] are actively working on obtaining all necessary instrumentation (see Core description). Imaging is vitally important in clinical diagnostics and can improve clinical care as

well as obtain objective metrics for research protocols.

Colony Management. Well-trained, highly experienced veterinarians in medical primatology and AHTs trained to the level of physician assistants will continue to provide preventive health care, medical care, and input into the CNPRC management programs. Preventive health care will remain a focus using an international CDC approved quarantine program, biannual TB testing, routine physical examinations, regular body weights, serum banking, and a vaccination program (measles and tetanus). New preventive health modality options under consideration include a trivalent vaccine for the three main pathogenic bacteria that cause diarrhea. Pre-project physicals will continue to be performed as a baseline and to screen for any potential underlying confounding factors. All colony animals are observed multiple times daily in an effort to quickly ascertain any clinical abnormalities. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Indoor-housed animals receive cageside evaluations to assess any reported clinical signs and remain in their home cages for treatment unless they require intensive care. Approximately 160 animals are reported on indoor morning health daily, ~60 animals require daily to weekly follow up care, ~40 animals are monitored monthly, and two animal care assessment requests are generally submitted daily. Project animals are most commonly housed indoors, therefore veterinarians work closely with investigators to mitigate the effects of treatment on animals assigned to projects. In addition, hundreds of infants are born annually at the CNPRC, and the Primate Medicine staff

Excluded by Requester closely with [REDACTED] **Reproductive Sciences and Regenerative Medicine Research Unit and Odal Imaging Core**) to address any issues that may arise prenatally. The foster dam, aunt, and uncle program has also reduced the number of infants raised in nurseries and provided social enrichment. New non-surgical and reversible methods for vasectomy are also being explored in collaboration with Excluded by Requester **(Reproductive Sciences and Regenerative Medicine Research Unit)** using a non-hormonal contraceptive to block the passage of sperm.

Staff veterinarians participate in management committees and in the decision-making process, providing input from preventive health measures to potential infectious concerns. Primate Medicine will continue to work closely with **Behavior Management Services** to optimize the psychological well-being of the animals, with the **Anatomic and Clinical Pathology Services** to diagnose clinical health problems and determine potential colony trends, with the **Genetics Management Services** to determine any genetic outliers, and with the Core Scientists in their respective domains of expertise.

The **Immunology and Pathogen Detection Resources Core** (see Core description) also plays an integral Excluded by Requester Primate Medicine [REDACTED] 2011 Excluded by Requester 2011 Excluded by Requester 2013], which will continue during the pending period. The Core provides diagnostic marker detection for a number of infectious agents including simian immunodeficiency virus (SIV), HVP2 (Herpes B surrogate marker), simian foamy virus, simian T-cell leukemia virus (STLV), SV40, TB (Primagam), rhesus cytomegalovirus, measles, and other nonhuman primate pathogens. The majority of infectious disease testing can be done in-house in the Core. In addition, Primate Medicine collaborates with the **Endocrine Core** (see Core description) to assess the hormonal and metabolic status of clinical cases. Having on-site Cores with unique expertise and knowledge fosters a collaborative approach that benefits the animals and the overall research enterprise at the CNPRC, which ultimately benefits investigators and the scientific community. These activities also result in costs savings by using pooled resources, skills, and expertise, which maximizes output and resources.

Reducing the number of animal treatments can also result in substantial financial and labor savings as well as the reduction of occupational health risks. Reduced treatments can be accomplished by employing new sustained release or long-acting antibiotics and analgesics. A Primate Medicine Clinical Trainee recently finished a pharmacokinetic study in collaboration with the UC Davis Maddy Equine Analytical Chemistry Laboratory. This study focused on a long acting, third generation cephalosporin which could potentially provide a wider spectrum of bacterial coverage, decreasing the standard number of antibiotic treatments from 10 to just one. Additionally, sustained release or long-term analgesics could prevent breakthrough pain as well as decrease the number of injections. The frequency and volume of treatments also increase the risk of exposure and/or injuries to animal handlers. Effective, long-term antibiotic coverage and/or sustained release analgesia could also facilitate early hospital discharge, thereby maintaining group social stability, reduced discomfort and distress to the individual and social group, and create time and financial savings while reducing occupational

hazards. Other long-acting drug efficacy studies are planned and will be performed in collaboration with **Behavior Management Services**, the Maddy Equine Analytical Chemistry Laboratory, and [Excluded by Requester] Director of the Master's in Preventive Veterinary Medicine Program, School of Veterinary Medicine.

While the CNPRC has begun a multidisciplinary investigation of ICD in nonhuman primates as well as the comparison with Inflammatory Bowel Disease in humans, another area of focus is alopecia. Alopecia is a common human affliction, and nonhuman primates are the best translational model for causes and treatment of alopecia, especially behavioral or psychological etiologies. The first step is to implement an alopecia scoring system to evaluate hair loss during annual physical examinations similar to Body Condition Scores that are currently performed [Excluded by Requester] 2012 [Excluded by Requester] et al., 20 [Excluded by Requester] standardized project template is under development to ensure that result-focused trials are performed consistently with limited confounding variables. In conjunction with **Anatomic and Clinical Pathology Services**, Primate Medicine will also monitor epizootics (*Streptococcus pneumoniae*, *Shigella*, *Listeria*, *Baylisascaris*), which have led to changes in colony management and preventive health treatments.

Information Technology. A paramount issue for Primate Medicine is the development of an electronic supply inventory system to link with the current electronic treatment program with the assistance of the Information Technology Services staff. With over 200 animal treatments daily, a precise inventory system is needed to closely monitor current stock and identify when to place orders as well as the amount required. It is typical for a veterinary practice to spend 15 to 18% of its budget on drugs and supplies. This percentage can be reduced to approximately 12% by decreasing the number of rush orders and expired drugs or supplies that can translate into considerable cost savings. Additionally, an electronic inventory system can prevent drug treatment errors.

An emphasis for the next funding period is integrating the Primate Services team with the extensive amount of information that is generated by colony animals and to work directly with Core Scientists, Cores Services, and Information Technology Services to implement an efficient process to ensure accessible anatomic, behavioral, and physiologic data of animals in the CNPRC populations. Primate Medicine collaborates closely with **Behavior Management Services** staff to assess potential clinical problems resulting from a behavioral issue and to further assess behavioral profiles. Since the CNPRC has biobehavioral assessments on several animals born in the field corrals (see **Behavior Research Services Core**), this information can be used to investigate if specific profiles are more predisposed to certain clinical problems such as chronic colitis or rhesus arthritis. Work has also begun to establish the microbiota of colony animals in order to understand the interaction between the microbiome and physiology, immunology, and/or behavior (see **Immunology and Pathogen Detection Resources Core** and **Infectious Diseases Research Unit**). The colony database is expanding from basic census information to incorporating information such as an animal's pedigree, behavioral reactivity, and eventually clinical and pathologic information such as the GI flora and changes over time. This information not only increases the value of the animals but also increases the complexity of colony management, veterinary care, and in some cases, how investigators design their projects.

Specific Aim 2. Provide expertise and research support to investigators locally, regionally, and nationally.

The goal of Primate Medicine is to continue to support the biomedical research community by providing the expertise needed to perform veterinary procedures required to support cutting edge science, and as new projects are developed. Primate Medicine performs approximately 300 major surgeries, 400 radiographs, 100 dental procedures, 100 endoscopic procedures, and participates in approximately 300 imaging studies and 100 pulmonary function tests annually. The goal of Primate Medicine is to continue to provide the research support needed, and it is anticipated that this need will increase over the next funding period with recruitment of new FTE positions and increased grant support. Multiple approaches will be used to continue the growth trajectory in this area to increase expertise of staff veterinarians in defined areas of diagnostics and surgery. For example, through collaborations with School of Veterinary Medicine colleagues, new procedures in ophthalmology and echocardiography are under consideration. Links with Core Scientists and their departmental faculty in the School of Medicine will also provide new avenues for training, and developing the level of expertise needed to support research with expansion of the CNPRC research portfolio as a result of new Core Scientists and growth of the Research Units (see **Overview**).

Specific Aim 3. Mentor and train the next generation of veterinarians with nonhuman primate expertise.

CNPRC veterinarians have been trained in ACLAM-approved LAM residency programs, and are ACLAM boarded. In addition, they each have acquired a vast amount of nonhuman primate experience. They utilize their considerable training and experiences to provide an avenue of educational growth (both didactic and clinical) for students, residents, researchers, veterinarians, and the nonhuman primate scientific community at large. Primate Medicine takes the responsibility to mentor and train the next generation very seriously. For example, UC Davis and the CNPRC have overseen the LAM Residency Program since 1974. The CNPRC has trained many highly successful experts and leaders in the field (see Table 6). Primate Medicine is a senior veterinary student clinical rotation specifically for UC Davis veterinary students, and the CNPRC is one of the few NPRCs that provide such opportunities for externs (see Table 7). Many of the externs have pursued careers in LAM and/or research. During discussions with the National Scientific Advisory Board, several students commented as follows: *"....how their early involvement in nonhuman primate research is likely to impact their future career path(s). Similarly, students involved in medical related training programs suggested the highly translational nature of research at the CNPRC made them more likely to continue pursuing research throughout their veterinary medical careers."* The program has also accepted international veterinarians that were in need of nonhuman primate training. Most notably, Primate Medicine trained two of the Mountain Gorilla Project Veterinarians, which was viewed by the trainees as invaluable to their success.

Table 6. UC Davis LAM Residents (May 1, 2010 to April 30, 2014)

Resident	Year	Boards	Employment	Support
Excluded by Requester	2010	ACLAM	Academia and industry	T32
	2010	<i>PhD recently completed</i>	UC Davis	R-25, APV Travel Grant
	2011	<i>(in PhD program currently)</i>	UC Davis	R-25, APV Travel Grant
	2012	ACLAM	Academia	None
	2012	Board Exam 2015	Industry	R-25, APV Travel Grant
	2012	ACLAM	UC Davis	R-25, APV Travel Grant
	2014	Board Exam 2015	Current Associate Veterinarian	GLAS Grant
	2014	Board Exam 2015	Current LAM Resident	None
	2015	Board Exam 2016	Current LAM Resident	None (P51 pilot project)
	2015	Board Exam 2016	Current LAM Resident	None

APV=Association of Primate Veterinarians

Primate Medicine also provides a significant amount of training to technicians, veterinary students, and other trainees, and has amassed a considerable amount of training information with specific algorithms. The plan is to improve formalized educational materials and documentation by ensuring all information is available in an electronic database, algorithms are available for commonly observed clinical problems, training presentations are archived, and quizzes to test concept understanding are compiled. With resident training, board learning, and extensive nonhuman primate experience, every member of the Primate Medicine staff is an integral part of the team training approach. The CNPRC is also working with **NPRC Consortium** to share clinical information and training materials/resources. Another component of the learning experience is the rationale for the choice of treatment for an individual animal because there is often more than one approach. With many staff veterinarians, Clinical Trainees and students learn different techniques to aid in building their own veterinary treatment arsenal. Trainees also receive considerable one-on-one training as they learn different treatment approaches and techniques, including through the Training Program for staff as described in the **Colony Management and Research Services** section.

In addition to their supportive role in research, the Primate Medicine veterinary staff members are involved in clinical research. The LAM Clinical Trainees typically conduct a study on a new treatment, vaccine, technique, or procedure to improve colony care and management. In the last few years, these studies have included clinical treatment trials for ICD, a measles vaccine trial, an investigation of outdoor housed animal fractures, normative blood pressure ranges and the accuracy of different blood pressure monitoring methods, a long acting antibiotic, and a new potential therapy for endometriosis (see Table 3).

All veterinarians are encouraged to present interesting cases, topics, or research at webinars and conferences as well as publish in pertinent scientific journals to increase the available information on nonhuman primates. The veterinary staff regularly present at national conferences such as the Association of Primate Veterinarians (APV), AAALAS, and the Charles River Short Course. Typically the veterinary staff members have published in Comparative Medicine, but with collaborations, new publications appear in many other journals.

Table 7. CNPRC Externs (May 1, 2010 to April 30, 2014)

Name	Year	Focus Area	Institution	Funding
Excluded by Requester	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010	Zoo Medicine	UC Davis	Veterinary Student Clinical Rotation
	2010	LAM	Private Source	
	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010		UCLA	Private Source
	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010	LAM	UC Davis	Veterinary Student Clinical Rotation
	2010	LAM	Univ of Wisconsin	Private Source
	2011	LAM	UC Davis	Veterinary Student Clinical Rotation
	2011	LAM	UC Davis	Veterinary Student Clinical Rotation
	2011	LAM	UC Davis	Veterinary Student Clinical Rotation
	2011	LAM	UC Davis	Veterinary Student Clinical Rotation
	2011		Private Source	
	2011			
	2011	LAM		
	2011			
	2011			
	2011	LAM	UC Davis	Veterinary Student Clinical Rotation
	2011	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	Private Source	
	2012	Primatology		
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012		UC San Francisco	Private Source
	2012		Private Source	
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2012	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013		Private Source	
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	Private Source	
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2013	Zoo Medicine	UC Davis	Veterinary Student Clinical Rotation
	2013	LAM	UC Davis	Veterinary Student Clinical Rotation
	2014	LAM	UC Davis	Veterinary Student Clinical Rotation
	2014	LAM	UC Davis	Veterinary Student Clinical Rotation
	2014	LAM	UC Davis	Veterinary Student Clinical Rotation
	2014	LAM	UC Davis	Veterinary Student Clinical Rotation

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

CNPRC staff veterinarians translate their vast nonhuman primate experiences into enhancement of animal care and research standards, and share this expertise with regulatory agencies and other governing bodies. Veterinary staff members work together with input from Core Scientists and CNPRC staff to provide optimal

colony management and psychological well-being. Working together in a creative and productive manner ensures that validated clinical data are used to refine policies, SOPs, guidelines, and future plans. One role of a LAM veterinarian is to cultivate good working relationships, be involved in management committees, and remain engaged in all aspects of the research process from IACUC protocol development to procedural support. Veterinarians collaborate with Core Scientists, primatologists, and other Primate Services staff to establish and facilitate research protocols, particularly for investigators new to nonhuman primate research.

A number of the **NPRC Consortium** Working Groups have shared best practices, regulatory questions and concerns, training methods and resources, as well as new ideas for collaborations including developing evidence-based performance standards. Primate Medicine will continue to develop algorithms to standardize care and reduce costs, and share these findings with the NPRC Consortium. Formation of the NPRC Consortium and the Working Group activities has changed many aspects of NPRC operations and communications, and these activities have facilitated and institutionalized collaborations between veterinarians and related personnel across many NPRC domains that benefit the entire NPRC program. As noted in the NPRC Consortium section, the Working Group education forums (Virtual Slide Conferences, Virtual Grand Rounds, Clinical and Surgical Techniques Conferences) will continue as important channels to disseminate NPRC expertise and share best practices across NPRCs, as well as outreach to the greater nonhuman primate research community. Currently, the CNPRC plays a leadership role in coordinating two high priority initiatives in the NPRC Consortium (*Virology Testing Quality Improvement Initiative*, and the multi-center *Measles Vaccination Safety and Efficacy Study*).

The value of nonhuman primate models also resides within their genetic diversity, behavioral complexity, and anatomy, immunology, and physiology, all of which closely simulate humans. The scientific resources that have been developed in genetics and genomics provide a means to better define individual rhesus monkeys over a lifespan, and to identify models of human disease. The **NPRC Consortium** has initiated an “Extreme Phenotype” survey, and plans are underway for a white paper on a program using targeted state-of-the-art genomics to discover genotype-phenotype relationships related to human disease. The primary goals are to identify common genetic variations across the NPRCs, develop an online searchable database as a resource to the research community, and establish a genome sequencing service that will generate whole genome or whole exome sequences for specific animals with significant phenotypes. As an active member of the NPRC Consortium, the CNPRC will participate in these efforts. For example, the identification of unique phenotypes integrates the highly efficient CNPRC WebVitals database (see **Information Technology Services**) and direct animal observation by Primate Medicine staff and Core Scientists. The database includes 32 different fields that comprise each animal’s individual veterinary and demographic record including:

- Birthdate, gender, generation, acquisition history
- Location history, body weight history, project assignments, pairing history and current cage mate
- Breeding and menstrual data, conceptions (sire, conception date, conception number), foster history
- Enrichment history, body condition scores, biobehavioral assessment (if done)
- Morning health observations, diarrhea history
- SNOMED entries (clinical treatments), discharge diagnosis, microbiology, biopsies
- Experimental interventions, surgeries
- SPF testing, viral testing, vaccinations, TB test history, serum banking
- Genetic data and Pedigrees

Since Primate Medicine has a daily interface with colony animals, the veterinarians and AHTs can aid in identifying animals of potential interest through the following activities: Screening animals prior to project assignment; veterinary observation from clinical health reports; routine preventive health programs such as weights, TB testing, and annual physical examinations; direct observation by staff pathologists during routine necropsies, and joint veterinary clinical/pathology rounds where interesting cases are presented (see **Anatomic and Clinical Pathology Services**); and daily observations by animal care and behavioral staff. Once animals of interest are identified, the WebVitals database for that animal will be reviewed, and a case summary prepared for discussion at the Colony Management Advisory Committee. The committee is composed of Core Scientists and Primate Medicine staff, and it provides an outstanding venue for multidisciplinary discussions of individual animals or groups of animals. The opportunity to observe animals from birth to old age and the quantity of information collected on each individual at different life stages provides many opportunities for Consortium activities focused on identifying translational disease models, particularly novel clinical phenotypes that potentially recapitulate comparable outcomes in humans

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

PUBLICATIONS (May 1, 2010 to April 30, 2014) Core Scientists in bold. Primate Medicine underlined

Excluded by Requester [redacted] Idiopathic microscopic colitis of rhesus macaques: Quantitative assessment of colonic mucosa. Anat Rec (Hoboken) 296:1169-1179, 2013. PMC Journal-in-Progress

Excluded by Requester [redacted] "Abdomen" in the Pocket Handbook of Nonhuman Primate Clinical Medicine, CRC Press, 2012. PMC Journal-in-progress

Excluded by Requester [redacted] Therapeutic helminth infection of macaques with idiopathic chronic diarrhea alters the inflammatory signature and mucosal microbiota of the colon. PLoS Pathog 8:e1003000, 2012. PMCID: PMC3499566

Excluded by Requester [redacted] Comparative pathogenesis of epidemic and enzootic Chikungunya viruses in a pregnant rhesus macaque model. Am J Trop Med Hyg 83:1249-1258, 2010. PMCID: PMC2990040

Excluded by Requester [redacted] Generalized seizure activity in an adult rhesus macaque (*Macaca mulatta*) during ketamine anesthesia and urodynamic studies. Comp Med 63:445-447, 2013. PMCID: PMC3796756

Excluded by Requester [redacted] Validation of a body condition scoring system in rhesus macaques (*Macaca mulatta*): inter- and intrarater variability. J Am Assoc Lab Anim Sci 51:31-36, 2012. PMCID: PMC3276963

Excluded by Requester [redacted] Genetic diversity and histo-blood group antigen interactions of rhesus enteric caliciviruses. J Virol 84: 8617-8625, 2010. PMCID: PMC2919043

Excluded by Requester [redacted] Genetic characterization of specific pathogen-free rhesus macaque (*Macaca mulatta*) populations at the California National Primate Research Center (CNPRC). Am J Primatol 72:587-599, 2010. PMCID: PMC2941796

Excluded by Requester [redacted] Efficacy of antibiotic-impregnated polymethylmethacrylate beads in a rhesus macaque (*Macaca mulatta*) with osteomyelitis. Comp Med 62: 311-315, 2012. PMCID: PMC3415374

Excluded by Requester [redacted] Pharmacokinetics of oxymorphone in titi monkeys (*Callicebus spp.*) and rhesus macaques (*Macaca mulatta*). J Am Assoc Lab Anim Sci 50:212-220, 2011. PMCID: PMC3061422

Excluded by Requester [redacted] Metastatic hepatocellular carcinoma in a juvenile rhesus macaque (*Macaca mulatta*). Comp Med 63:448-453, 2013. PMCID: PMC3796757

Excluded by Requester [redacted] Meningoencephalitis due to *Listeria monocytogenes* in a pregnant rhesus macaque (*Macaca mulatta*). Comp Med 62:443-447, 2012. PMCID: PMC3472610

Excluded by Requester [redacted] Reference intervals for preprandial and postprandial serum bile acid in adult rhesus macaques (*Macaca mulatta*). J Am Assoc Lab Anim Sci 52:444-447, 2013. PMCID: PMC3725928

Excluded by Requester [redacted] Simian retroviruses: infection and disease--implications for immunotoxicology research in rhesus macaques. J Immunotoxicol 7:93-101, 2010. PMC Journal-in-progress

Excluded by Requester [redacted] Simultaneous detection of antibodies to five simian viruses in nonhuman primates using recombinant viral protein based multiplex microbead immunoassays. J Virol Methods 178:143-152, 2011. PMCID: PMC3213204

Excluded by Requester [redacted] Stereologic analysis of bacterial load and lung lesions in nonhuman primates (rhesus macaques) experimentally infected with *Mycobacterium tuberculosis*. Am J Physiol Lung Cell Mol Physiol 301:731-738, 2011. PMC Journal-in-progress

Excluded by Requester [redacted] Effects of simian betaretrovirus serotype 1 (SRV1) infection on the differentiation of hematopoietic progenitor cells (CD34+) derived from bone marrow of rhesus macaques (*Macaca mulatta*). Comp Med 62:61-68, 2012. PMCID: PMC3276394

Excluded by Requester [redacted] Naturally occurring infections in non-human primates (NHP) and immunotoxicity

implications: discussion sessions. J Immunotoxicol 7:138-146, 2010. PMC Journal-in-progress

Excluded by Requester

Plasma antibody profiles in non-human primate tuberculosis. J Med Primatol 43:59-71 2014. PMC Journal-in-progress

Excluded by Requester

Investigation of tularemia outbreak after natural infection of outdoor-housed rhesus macaques (*Macaca mulatta*) with *Francisella tularensis*. Comp Med 63:183-190, 2013. PMCID: PMC3625059

Excluded by Requester

Validation of a body condition scoring system in rhesus macaques (*Macaca mulatta*): assessment of body composition by using dual-energy X-ray absorptiometry. JAALAS 51:88-93, 2012. PMCID: PMC3276972

Excluded by Requester

Intracranial meningioma with ophthalmoplegia in a rhesus macaque (*Macaca mulatta*). Comp Med 62:439-442, 2012. PMCID: PMC3472609

Excluded by Requester

Specific-pathogen-free status is associated with lower infant mortality rate in rhesus macaque (*Macaca mulatta*) colonies at the California National Primate Research Center. J Med Primatol 42:186-191, 2013. PMC Journal-in-progress

Excluded by Requester

Longitudinal patterns of viremia and oral shedding of rhesus rhadinovirus and retroperitoneal fibromatosis herpesviruses in age-structured captive breeding populations of rhesus Macaques (*Macaca mulatta*). Comp Med 61:60-70, 2011. PMCID: PMC3060420

Excluded by Requester

Constitutive release of IFNgamma and IL2 from peripheral blood mononuclear cells of rhesus macaques (*Macaca mulatta*) infected with Simian T-Lymphotropic Virus Type 1. Comp Med 63:508-514, 2013. PMC Journal-in-progress

Excluded by Requester

The complete genome and genetic characteristics of SRV-4 isolated from cynomolgus monkeys (*Macaca fascicularis*). Virology 405:390-396, 2010. PMCID: PMC2941434

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC.

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Excluded by Requester] indoor animal [Specific Animal Location] [Excluded by Requester] field corrals [Specific Animal Location] [Excluded by Requester] corn cribs [Specific Animal Location] [Excluded by Requester] outdoor space is used primarily to support the long-term breeding program. The rhesus production [Specific Animal Location] provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian [Excluded by Requester]). Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an

approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Housing and Environmental Monitoring. Animal rooms are maintained within the recommended guidelines established by the current edition of the *ILAR Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. Typical nonhuman primate rooms provide 10-15 air changes per hour and are negatively pressurized relative to anterooms/corridors and the outside. Lighting is provided by fluorescent lights, which are controlled by timers (12 hours on/12 hours off). Room temperature is maintained between 68°F and 80°F, depending on the species and age of the animals in the room, and are checked and recorded daily. Emergency generator power is provided for all animal rooms. Indoor animal housing is monitored on a daily basis for temperature, light, and humidity. Power failures, major temperature fluctuation, and other environmental disturbances are either alarmed directly to Campus Physical Plant Services or monitored by CNPRC personnel on a daily basis. The Colony Operations Supervisor and the Maintenance Shop Supervisor carry pagers 24 hours/day and are alerted to environmental monitoring alarms and rooms that are out of temperature and humidity range.

Caging Systems. Indoor cages are stainless steel construction and either wall or rolling rack mounted. Cages incorporate a squeeze mechanism to bring the animal to the front of the cage for manipulation. Cage sizes are determined by the USDA and NIH policies. Cage designs incorporate sliding partitions to allow socialization or pair housing.

Environmental Enrichment. The Environmental Enrichment program is part of the Colony Management and Research Services component of Primate Services, is integrated with Behavior Management Services, and includes all animals, with emphasis placed on indoor-housed animals on research projects. Indoor cages are outfitted with a variety of enrichment options including manipulation mirrors (allowing the animal to view adjacent animals), and cage toys. Perches are present in all indoor cages. Low caloric items, such as forage, are provided on forage boards located on each cage. Animals also receive fruit or vegetables twice weekly. Non-food enrichment is also emphasized. One example of such enrichment is the placement of televisions, which provide visual stimulus to colony animals. Socialization can provide substantial benefit to the animals and is generally accomplished within the limitations of research protocols and daily management practices. Cages have been retrofitted or purchased with sliding partitions to allow pairing. The current strategy is to pair animals during the day and separate them at night to facilitate the assessment of physical signs each morning. Animals are paired early in the morning when animal care staff members begin daily activities, animals are then separated at night when there are limited personnel available to monitor for potential aggressive interactions. The ability to observe each animal's individual daily physical signs is essential to many research programs and overall clinical care. Behavior Management Services staff members view every animal in the colony during morning health rounds and ensure they receive daily enrichment items targeting their specific behavior aberration. All indoor animals are also assessed monthly to identify any abnormal behaviors; these animals receive a detailed behavioral assessment monthly to monitor their status and progress.

Surveillance. The majority of animals at the CNPRC are from the production colony of 24 half-acre outdoor field corrals. Animals brought into the CNPRC from off-site facilities complete a 90-day quarantine at the CNPRC Quarantine Facility. During this time, animals undergo a complete physical examination with complete blood counts, blood and fecal parasitology, and rectal culture. Five tuberculin tests are completed, and animals are screened for simian retroviruses including Type D simian retrovirus (SRV), Simian Immunodeficiency Virus (SIV), and simian T-cell leukemia virus (STLV). Animals of foreign origin are treated for malaria and intestinal parasites. Animals with positive tuberculosis tests and SRV assays, or

demonstrating signs of clinical illness, are humanely euthanized and a complete necropsy performed.

Feeding. The animals are fed commercial monkey chow twice daily. Monkey Chow is pre-analyzed for content. The analysis of each lot of feed is reviewed by CNPRC Quality Assurance and a Senior Veterinarian. Animals are supplemented with fruit or vegetables twice weekly. Water is provided by automatic lixits, which are checked daily for proper operation. Portable caging with detachable waterlines is checked daily. The CNPRC potable water supply is obtained from wells operated by UC Davis. All UC Davis wells are monitored by the Office of Environmental Health and Safety quarterly. The water is tested for chloroforms, a variety of chemical markers including heavy metals and a variety of toxic minerals, pesticides, and chemical contaminants. Additionally, the CNPRC tests for general mineral, organic, and inorganic contamination annually.

Sanitation. Indoor cages are hosed daily with a quaternary ammonium detergent/disinfectant and are sanitized every 2 weeks in a mechanical cage-washer. A microbiological monitoring program is in place to ensure efficacy of sanitation practices. Each animal area is monitored twice per year. Microbiological monitoring results are reviewed and signed off by each area supervisor, a Senior Veterinarian, and the Assistant Director for Colony Management and Research Services. Monitoring of caging pH during cage washing is included in the cage sanitation surveillance program. In addition, water lines in both the indoor and outdoor colony are monitored with microbiological testing on a rotational basis in conjunction with cage change activities.

Record Keeping. Record keeping includes a written individual animal record and entry of specific information into a computerized Vitals database (see **Information Technology Services**). Maintenance of the animal colony database, including information on project history, reproductive history, clinical data, viral status, as well as genealogical data is included. Also included are the current location of the animals, weight history, date of last tuberculosis test, and the date of the last serum banking. These data are available to aid in project design and animal selection by investigators. This database has also been critical to several retrospective studies involving prenatal mortality, transmission of retroviral agents in colony management, effects of housing changes on health, and risk factors for spontaneous diseases such as endometriosis. Management of this informational database represents a valuable resource to the entire biomedical research community. Historical animal-related data are maintained on a yearly basis to reflect the production statistics of the colonies including: conception rates, live birth rates, pregnancy loss, and infant mortality.

Animal Health Program. A health check is performed each morning by the colony management staff. Each animal has a location and animal identification barcode that is scanned, and an animal technician records physical signs listed on a menu using a portable barcode reader. After completion of the health check, the information is downloaded onto the main computer, and a morning health report is generated directly to the veterinary staff. Veterinarians or Animal Health Technicians perform a visual examination of each animal on health report. Results of the health check and assessment by the veterinary clinician are then recorded in the animal's record. For animals on study, a report is generated to the investigator on a daily basis by electronic mail. Animals in the outdoor colony are also checked twice each day, once in the morning and afternoon. Identification of animals in the field corrals is performed by individual dye mark. Technicians check each cage closely for animals potentially requiring medical attention. The afternoon health check was added to the outdoor colony in 2012, and increased health surveillance is particularly important during the birth season.

Centralized Research Support. The various services represented in Primate Services work synergistically to provide high quality, technical research support to all investigators utilizing the CNPRC, as needed, whether located locally or at a distant site. Staff veterinarians also provide extensive clinical support to animals on long-term research protocols (see Primate Medicine Services).

Staff Training. The program emphasizes occupational safety, as well as increasing demands for technical expertise in the care and research support of nonhuman primates. Training is viewed not only as the initial step at hire, but as an ongoing process through in-house classes and support to attend relevant training programs, meetings, and conferences. A spectrum of training opportunities is available specific to the

CNPRC and to meet campus-wide training requirements. These include: UC Davis Primate Handling and Husbandry Training, Campus Laboratory Animal Care Classes (AAALAC preparation); Injury / Illness Prevention Plan; Infection Control Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management; Campus Back Safety Class; Campus Radiation Safety Class; Pesticide and Antimicrobial Safety; Training in Good Laboratory Practices; Supervisor Training with Job Skills Worksheet; and position specific training for all levels of husbandry, animal care, and technical skills. The training program also includes a series of "*Attention to Detail*" documents that provide very detailed information for each of the training and skill areas the staff is expected to meet including information to enhance understanding and the need to adhere to defined guidelines for critical procedures.

Standard Operating Procedures (SOPs). Primate Services has an extensive collection of 185 SOPs that provide detail on all operational procedures including: husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by all staff and undergo full review and revision every three years. SOPs are available in an electronic format online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC, and SOPs by number can be noted in IACUC protocol submissions.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

BIBLIOGRAPHY AND REFERENCES CITED

- Excluded by Requester
 rhesus macaques: Quantitative assessment of colonic mucosa. *Anat Rec* (Hoboken) 296:1169-1179, 2013. PMC Journal-in-Progress
- Excluded by Requester
 Excluded by Requester
 Therapeutic helminth infection of macaques with idiopathic chronic diarrhea alters the inflammatory signature and mucosal microbiota of the colon. *PLoS Pathog* 8:e1003000, 2012. PMCID: PMC3499566
- Excluded by Requester
 Validation of a body condition scoring system in rhesus macaques (*Macaca mulatta*): inter- and intrarater variability. *J Am Assoc Lab Anim Sci* 51:31-36, 2012. PMCID: PMC3276963
- Excluded by Requester
 Simultaneous detection of antibodies to five simian viruses in nonhuman primates using recombinant viral protein based multiplex microbead immunoassays. *J Virol Methods* 178:143-152, 2011. PMCID: PMC3213204
- Excluded by Requester
 Validation of a body condition scoring system in rhesus macaques (*Macaca mulatta*): assessment of body composition by using dual-energy X-ray absorptiometry. *JAALAS* 51: 88-93, 2012. PMCID: PMC3276972
- Excluded by Requester
 Longitudinal patterns of viremia and oral shedding of rhesus rhadinovirus and retroperitoneal fibromatosis herpesviruses in age-structured captive breeding populations of rhesus Macaques (*Macaca mulatta*). *Comp Med* 61:60-70, 2011. PMCID: PMC3060420
- Excluded by Requester
 Constitutive release of IFNgamma and IL2 from peripheral blood mononuclear cells of rhesus macaques (*Macaca mulatta*) infected with Simian T-Lymphotropic Virus Type 1. *Comp Med* 63:508-514, 2013. PMC Journal-in-progress

PRIMATE SERVICES: PRIMATE MEDICINE SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Anatomic and Clinical Pathology Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename ACPS_abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	ACPS_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	ACPS_FacilitiesOtherResources.pdf
11. Equipment	ACPS_Equipment.pdf

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

ABSTRACT

The primary goal of Primate Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. Animal care and research service is provided by a highly trained staff of veterinarians, Core Scientists, technicians, and administrators to meet the needs of the animals as well as the investigators using the CNPRC resource. **Anatomic and Clinical Pathology Services** is aligned with the strategic focus of the CNPRC to support multidisciplinary research that optimizes the development and use of nonhuman primate models of human health and disease. Extensive expertise in clinical, gross, and microscopic diagnostic pathology is utilized to promote colony health and disease surveillance to ensure that high quality animals are available for biomedical research, and to provide research support for projects requiring pathology expertise, either collaboratively or on a recharge basis. The Specific Aims for Anatomic and Clinical Pathology Services are to: (1) Provide pathology expertise for state-of-art research and scientifically contribute to the understanding and treatment of human disease with nonhuman primate models, (2) Provide exceptional nonhuman primate resources and pathology services to investigators at the regional and national levels to advance NIH-supported research excellence, (3) Mentor and train the next generation of nonhuman primate pathologists and translational investigators, and (4) Maintain the production of high quality, healthy animals for research.

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: A wet tissue processing laboratory and an equipment and prep room totaling 466 sq. ft. is available.

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites (3). The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology.

Animal: The CNPRC currently has an animal census of approximately 5,000 rhesus monkeys, 12 long-tailed monkeys, and 86 titi monkeys. The vivarium includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, necropsy suites (3), and infectious animal housing. The outdoor animal housing area includes field corrals and corn cribs as described in other sections of the application. The Clinical Pathology Laboratory provides diagnostic support services as noted, and the veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in this and other sections of the application.

Specific Animal
Location

Computer: Pathology Services is equipped with networked PCs (15 workstations).

Office: Office space is provided for [Excluded by Requester] and shared space is provided for the pathology residents and support staff.

Other: The CNPRC is a part of the UC Davis AAALAC-accredited program.

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

EQUIPMENT

Major equipment for the **Clinical Pathology Laboratory** includes a Horiba Inc. Pentra 60C+ hematology analyzer, Scil Hematology Analyzer, Beckman Coulter AU480 chemistry analyzer, NOVA Stat Whole Blood chemistry analyzer, fluorescent microscope, light microscopes (2), $\leq -80^{\circ}\text{C}$ freezers (2), Beckman Coulter TQ prep workstation for flow cytometry, BD Bioscience FACS Calibur, FACS Aria in a biocontainment hood for cell sorting, and LSR Fortessa.

Anatomic Pathology includes down-draft necropsy tables (3), fume/trimming hoods (2), biosafety cabinets (3), microwriter (1), Nikon digital camera and photography stand with lights and polarizing filters (1), $\leq -80^{\circ}\text{C}$ freezer (1), microscopes with cameras and imaging software (3), additional microscopes (2), multi-headed microscope with camera, and imaging software and high definition monitors (1).

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	1,810.00	6,348.00
2.					Pathology Senior Manager			0.0	0.0	22,174.00	8,844.00	31,018.00
3.					Senior Veterinary Pathologist			0.0	0.0	16,702.00	6,661.00	23,363.00
4.					Associate Veterinary Pathologist			0.0	0.0	14,874.00	7,868.00	22,742.00
5.					Postdoc Pathologist			0.0	0.0	4,628.00	779.00	5,407.00

Total Funds Requested for all Senior Key Persons in the attached file**Additional Senior Key Persons:**

File Name:

Total Senior/Key Person**88,878.00****B. Other Personnel**

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Pathology Assistant Excluded by Requester	EFFORT			43,690.00	17,425.00	61,115.00
1	Clinical Laboratory Manager: Excluded by Requester				30,321.00	16,040.00	46,361.00
2	Clinical Laboratory Specialists: Excluded by Requester				37,729.00	19,959.00	57,688.00
6	Total Number Other Personnel					Total Other Personnel	165,164.00
Total Salary, Wages and Fringe Benefits (A+B)							254,042.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	6,000.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	500.00
9. Pathology Imaging Database Expenses	20,000.00
Total Other Direct Costs	31,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	291,542.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	291,542.00	66,180.00
		Total Indirect Costs	66,180.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	357,722.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ACPS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	1,915.00	6,453.00
2.					Pathology Senior Manager			0.0	0.0	23,061.00	9,732.00	32,793.00
3.					Senior Veterinary Pathologist			0.0	0.0	17,370.00	7,330.00	24,700.00
4.					Associate Veterinary Pathologist			0.0	0.0	15,469.00	8,557.00	24,026.00
5.					Postdoc Pathologist			0.0	0.0	4,813.00	858.00	5,671.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

93,643.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Pathology Residents	Excluded by Requester	EFFORT		45,001.00	18,990.00	63,991.00
	Excluded by Requester						
1	Clinical Laboratory Manager:				31,230.00	17,275.00	48,505.00
	Excluded by Requester						
2	Clinical Laboratory Specialists:				38,862.00	21,497.00	60,359.00
	Excluded by Requester						
6	Total Number Other Personnel					Total Other Personnel	172,855.00
						Total Salary, Wages and Fringe Benefits (A+B)	266,498.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,180.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,180.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,300.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	515.00
9. Pathology Imaging Database Expenses	20,600.00
Total Other Direct Costs	32,445.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	305,123.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	305,123.00	<u>69,263.00</u>
		Total Indirect Costs	69,263.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	374,386.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ACPS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	1,982.00	6,520.00
2.					Pathology Senior Manager			0.0	0.0	23,292.00	10,175.00	33,467.00
3.					Senior Veterinary Pathologist			0.0	0.0	17,718.00	7,740.00	25,458.00
4.					Associate Veterinary Pathologist			0.0	0.0	15,779.00	9,012.00	24,791.00
5.					Postdoc Pathologist			0.0	0.0	4,909.00	904.00	5,813.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

96,049.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Pathology Residents	Excluded by Requester	EFFORT		45,565.00	19,905.00	65,470.00
	Excluded by Requester						
1	Clinical Laboratory Manager	Excluded by Requester			31,855.00	18,195.00	50,050.00
	Excluded by Requester						
2	Clinical Laboratory Specialists	Excluded by Requester			39,249.00	22,417.00	61,666.00
	Excluded by Requester						
6	Total Number Other Personnel					Total Other Personnel	177,186.00
						Total Salary, Wages and Fringe Benefits (A+B)	273,235.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,365.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,365.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,609.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	530.00
9. Pathology Imaging Database Expenses	21,218.00
Total Other Direct Costs	33,418.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	313,018.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	313,018.00	71,056.00
Total Indirect Costs			71,056.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	384,074.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ACPS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	2,041.00	6,579.00
2.					Pathology Senior Manager			0.0	0.0	24,223.00	10,896.00	35,119.00
3.					Senior Veterinary Pathologist			0.0	0.0	18,245.00	8,207.00	26,452.00
4.					Associate Veterinary Pathologist			0.0	0.0	16,248.00	9,557.00	25,805.00
5.					Postdoc Pathologist			0.0	0.0	5,056.00	961.00	6,017.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

99,972.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Pathology Residents	Excluded by Requester	EFFORT		46,814.00	21,058.00	67,872.00
1	Clinical Laboratory Manager:	Excluded by Requester			32,489.00	19,109.00	51,598.00
2	Clinical Laboratory Specialists:	Excluded by Requester			40,427.00	23,778.00	64,205.00
6	Total Number Other Personnel					Total Other Personnel	183,675.00
					Total Salary, Wages and Fringe Benefits (A+B)		283,647.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

6,556.00

2. Foreign Travel Costs

0.00

Total Travel Cost 6,556.00**E. Participant/Trainee Support Costs**

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other:

0 Number of Participants/Trainees**Total Participant Trainee Support Costs****0.00**

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,927.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	546.00
9. Pathology Imaging Database Expenses	21,855.00
Total Other Direct Costs	34,421.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	324,624.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	324,624.00	73,690.00
Total Indirect Costs			73,690.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	398,314.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ACPS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Primate Services	Institutional Base Salary	EFFORT	0.0	0.0	4,538.00	2,104.00	6,642.00
2.					Pathology Senior Manager			0.0	0.0	25,193.00	11,681.00	36,874.00
3.					Senior Veterinary Pathologist			0.0	0.0	18,975.00	8,798.00	27,773.00
4.					Associate Veterinary Pathologist			0.0	0.0	16,899.00	10,241.00	27,140.00
5.					Postdoc Pathologist			0.0	0.0	5,258.00	1,031.00	6,289.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						104,718.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Pathology Residents Excluded by Requester	EFFORT			48,218.00	22,357.00	70,575.00
1	Clinical Laboratory Manager: Excluded by Requester				33,463.00	20,279.00	53,742.00
2	Clinical Laboratory Specialists: Excluded by Requester				41,640.00	25,234.00	66,874.00
6	Total Number Other Personnel					Total Other Personnel	191,191.00
Total Salary, Wages and Fringe Benefits (A+B)							295,909.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	6,753.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	6,753.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	11,255.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	562.00
9. Pathology Imaging Database Expenses	22,511.00
Total Other Direct Costs	35,454.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	338,116.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	338,116.00	76,752.00
Total Indirect Costs			76,752.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	414,868.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ACPS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Associate Director for Primate Services	% Effort			
	Senior Veterinary Manager				
	Associate Veterinary Pathologist				
	Postdoctoral Fellow				
	Senior Veterinary Pathologist				
	Pathology Resident				
	Pathology Resident				
	Pathology Resident				
	Clinical Pathology Laboratory Supervisor				
	Clinical Laboratory Technician				
	Clinical Laboratory Technician				
	Senior Veterinary Pathologist				
	Clinical Pathology Technician				
<i>Technicians (4)</i>	<i>Anatomic Pathology Technicians</i>	0	100	0	100

Individuals shown in italics are not supported by the P51 base grant; their salary support is provided by Program Income

Excluded by Requester **DVM, DACLAM, Associate Director for Primate Services** EFFORT months % Effort

Excluded by Requester Associate Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine, the Associate Director for Primate Services, and Chief Veterinarian. He has responsibilities for all aspects of the nonhuman primate colonies and related services provided through Anatomic and Clinical Pathology Services.

Excluded by Requester **BVSc, PhD, DACVP, Senior Veterinary Manager** EFFORT months % Effort Dr.

Excluded by Requester the Senior Veterinary Manager for Anatomic and Clinical Pathology Services. She manages the pathology service and is responsible for routine necropsies and biopsies in support of colony health and disease surveillance. She also provides pathology support for research protocols. serves as Excluded by Requester for the laboratory animal veterinary pathology residents. She is a veterinary pathologist with 18 years experience as an anatomic laboratory animal pathologist, and nearly 5 of those years exclusively as a nonhuman primate pathologist.

Excluded by Requester **DVM, DACVP, Associate Veterinary Pathologist** EFFORT months % Effort Dr.

Excluded by Requester responsible for routine necropsies and biopsies in support of colony health and disease surveillance and provides pathology support for research protocols. Excluded by Requester also serves as mentor for the laboratory animal veterinary pathology residents. She is a veterinary anatomic pathologist with 5 years experience working across a wide range of species, and she previously held a teaching position at the Private Source

Excluded by Requester **BVMS, PhD, DACVP, Postdoctoral Fellow** EFFORT months % Effort Excluded by Requester

Excluded by Requester Postdoctoral Fellow conducting research in support of colony health under the guidance of (Infectious Diseases Research Unit). He is also responsible for routine necropsies and biopsies in support of colony health and disease surveillance, and pathology support for research protocols.

Excluded by Requester

EFFORT

% Effort

Excluded by Requester

DVM, PhD, DACVP, Senior Veterinary Pathologist

months –

responsible for routine necropsies and biopsies in support of colony health and disease surveillance, and also provides pathology support for research projects. He serves as mentor for the laboratory animal veterinary pathology residents, and has more than 24 years experience in nonhuman primate anatomic pathology.

EFFORT

% Effort

Pathology Residents

months each

The Laboratory Animal Training Program trains future comparative pathologists with a primate pathology focus. As part of the training program, residents will perform routine necropsies and biopsies in support of colony health and disease surveillance under the supervision of experienced senior pathologists. Three residents are currently in the program

Excluded by Requester

Excluded by Requester

Excluded by Requester

EFFORT

months –

% Effort

Excluded by Requester

MS, MLS (ASCP), Clinical Pathology Laboratory Supervisor

manages the Clinical Pathology Laboratory, and is responsible for the oversight of routine laboratory tests as well as the research and development of non-routine assays. She also serves as the manager and key operator for the flow cytometry systems and facility (see Immunology and Pathogen Detection Resources Core). She has over 30 years of nonhuman primate clinical pathology experience, and serves as a mentor to undergraduate and graduate students, and to postdoctoral and clinical fellows interested in clinical laboratory science. She is a nationally renowned consultant and resource in the field of diagnostic testing for nonhuman primate researchers and clinicians based on her extensive and unique expertise.

Excluded by Requester

CLS, Clinical Laboratory Technician

EFFORT

months

% Effort

Excluded by Requester

is responsible for performance of routine clinical laboratory testing in areas of microbiology, parasitology, hematology, chemistry, and flow cytometry.

Excluded by Requester

CLS, Clinical Laboratory Technician

EFFORT

months

% Effort

Excluded by Requester

is responsible for performance of routine clinical laboratory testing in areas of microbiology, parasitology, hematology, chemistry, and flow cytometry.

Excluded by Requester

DVM, Senior Veterinary Pathologist

Excluded by Requester

is responsible for routine necropsies and biopsies in support of colony health and disease surveillance, and also provides pathology support for research projects. She has more than 30 years of expertise in nonhuman primate anatomic pathology, and is primarily supported through recharge.

Excluded by Requester

Clinical Laboratory Technician, and the Anatomic Pathology Technicians (4) provide daily support to the Clinical Pathology Laboratory and to the Pathologists, respectively.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are listed in the **Facilities Improvement** section.

TRAVEL

\$6,000 is requested (4 x \$1,500) for four pathologists to attend one professional meeting annually.

SUPPLIES

\$10,000 is requested for essential pathology supplies to develop new techniques and applications related to colony management.

OTHER EXPENSES

\$20,000 is requested for the Primate Pathology Imaging Database for scanning slides through the services provided in the Multimodal Imaging Core (see Core).

\$500 is requested for shipping containers for specimens sent to investigators.

\$1,000 is requested for manuscript submission.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		483,260.00
Section B, Other Personnel		890,071.00
Total Number Other Personnel	30	
Total Salary, Wages and Fringe Benefits (A+B)		1,373,331.00
Section C, Equipment		0.00
Section D, Travel		31,854.00
1. Domestic	31,854.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		167,238.00
1. Materials and Supplies	53,091.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	2,653.00	
9. Other 2	106,184.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,572,423.00
Section H, Indirect Costs		356,941.00
Section I, Total Direct and Indirect Costs (G + H)		1,929,364.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	450,000.00	Services
2	474,750.00	Services
3	500,861.00	Services
4	528,408.00	Services
5	557,470.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

ACPS_SpecificAims.pdf

3. Research Strategy*

ACPS_ResearchStrategy.pdf

4. Progress Report Publication List

ACPS_ProgressReport_Pubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

ACPS_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

ACP_LettersofSupport.pdf

13. Resource Sharing Plan(s)

ACPS_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

SPECIFIC AIMS

Anatomic and Clinical Pathology Services is aligned with the strategic focus of the California National Primate Research Center (CNPRC) to support multidisciplinary research that optimizes the development and use of nonhuman primate models of human health and disease. Extensive expertise in clinical, gross, and microscopic diagnostic pathology is utilized to promote colony health and disease surveillance to ensure that high quality animals are available for biomedical research, and to provide research support for projects requiring pathology expertise, either collaboratively or on a recharge basis. Pathology is closely aligned with the overall CNPRC goals for the next funding period, which are reflected in the following Specific Aims.

Specific Aim 1. Provide pathology expertise for state-of-art research and scientifically contribute to the understanding and treatment of human disease with nonhuman primate models.

Plan. Pathology services support multidisciplinary research by providing anatomic and clinical pathology expertise either collaboratively or on a recharge basis. Pathologists with strong comparative pathology backgrounds and PhD training are ideally positioned to work effectively at the interface of animal models and their translation to human disease. Currently within these services, there is additional expertise in gastric pathology, mucosal immunity, and intestinal disease, respiratory pathology, stereology, and naturally occurring infectious disease. Collaborative relationships to capitalize on individual expertise are encouraged.

Specific Aim 2. Provide exceptional nonhuman primate resources and pathology services to investigators at the regional and national levels to advance NIH-supported research excellence.

Plan. The primary goal is to facilitate research and ensure a supportive environment for investigators by providing pathology expertise in study design and evaluation of animals on experimental protocols. High quality technical support can facilitate extensive or specialized tissue collection and handling techniques including specific organ perfusion for fixation, or immediate antemortem collection of tissues needed for *in vitro* studies. The Clinical Pathology Laboratory provides a wide range of ancillary testing to both intramural and extramural investigators. Additionally, the Biological Specimen Request Program distributes tissues collected at necropsy from colony animals to local and national investigators requesting specific biological samples, and the service maintains repositories of fixed nonhuman primate tissue and a serum bank. These resources provide important opportunities for collaborative research, training, pilot projects, and new NIH grants.

Specific Aim 3. Mentor and train the next generation of nonhuman primate pathologists and translational investigators.

Plan. A central mission is to mentor and train pathologists early in their careers to become strong comparative pathologists with an emphasis in nonhuman primate pathology to ensure they will be able to provide both diagnostic pathology services and become key players in team science in the nonhuman primate community.

Specific Aim 4. Maintain the production of high quality, healthy animals for research.

Plan. The CNPRC will continue to deliver high quality pathology services by performing post-mortem examinations and ancillary clinical pathology testing. As a result, the pathology service, in close cooperation with Primate Medicine, provides surveillance for infectious diseases and other conditions having a deleterious effect on colony health, epidemiological data on the incidence and prevalence of disease, and early recognition of potential spontaneous animal models of human diseases.

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

RESEARCH STRATEGY

INTRODUCTION

The California National Primate Research Center (CNPRC) is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited Animal Care Program. The pivotal role of the Anatomic and Clinical Pathology Services team is to provide clinical, gross, and microscopic diagnostic pathology services in support of colony health and disease surveillance, as well as support for projects requiring pathology expertise, either collaboratively or on a recharge basis. Professional staff of the Anatomic Pathology service comprises highly experienced staff pathologists and a postdoctoral fellow who are supported by a competent team of technical staff, and includes the Clinical Pathology Laboratory (Figure 1). The pathologists are all highly skilled comparative pathologists equipped to provide intellectual and scientific contributions to colony health and translational research. The diagnostic services provided include post-mortem examinations on every animal at the CNPRC. As a result, the Pathology service provides surveillance for infectious diseases and other conditions having a deleterious impact on colony health, epidemiological data on the incidence and prevalence of spontaneously occurring congenital anomalies and other developmental defects, and recognition of potential spontaneous animal models of human diseases. Professional staff members provide consultation and collaborative services to CNPRC Core and Affiliate Scientists in study design and evaluation of animals on experimental protocols. Research support services provided by technical staff often require extensive or specialized tissue collection and handling techniques including specific organ perfusion for fixation, or immediate antemortem collection of tissues needed for *in vitro* studies. Pathology staff members administer a number of other important resources including a biospecimen distribution program, extensive tissue archives, a serum bank, and a growing collection of photographs and electronic images of both common and unusual lesions. Members of Anatomic and Clinical Pathology Services are shown in Table 1.

Figure 1. Organizational Chart: Anatomic and Clinical Pathology Services

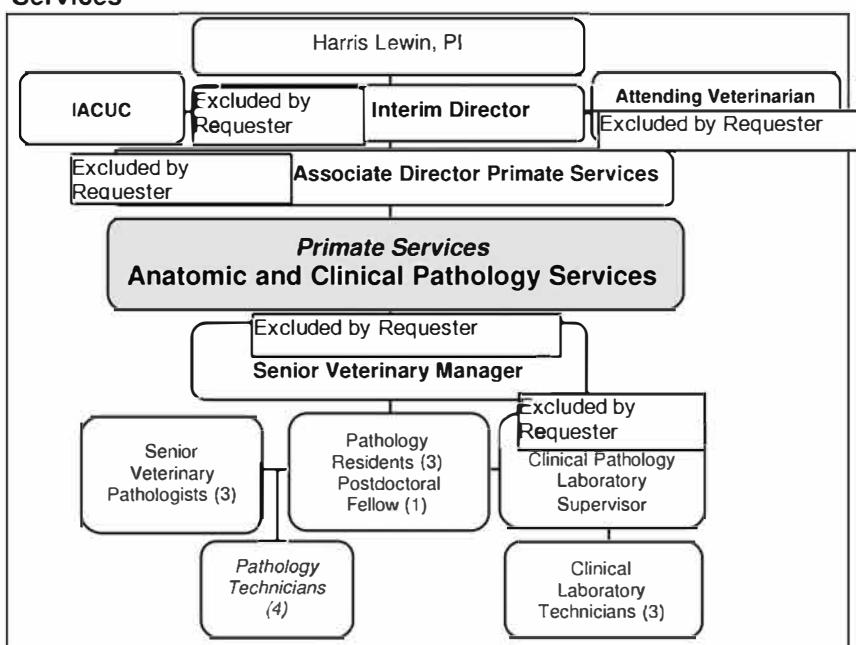


Table 1. Anatomic and Clinical Pathology Services Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Excluded by Requester	Department of Medicine and Epidemiology, School of Veterinary Medicine	Associate Director for Primate Services
	Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine	Senior Veterinary Manager
	CNPRC	Associate Veterinary Pathologist
	CNPRC	Postdoctoral Fellow
	CNPRC	Senior Veterinary Pathologist
	CNPRC	Pathology Residents
	CNPRC	Clinical Pathology Laboratory Supervisor
	CNPRC	Clinical Laboratory Technician
	CNPRC	Clinical Laboratory Technician
	CNPRC	Senior Veterinary Pathologist
	CNPRC	Clinical Pathology Technician
Technicians (4)	CNPRC	Anatomic Pathology Technicians

Additionally, personnel provide teaching and training across many different sectors, but most notably the Laboratory Animal Pathology Postdoctoral Training Program in conjunction with the School of Veterinary Medicine, a highly sought after program.

The sources of support for the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 2. Support for Anatomic and Clinical Pathology Services

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$278,898	\$291,542
Program Income from P51	\$430,000	\$450,000
Other Sources	\$0	\$0
TOTAL	\$708,898	\$741,542

Response to Summary Statement.

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

The Pathology service plays a pivotal role in the maintenance of colony health and provision of research support. To achieve this end, the service has extensive interactions with **Primate Medicine Services**, **Colony Management and Research Services**, and the **Multimodal Imaging Core**. The service is staffed by a highly experienced, well-trained group of veterinary pathologists and technicians who are all adept at working in a fast paced, dynamic environment. The combination of experienced, highly trained pathologists, highly skilled technical staff with numerous years of experience, and close interactions with the specialized Scientific Research Units and Cores provides a unique resource, particularly for off-site investigators that conduct studies at the CNPRC.

Personnel. The personnel structure within Pathology has undergone considerable re-organization during the current funding period. [Excluded by Requester] became the managing pathologist in April 2011 as noted above. Dr.

[Excluded by Requester] a highly experienced primate pathologist, continues to serve as a senior pathologist and [Excluded by Requester] although [Excluded by Requester] the other long-serving pathologist, [Personal Info] to

work [Excluded by Requester] to ease the transition and continue to provide support to several investigators with which he has established collaborations. A search to recruit a replacement pathologist has been successful and [Excluded by Requester]

[Excluded by Requester] from the [Private Source] joined the team on July 1, 2014. Additionally, as described [Excluded by Requester] a postdoctoral fellowship, filled by [Excluded by Requester] was created in August 2013 to assist with

necropsy duty and allow latitude for the development of research projects. Among the pathology staff [Excluded by Requester] longstanding technician in the service, was promoted in July 2012 to serve as supervising [Excluded by Requester]

ian. Since the prior review [Private Source] has been hired. A long-standing technician [Excluded by Requester] remains on the staff. Recently, the Clinical Pathology Laboratory has

been added to the Anatomic and Clinical Pathology Services. The Clinical Pathology Laboratory is led by [Excluded by Requester] a Licensed Senior Clinical Laboratory Specialist who supervises a staff of three (two licensed

Medical Laboratory Scientists and one Laboratory Assistant). [Excluded by Requester] also plays an important role in the

supervision of flow cytometry services in the **Immunology and Pathogen Detection Resources Core** (see Core description).

Every animal culled from the colony and each animal on a terminal research protocol receives a post-mortem examination, which may include appropriate additional ancillary testing provided by the Clinical Pathology Service. Primate Medicine clinicians also regularly submit biopsies for diagnostic purposes, with skin and liver biopsies being the most common. As a result, the Pathology service provides surveillance for infectious diseases and other conditions having a deleterious effect on colony health, epidemiological data on the incidence and prevalence of spontaneously occurring congenital anomalies and other developmental defects, and recognition of potential spontaneous animal models of human diseases. Experimental protocols and scheduled cull animals are planned, however some necropsies cannot be scheduled. Hence the workload can fluctuate dramatically and unpredictably on any given day or week, and the service must ensure flexibility to respond to emergencies. Colony necropsies are conducted by the pathologist on duty who makes a decision on the extent of tissue processing and collection for any particular case. Routine necropsies for animals that are culled, such as those that result from idiopathic chronic diarrhea (ICD) have a set protocol for tissue collection and reporting, and may be carried out by an experienced technician with a pathologist present in the necropsy room as necessary.

The Clinical Pathology Laboratory provides microbiology, clinical chemistry, hematology, urinalysis, parasitology, and basic flow cytometry services (Figure 2, Table 3), which may be used as additional diagnostic tools for colony necropsies (Figure 3) or to monitor and define the health status of the colony. Flow cytometry services to support research are overseen by the **Immunology and Pathogen Detection Resources Core**.

Figure 2. Clinical Laboratory (May 1, 2010-April 30, 2014)

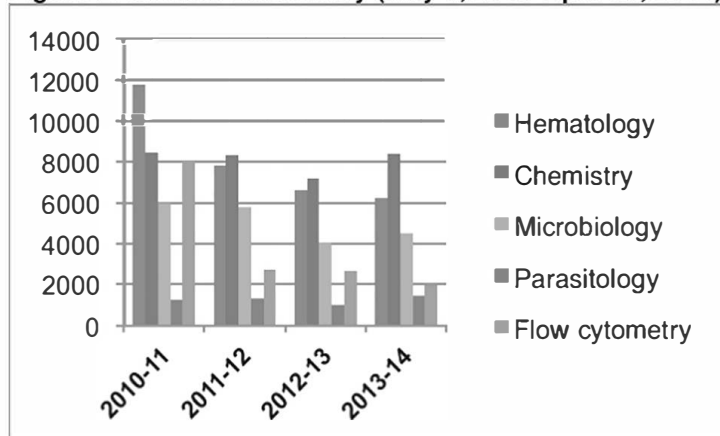


Figure 3. Necropsies (May 1, 2010-April 30, 2014)

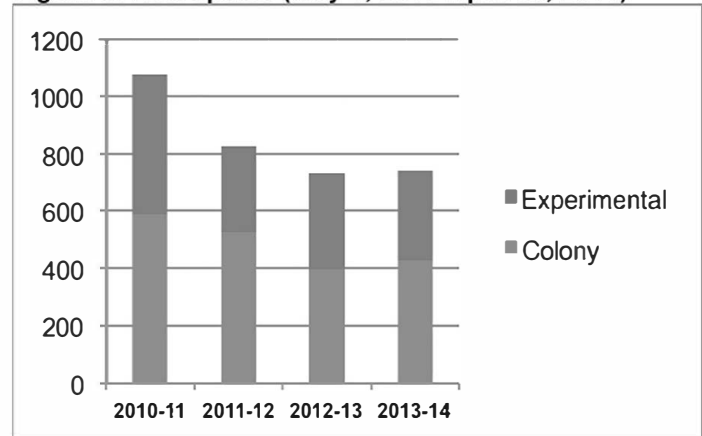


Table 3. Service Use: Clinical Laboratory (May 1, 2010 to April 30, 2014)

Grant Year	# Users	Investigators (N)	Service Cost (\$)	Total Cost (\$)
2010 - 2011	59	Core Scientists (13)	446,501	1,167,985
		UC Davis (23)	442,782	
		External (23)	278,702	
2011 - 2012	60	Core Scientists (12)	82,273	663,697
		UC Davis (21)	358,071	
		External (27)	223,353	
2012 - 2013	61	Core Scientists (11)	116,976	604,294
		UC Davis (22)	367,566	
		External (28)	119,752	
2013 - 2014	67	Core Scientists (13)	60,651	578,971
		UC Davis (20)	410,058	
		External (34)	108,262	
TOTAL				\$3,014,947

In the late 1970's, a serum bank including several nonhuman primate species was initiated. This has proven invaluable in epidemiological studies as well as for retrospective analysis of disease states. Scheduling and

tissue collection protocols for experimental necropsies are coordinated with investigators or **Colony Management and Research Services** staff. The service is capable of handling projects with large complex tissue collection requirements and can provide expert technical advice (Table 4). Some protocols require special procedures, such as whole body or brain only perfusions followed by complex tissue collection protocols using multiple specialized techniques (e.g., OCT frozen, snap frozen, sterile collections, RNAase free collections), which the technical staff are highly capable of performing. Other examples of technically complex projects that illustrate the scope of expertise in the Pathology service include projects for Core Scientist [REDACTED] in the Brain, Mind, and Behavior Research Unit:

- Epigenomic modifications in neurodevelopment: Sectioning the entire brain, organizing and cataloging the sections with photography, then dissecting out precise regions.
- Serotonergic modulation of brain development: Whole body perfusion of late second trimester fetuses

Table 4. Service Use: Anatomic Pathology (May 1, 2010 to April 30, 2014)

Grant Year	# Users	Investigators (N)	Service Cost (\$)	Total Cost (\$)
2010 - 2011	35	Core Scientists (11)	100,429	209,407
		UC Davis (9)	37,568	
		External (15)	71,410	
2011 - 2012	35	Core Scientists (10)	50,213	155,745
		UC Davis (7)	27,840	
		External (18)	77,692	
2012 - 2013	36	Core Scientists (9)	41,555	149,790
		UC Davis (9)	35,052	
		External (18)	73,182	
2013 - 2014	39	Core Scientists (8)	38,385	139,403
		UC Davis (7)	38,007	
		External (24)	63,010	
TOTAL				\$654,345

A project for a local biotechnology company was also conducted under Good Laboratory Practice (GLP) conditions. Many of these research projects also utilize the resources of the Clinical Pathology Laboratory, which has continued to serve as an invaluable national resource with expertise in the analysis of primate blood,

and cells [REDACTED] has more than 32 years of experience analyzing primate samples, and she rates with the Clinical Pathology Laboratory in the School of Veterinary Medicine as well as other facilities throughout the nation to share information and obtain other opinions on challenging cases. Another critical function of the Clinical Pathology Laboratory is to provide customized tests for pre-project evaluations to ensure avoiding any potential health issues that may confound the research protocol. Several tests are developed in collaboration with the **Endocrine Core** (see Core). [REDACTED] are also members of the Morbidity and Mortality Review Committee, a multi-disciplinary committee meeting every quarter with the purpose to review spontaneous deaths in the colony and any emerging trends in the data and potential follow-up actions.

The reporting system for cases that come through the necropsy suites includes a running log of animals, which is transferred into an Excel format containing preliminary diagnoses, and filed as soon as the necropsy is completed. A necropsy report that consists of gross anatomy and microscopic findings with associated SNOMED codes is generated and entered into the electronic pathology database. Any images taken during necropsy or histological images obtained are uploaded to the image database and subsequently linked to the necropsy report. Similarly, the Clinical Pathology Laboratory enters microbiology, parasitology, hematology, and serum banking results onto the main server which links to the animal record (see **Information Technology Services**). Histological tissue processing and any further special stains and immunohistochemistry is carried out at the Veterinary Medical Teaching Hospital histology laboratory since they have the wide range of immunohistochemical and special stains that are regularly required for diagnostic pathology fully optimized with a good turn-around time. Cases are prioritized so that any necropsy case with a potential large colony impact and biopsies are expedited for processing and can be returned from the histology laboratory within 24 hours. Standard Operating Procedures (SOPs) addressing necropsy procedures, the use of PPE (personal protective equipment), sample collection, and tissue shipping are maintained current, and reviewed annually. Health and safety requirements for each employee are tracked and updated as required.

Re-organization of Daily Operations. Since taking on a management role in the Pathology service in 2011,

Excluded by Requester has reviewed SOPs and organizational structure involved in day-to-day running of these services. A number of strategies have been employed aimed at releasing pathologist time, allowing more involvement in research, writing manuscripts, and the resident training program. Additionally, streamlining the operation of the service has reduced waste and improved efficiency. Implementing the following strategies has begun to achieve the stated goals.

- As described above, technical staff has been given more delegated authority and independence. They have been trained to carry out certain categories of routine necropsies with minimal supervision and special technical procedures (e.g., perfusions) unsupervised.
- Bottlenecks hampering service operations have been identified and removed. The processing of tissues upon removal from the necropsy room for submission to the histology laboratory is now carried out by technical staff members. The staff members also provide transcription assistance for report entry into the database as other primary duties allow.
- A well-organized organizational structure for technical staff has been developed. Roles, duties, and work expectations are been re-defined and responsibilities are clear.
- A triage system has been implemented to reduce the number of cases that are given a full necropsy, and tissues that are saved. Cases are triaged at the pathologist's discretion. Cases deemed to be more informative receive a full work-up whereas more routine cases may receive a more limited tissue collection with only select tissues processed for histopathology or alternatively, a gross necropsy alone with no tissues collected. Generally middle-aged and older animals receive a full necropsy. Standardized protocols have been set up to handle cases of ICD and spontaneous fetal loss.
- The creation of a technical supervisor position has allowed the Senior Veterinary Manager to spend much less time supervising the technical staff. Further delegation of responsibilities, such as health and safety monitoring, protocol maintenance, and billing, as well as other organizational responsibilities has greatly assisted in improving her workload.
- The Clinical Pathology Laboratory computerization of daily entries for microbiology, parasitology, and serum bank data has greatly improved overall efficiency.

Infrastructure and Equipment. Critically needed equipment has been purchased over the past 2 years to replace old and out-of-date equipment primarily using program income. A five-head microscope linked to a high quality camera and two high definition monitors has transformed communication between pathologists and teaching capabilities both within and outside the service. Additionally, three new microscopes with cameras have been purchased, allowing pathologists to easily add histology images to pathology reports. A chemistry analyzer was leased last year by the Clinical Pathology Laboratory, and now accommodates routine chemistry panels including the high sensitivity C Reactive Protein assay, a frequently requested test. This acquisition has provided a substantial cost savings to both investigators and clinicians, and the turnaround time has been greatly reduced.

Research. Progress has been made towards increasing the involvement of pathologists in research, with 14 publications cited in the current funding period. The clinical veterinarians and Pathology service have also worked together to develop an atmosphere of increasing collaboration, which has already resulted in a number of joint publications and with more in the pipeline. Excluded by Requester continued his fruitful collaboration with Core Scientist Excluded by Requester (**Infectious Diseases Research Unit**), Excluded by Requester is well recognized as an expert in gastric pathology and helicobacteriosis Excluded by Requester [2013]. The collaboration between Excluded by Requester

Excluded by Requester is a model for the development of future collaborations between pathologists and investigators. Dr. Excluded by Requester is involved in a number of collaborative interactions. He works with Core Scientist Excluded by Requester Affiliate Scientist Excluded by Requester (UC Irvine) (**Infectious Diseases Research Unit**) on the morphologic

characterization of chlamydia infection in the reproductive tract of female rhesus monkeys, and with Excluded by Requester (Cornell University) on serologic diagnosis of *Campylobacter jejuni* infection in rhesus monkeys by testing for cytolethal distending toxin. He has ongoing collaborations with Excluded by Requester (UC Davis) to characterize the oral microbiome and morphologic appearance of the mucosa in the rhesus monkey Excluded by Requester al., 2013], and with Core Scientist Excluded by Requester (**Genetics Management Services**) and Excluded by Requester Roodgar (UC Davis) to explore evolutionary immunology with particular emphasis on the morphologic expression of infectious disease influenced by the genome. Excluded by Requester has been developing interactions with

investigators in the **Respiratory Diseases Research Unit**, which has recently resulted in collaboration and a publication on the subject of infant influenza [Excluded by Requester 2014].

Anatomic and Clinical Pathology Services has also been promoting the investigation of naturally occurring disease within the colony, particularly chronic colitis associated with ICD. One of the most significant developments is creation of a postdoctoral position for a junior pathologist, which will address a number of previous criticisms of the service as noted above. The position is aimed at developing junior pathologists as scientific collaborators in their own right, and providing the stepping-stone to a junior faculty position. In addition to providing a percentage of pathology duty for the service, the incumbent is actively involved in research, working with Principal Investigator (PI) and mentor, Core Scientist [Excluded by Requester].

(Infectious Diseases Research Unit) [Excluded by Requester] a former laboratory animal pathology resident in the School of Veterinary Medicine pathology program at UC Davis, and who obtained a PhD from [Private Source].

[Private Source] has recently achieved American College of Veterinary Pathologists (ACVP) board certification, and has been appointed to this position. Under the supervision of [Excluded by Requester] he is studying immune cell populations present in the intestine in the setting of inflammation caused by chronic colitis. [Excluded by Requester]

[Excluded by Requester] also working on a colony pilot project supported by the P51 base grant to better characterize the pathological lesions of ICD within the colony. It is anticipated that within 1-2 years extramural support for [Excluded by Requester] will come from other sources while he continues to maintain his skills as a pathologist. This approach underscores the advantageous position by pathologists to contribute to high-quality science allowing them the time and resources for career development.

Teaching. Teaching is an essential mission of the service, and over the past 3 years efforts in this area have been refocused and revitalized. Communications and interactions with the pathology service in the School of Veterinary Medicine have greatly improved, thus increasing awareness of the CNPRC and potential for expansion of its role as a teaching resource. The majority of the teaching carried out by pathologists is focused within the Postgraduate Pathology Residency Training Program associated with the School of Veterinary Medicine. The CNPRC is now better integrated into the larger pathology residency program and is taking a leading role in this program. At any one time, there are 6-8 residents in the program as well as residents who have moved into PhD research. The 3-year Laboratory Animal Pathology Track is supported by the School of Veterinary Medicine, CNPRC, and the UC Davis Comparative Pathology Laboratory, and admits one student each year from a highly competitive pool of outstanding candidates. The program provides a unique mix of general pathology training geared towards ACVP board certification along with specialized training with laboratory animal species. This program is unique and is not available anywhere else in the U.S. Trainees gain hands-on experience and many hours of one-on-one mentoring in primate pathology during their 10-month

[Excluded by Requester] at the CNPRC (Table 5) [Excluded by Requester] in particular has been an outstanding educator asset to this program. In addition to his extensive expertise in primate pathology, he has been recognized by all the recent residents in the Laboratory Animal Pathology Training Program as an exceptional teacher and mentor. The program is producing veterinary pathologists with specialized laboratory animal training who have a very high success rate achieving Board certification with the ACVP. Importantly, the majority of program graduates have continued on to PhD programs.

Table 5. Residents Trained (May 1, 2010 to April 30, 2014)

Resident	Completed Residency	Board Certification	Current Position
[Excluded by Requester]	2010	2011	PhD student, UC Davis
	2011	2011	PhD student, North Carolina State
	2012	In progress	PhD student, Stanford University
	2013	2013	PhD Student, NIH
	2013	2013	Postdoctoral fellow CNPRC (PhD 2010)

As well as enhancing mentoring and teaching capabilities at the CNPRC, pathologists and laboratory animal pathology residents are playing an important role in the pathology community in the School of Veterinary Medicine, both in teaching and by providing exposure to primate pathology case material. The CNPRC is now represented at all major pathology rounds at the Veterinary Medical Teaching Hospital, regularly providing interesting nonhuman primate cases for Friday biopsy conference. CNPRC residents and pathologists contribute regularly to biweekly laboratory animal rounds, which provide more in-depth training in laboratory animal pathology of nonhuman primates and rodents. Primate pathologists provide training for ACVP board

Excluded by
Requester

examinations to all the residents. In 2013, [redacted] was appointed as Assistant Adjunct Clinical Professor in the Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, in recognition of her role as a pathology resident trainer, and involvement with teaching residents in the pathology department in the School of Veterinary Medicine. Additionally she took on more formal teaching responsibilities in the Comparative Pathology Graduate Group in 2013, and teaches in a graduate level course in the winter quarter.

Both pathologists and technical staff serve as educators in many other forums. PIs and their laboratory staff come to pathology services for technical training in tissue handling and processing. Veterinary students also sign up for rotations.

Other Resources. The Pathology service maintains and administers valuable resources, which are used by an extensive network of investigators. The most highly utilized resource is the large Biospecimen Distribution Program, run efficiently by the technical staff, which allows the full use of animals that are culled from the colony for a variety of reasons. This service is used extensively by investigators nationally. Regular recipients include 13 Core and Affiliate Scientists at the CNPRC, 12 investigators on the UC Davis campus, and 15 investigators from external institutions throughout the U.S. (see Figure 4 and Tables 6 and 7). The program distributes organs and tissue samples as well as other biological samples such as blood, bone marrow, and cerebrospinal fluid. The program is publicized on the external website, through outreach efforts, and is viewed as a service and resource for investigators rather than a primary income generator. Samples can be collected and prepared according to the investigators needs and then either collected by or shipped to the investigator. The income generated from the Biospecimen Program (specimen fee, labor for processing and shipping, consumables) is placed back into program income to support the nonhuman primate colony. In collaboration with the **Information Technology Services**, a program to streamline the distribution of biospecimens has been developed and is in the testing and refinement stage. This program will dramatically reduce the number of technician hours invested in the program. Additionally, a highly organized archive of formalin-fixed tissue, paraffin blocked tissue, and glass slides are housed in temperature-controlled trailers. The catalogued database of this archive allows for easy retrieval of requested samples.

Figure 4. Biospecimens Distributed Annually (May 1, 2010-April 30, 2014)

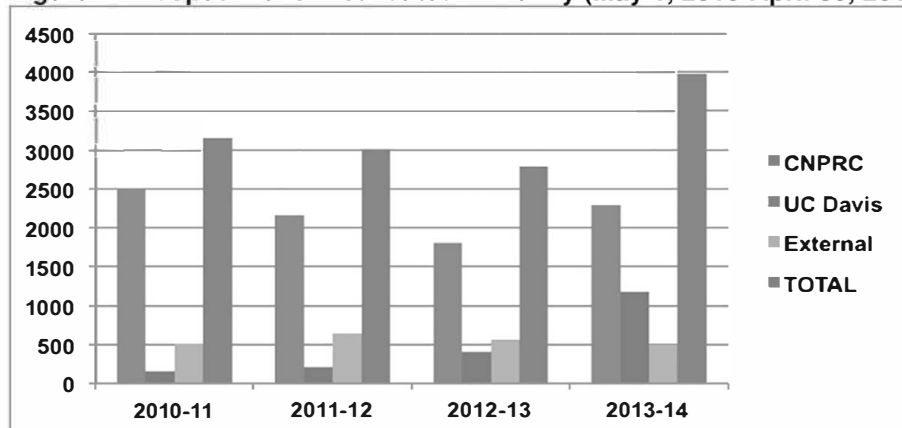


Table 6. Biospecimen Program: Investigators and Institutions (May 1, 2010 to April 30, 2014)

Grant Year	Investigators Served	Institutions Served
2010 - 2011	36	14
2011 - 2012	38	16
2012 - 2013	42	20
2013 - 2014	38	19
TOTAL	154	69

Table 7. Biospecimen Program: Income (May 1, 2010 to April 30, 2014)

Grant Year	Income (\$)
2010 - 2011	6,300
2011 - 2012	11,225
2012 - 2013	11,650
2013 - 2014	14,100
TOTAL	\$43,275

Interaction with Clinical Veterinarians. Over the past 2 years, there has been a particular focus on improved communication and interaction with the clinical medicine veterinary staff. In addition to rounds, which have been in place for many years, histopathology rounds were added about a year ago, enabled by a new multihead microscope and imaging system. Communication has improved prior to interesting cases arriving at necropsy, providing a means to address the interests of the clinical veterinarians and the pathologists at the time of necropsy.

Interaction with other NPRCs. During the current funding period the Pathology Working Group of the **NPRC Consortium** has continued to hold very well attended, monthly slide conferences using internet teleconferencing. For the past 2 years, there has also been an annual face-to-face meeting. The Working Group has established a **Primate Pathology Image Database** to allow sharing of images from informative or classical cases between the NPRCs. The CNPRC has played a leading role in the design of this database (see **Multimodal Imaging Core**). The culmination of the project this year has resulted in the upload of interesting cases to the database to be shared between all NPRCs for the purposes of teaching.

The implementation of the changes and enhancements to the Anatomic and Clinical Pathology Services described in detail above have resulted in a more focused and efficient service that is now able to handle the daily workload and is recognized as an outstanding teaching resource.

INNOVATION

Innovative strategies have been implemented to use resources wisely, and to improve the service in the face of an increasing workload. The primary strategies implemented to achieve these goals are detailed in the section below, and can be summarized as follows:

- Development of protocols to handle common cases with much of the work associated with these cases carried out by technical staff in a consistent way with oversight by the pathologists.
- Train senior technical staff to take on more responsibility and carry out necropsies (especially those with defined protocols such as whole-body and brain perfusions), and perform technical procedures with minimal oversight from pathologists. Triaging of cases has significantly reduced the routine histopathology expenses and also made better use of the pathologist's time reading out slides and writing up case reports.

Innovative approaches to expand our knowledge of two relatively common diseases in the colony include the following:

Idiopathic Chronic Diarrhea is a long-standing clinical issue that remains the primary cause for euthanasia of macaques in the CNPRC colony. The majority of animals submitted to necropsy for this reason have tested negative for known pathogens, and are given the clinical diagnosis of ICD. The pathogenesis of this syndrome remains elusive, as does a reliable antemortem diagnostic test. For these reasons, and under the leadership of

the Pathology service has designed a comprehensive necropsy and sampling protocol aimed at better understanding ICD and identifying potential markers of disease. This protocol is employed across the CNPRC to ensure more uniform tissue and data collection from affected animals, including interventional trials described in the **Primate Medicine Services** section. With a long-term view of a systematic investigation into the etiology of ICD, the primary emphasis is placed on tissue banking so that comprehensive studies can be conducted in the future in collaboration with clinicians, colony management, Core Scientists, and extramural investigators. The protocol includes:

- Develop biomarkers predictive of chronic diarrhea in collaboration with clinician veterinarians.
- Systematic and consistent sampling of the entire gastrointestinal tract for examination and grading of hematoxylin and eosin (H&E) sections from all affected animals and appropriate control animals.
- Banking of fresh colonic tissue to assess the colonic mucus layer, and for future immunofluorescence studies.
- Banking of plasma for future metabolomics studies.
- Banking of feces to examine changes in the microbiome associated with ICD.
- Banking of peripheral blood mononuclear cells and lymphocytes extracted from the ileum and colon to assess the immunology of chronic diarrhea.
- Investigation of potential immunohistochemical markers of disease (e.g., chromogranin-A).

Left Ventricular Hypertrophy (LVH) is responsible for a small but consistent number of spontaneous deaths in the colony each year (see **Genetics Management Services**), and can also be found incidentally at a

necropsy for other reasons. The Anatomic and Clinical Pathology Service has been working with Core and Affiliate Scientists to characterize this disease better, and investigate its potential as a disease model with the approaches outlined below:

- Examination of clinical records and pathology reports to develop an epidemiological picture of LVH.
- Develop a collaboration Excluded by Requester Assistant Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine, who specializes in the genetics of cardiac disease (see letter).
- With the assistance of Core Scientist Excluded by Requester develop design-based stereological techniques to assess cardiac myocytes in animals with LVH (see **Multimodal Imaging Core**).
- In collaboration Excluded by Requester examine the pedigrees of animals with LVH to identify genetic propensity to develop disease (see **Genetics Management Services**).

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Provide pathology expertise for state-of-art research and scientifically contribute to the understanding and treatment of human disease with nonhuman primate models.

Anatomic and Clinical Pathology Services currently supports and produces high quality multidisciplinary research either collaboratively or on a recharge basis. It is ideally poised to extend and promote collaborations with scientists whose programs would be significantly enhanced by the contributions of a pathologist during the next funding period. To achieve this aim the service will:

- Identify and characterize the histopathology of novel phenotypes with potential as models of human diseases. The ability to integrate information gathered at necropsy with clinical, genetic, and behavioral data can shed new light on the pathogenesis of disease processes, identify phenotypes that may not be immediately apparent with a single discipline approach, and aid in the development of new disease models. Initially, the service will focus on interaction with the **Genetics Management Services** to further characterize disease entities that preliminary data suggest may have a genetic component to their pathogenesis. To this end after initial consultations with this group, Pathology will initiate basic collection and storage of tissues suitable for genetic analysis and outreach to potential investigators to attract interest in further exploration of these cases.
- Support of pathologist-initiated research projects to take advantage of the extensive tissue banks available to investigate spontaneous disease within the colony.

Specific Aim 2. Provide exceptional nonhuman primate resources and pathology services to investigators at the regional and national levels to advance NIH-supported research excellence.

Anatomic and Clinical Pathology Services will continue to facilitate research and ensure a supportive environment for investigators by providing pathology expertise in study design and evaluation of animals on experimental protocols. High quality technical support can facilitate extensive or specialized tissue collection and handling techniques, for example specific organ perfusions and the immediate antemortem collection of tissues for *in vitro* studies. The Clinical Pathology Laboratory can support a wide range of both antemortem and postmortem testing, for example hematology, clinical chemistry, microbiology, parasitology, and urinalysis. Anatomic Pathology will continue to serve as a national resource for nonhuman primate tissue through the maintenance of the bank of preserved tissue and biospecimens harvested from culled animals. Reorganization of banks of fixed tissue, and paraffin-embedded blocks and slides has facilitated the retrieval of resources requested. The service will enhance research support and training in specialized technical skills to a wide variety of researchers:

- The computer program developed with **Information Technology Services** to assist with administering the Biospecimen Tissue Distribution Program will be a major enhancement once it is fully operational.
- Secure funding for a Laboratory Information System (LIMS) geared towards handling clinical laboratory data and an upgrade for the hematology analyzer to enable electronic data transfer. Advancements in computerization of data and instrument upgrades will enable the laboratory to remain GLP compliant.
- The Clinical Pathology Laboratory will actively work to stay current in providing up-to-date tests that will benefit investigators as well as the health of the colony.
- Outreach via the **NPRC Consortium** to alert investigators to novel potential models of human diseases.

Specific Aim 3. Mentor and train the next generation of nonhuman primate pathologists and translational investigators.

The Pathology service is ideally positioned to mentor and train the next generation of Veterinary Pathologists as strong comparative pathologists with an emphasis on primate pathology so that they will be able to both provide diagnostic pathology services and become key players in team science utilizing nonhuman primate models of human disease. We will enhance our ability to serve as an educational resource to trainee pathologists, veterinarians, laboratory animal professionals, and investigators by:

- Seeking opportunities to develop our contribution to the pathology training program at the School of Veterinary Medicine and the integration of other pathologists into other more formal teaching opportunities as they arise. Excluded by Requester new pathologist has extensive mentoring experience, a passion for teaching, and an additional teaching certification. Private Source
- Encourage attendance at gross pathology and microscope rounds and virtual slide conference to promote interaction between pathologists and with the clinical veterinary staff.
- The service will provide further cases to the Primate Pathology Image Database so that good quality teaching material can be shared at a national level.

Specific Aim 4. Maintain the production of high quality, healthy animals for research.

In close cooperation with the clinical veterinary staff, the service will continue to provide disease diagnosis and surveillance for the colony by performing diagnostic necropsies and biopsies, and the coordination of testing for specific pathogens. This activity is crucial to maintain a healthy colony and provide high quality animals for research. Surveillance information produced by the Anatomic and Clinical Pathology Services helps the clinical veterinary staff manage disease outbreaks and locate which field corrals or groups of animals may be involved or at risk. Examples of infectious disease outbreaks where this information has been crucial include the management of Listeriosis and stillbirths in the field cages, a Tularemia outbreak in 2010 in the corn cribs and the monitoring of infectious causes of enterocolitis in the colony. This aim will be enhanced as follows:

- In the future, as openings for pathologists arise, we will endeavor to fill them with pathologists who have clinical pathology expertise in addition to anatomic pathology training.
- Develop the ARMS database to include pathology reports and images with particular emphasis on enhancing searching capabilities of the database.
- Evaluation of further areas for efficiency in necropsy procedures and report preparation.
- Work closely with the clinical veterinarians to identify potentially useful clinical and pathological markers of disease.

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

PUBLICATIONS (May 1, 2010 to April 30, 2014) Core Scientists in bold, Pathologists underlined

Excluded by Requester

Excluded by Requester

Cross-species transmission of a novel adenovirus associated with a fulminant pneumonia outbreak in a new world monkey colony. PLoS Pathog 7:e1002155, 2011. PMID: PMC3136464

Excluded by Requester

Enhanced viral replication and modulated innate immune responses in infant airway epithelium following H1N1 infection. J Virol 2014 [Epub ahead of print]

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A recombinant attenuated Mycobacterium tuberculosis vaccine strain is safe in immunosuppressed simian immunodeficiency virus-infected infant macaques. Clin Vaccine Immunol 19:1170-1181, 2012. PMID: PMC3416096

In Press

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Metastatic hepatocellular carcinoma in a juvenile rhesus macaque (*Macaca mulatta*). Comp Med 65:448-453, 2013. PMID: PMC3796757

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The impact of *Helicobacter pylori* infection on the gastric microbiota of the rhesus macaque. PLoS One 8:e76375, 2013. PMID: PMC3792980

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Transcription profiling reveals potential mechanisms of dysbiosis in the oral microbiome of rhesus macaques with chronic untreated SIV infection. PLoS One 8:e80863, 2013. PMID: PMC3843670

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Excluded by Requester

Excluded by Requester

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Persistence of gut mucosal innate immune defenses by enteric α -defensin expression in the simian immunodeficiency virus model of AIDS. Immunol 186:1589-2597, 2011. PMC Journal-in-Progress

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian and the IACUC.

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of _____ of indoor animal _____ outdoor animal housing area includes _____ field corrals _____ corn cribs _____ floor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) _____ Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an

approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Housing and Environmental Monitoring. Animal rooms are maintained within the recommended guidelines established by the current edition of the *ILAR Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. Typical nonhuman primate rooms provide 10-15 air changes per hour and are negatively pressurized relative to anterooms/corridors and the outside. Lighting is provided by fluorescent lights, which are controlled by timers (12 hours on/12 hours off). Room temperature is maintained between 68°F and 80°F, depending on the species and age of the animals in the room, and are checked and recorded daily. Emergency generator power is provided for all animal rooms. Indoor animal housing is monitored on a daily basis for temperature, light, and humidity. Power failures, major temperature fluctuation, and other environmental disturbances are either alarmed directly to Campus Physical Plant Services or monitored by CNPRC personnel on a daily basis. The Colony Operations Supervisor and the Maintenance Shop Supervisor carry pagers 24 hours/day and are alerted to environmental monitoring alarms and rooms that are out of temperature and humidity range.

Caging Systems. Indoor cages are stainless steel construction and either wall or rolling rack mounted. Cages incorporate a squeeze mechanism to bring the animal to the front of the cage for manipulation. Cage sizes are determined by the USDA and NIH policies. Cage designs incorporate sliding partitions to allow socialization or pair housing.

Environmental Enrichment. The Environmental Enrichment program is part of the Colony Management and Research Services component of Primate Services, is integrated with Behavior Management Services, and includes all animals, with emphasis placed on indoor-housed animals on research projects. Indoor cages are outfitted with a variety of enrichment options including manipulation mirrors (allowing the animal to view adjacent animals), and cage toys. Perches are present in all indoor cages. Low caloric items, such as forage, are provided on forage boards located on each cage. Animals also receive fruit or vegetables twice weekly. Non-food enrichment is also emphasized. One example of such enrichment is the placement of televisions, which provide visual stimulus to colony animals. Socialization can provide substantial benefit to the animals and is generally accomplished within the limitations of research protocols and daily management practices. Cages have been retrofitted or purchased with sliding partitions to allow pairing. The current strategy is to pair animals during the day and separate them at night to facilitate the assessment of physical signs each morning. Animals are paired early in the morning when animal care staff members begin daily animal care activities, animals are then separated at night when there are limited personnel available to monitor for potential aggressive interactions. The ability to observe each animal's individual daily physical signs is essential to many research programs and overall clinical care. Behavior Management Services staff members view every animal in the colony during morning health rounds and ensure they receive daily enrichment items targeting their specific behavior aberration. All indoor animals are also assessed monthly to identify any abnormal behaviors; these animals receive a detailed behavioral assessment monthly to monitor their status and progress.

Surveillance. The majority of animals at the CNPRC are from the production colony. Specific Animal Location outdoor field corrals. Animals brought into the CNPRC from off-site facilities complete a 90-day quarantine at the CNPRC Quarantine Facility. During this time, animals undergo a complete physical examination with complete blood counts, blood and fecal parasitology, and rectal culture. Five tuberculin tests are completed, and animals are screened for simian retroviruses including Type D simian retrovirus (SRV), Simian Immunodeficiency Virus (SIV), and simian T-cell leukemia virus (STLV). Animals of foreign origin are treated for malaria and intestinal parasites. Animals with positive tuberculosis tests and SRV assays, or

demonstrating signs of clinical illness, are humanely euthanized and a complete necropsy performed.

Feeding. The animals are fed commercial monkey chow twice daily. Monkey Chow is pre-analyzed for content. The analysis of each lot of feed is reviewed by CNPRC Quality Assurance and a Senior Veterinarian. Animals are supplemented with fruit or vegetables twice weekly. Water is provided by automatic lixits, which are checked daily for proper operation. Portable caging with detachable waterlines is checked daily. The CNPRC potable water supply is obtained from wells operated by UC Davis. All UC Davis wells are monitored by the Office of Environmental Health and Safety quarterly. The water is tested for chloroforms, a variety of chemical markers including heavy metals and a variety of toxic minerals, pesticides, and chemical contaminants. Additionally, the CNPRC tests for general mineral, organic, and inorganic contamination annually.

Sanitation. Indoor cages are hosed daily with a quaternary ammonium detergent/disinfectant and are sanitized every 2 weeks in a mechanical cage-washer. A microbiological monitoring program is in place to ensure efficacy of sanitation practices. Each animal area is monitored twice per year. Microbiological monitoring results are reviewed and signed off by each area supervisor, a Senior Veterinarian, and the Assistant Director for Colony Management and Research Services. Monitoring of caging pH during cage washing is included in the cage sanitation surveillance program. In addition, water lines in both the indoor and outdoor colony are monitored with microbiological testing on a rotational basis in conjunction with cage change activities.

Record Keeping. Record keeping includes a written individual animal record and entry of specific information into a computerized Vitals database (see **Information Technology Services**). Maintenance of the animal colony database, including information on project history, reproductive history, clinical data, viral status, as well as genealogical data is included. Also included are the current location of the animals, weight history, date of last tuberculosis test, and the date of the last serum banking. These data are available to aid in project design and animal selection by investigators. This database has also been critical to several retrospective studies involving prenatal mortality, transmission of retroviral agents in colony management, effects of housing changes on health, and risk factors for spontaneous diseases such as endometriosis. Management of this informational database represents a valuable resource to the entire biomedical research community. Historical animal-related data are maintained on a yearly basis to reflect the production statistics of the colonies including: conception rates, live birth rates, pregnancy loss, and infant mortality.

Animal Health Program. A health check is performed each morning by the colony management staff. Each animal has a location and animal identification barcode that is scanned, and an animal technician records physical signs listed on a menu using a portable barcode reader. After completion of the health check, the information is downloaded onto the main computer, and a morning health report is generated directly to the veterinary staff. Veterinarians or Animal Health Technicians perform a visual examination of each animal on health report. Results of the health check and assessment by the veterinary clinician are then recorded in the animal's record. For animals on study, a report is generated to the investigator on a daily basis by electronic mail. Animals in the outdoor colony are also checked twice each day, once in the morning and afternoon. Identification of animals in the field corrals is performed by individual dye mark. Technicians check each cage closely for animals potentially requiring medical attention. The afternoon health check was added to the outdoor colony in 2012, and increased health surveillance is particularly important during the birth season.

Centralized Research Support. The various services represented in Primate Services work synergistically to provide high quality, technical research support to all investigators utilizing the CNPRC, as needed, whether located locally or at a distant site. Staff veterinarians also provide extensive clinical support to animals on long-term research protocols (see Primate Medicine Services).

Staff Training. The program emphasizes occupational safety, as well as increasing demands for technical expertise in the care and research support of nonhuman primates. Training is viewed not only as the initial step at hire, but as an ongoing process through in-house classes and support to attend relevant training programs, meetings, and conferences. A spectrum of training opportunities is available specific to the

CNPRC and to meet campus-wide training requirements. These include: UC Davis Primate Handling and Husbandry Training, Campus Laboratory Animal Care Classes (AAALAC preparation); Injury / Illness Prevention Plan; Infection Control Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management; Campus Back Safety Class; Campus Radiation Safety Class; Pesticide and Antimicrobial Safety; Training in Good Laboratory Practices; Supervisor Training with Job Skills Worksheet; and position specific training for all levels of husbandry, animal care, and technical skills. The training program also includes a series of "*Attention to Detail*" documents that provide very detailed information for each of the training and skill areas the staff is expected to meet including information to enhance understanding and the need to adhere to defined guidelines for critical procedures.

Standard Operating Procedures (SOPs). Primate Services has an extensive collection of 185 SOPs that provide detail on all operational procedures including: husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by all staff and undergo full review and revision every three years. SOPs are available in an electronic format online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC, and SOPs by number can be noted in IACUC protocol submissions.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

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Enhanced viral replication and modulated innate immune responses in infant airway epithelium following H1N1 infection. J Virol 2014 [Epub ahead of print].

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ANIMAL RESOURCES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

LETTERS OF SUPPORT

Letters of support from the individuals named below are provided on the pages that follow.

1 <div>Excluded by Requester</div>	DVM, PhD, Diplomate ACVIM (Cardiology), Assistant Professor, Department of Medicine and Epidemiology; Chief of Service: Cardiology, School of Veterinary Medicine, University of California, Davis
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 DAVIS, CALIFORNIA 95616-8734

July 11, 2014

Excluded by Requester

DVM DACLAM

Associate Director Primate Services
 California National Primate Research Center
 University of California Davis
 Davis California

Dear

Excluded by Requester

I am writing to let you know of my strong interest in the cases of spontaneous left ventricular hypertrophy (LVH) and sudden cardiac deaths that you have observed in the rhesus macaque colony at the California National Primate Research Center (CNPRC). The data that Primate Services has collected on the pedigree of affected individuals as well as the pathology findings indicate that this may be a potential model of LVH in humans. I look forward to working with your clinical veterinarians to develop cardiac evaluation algorithms to evaluate family members of affected animals. As a veterinary cardiac geneticist I hope to help fully describe this model from a cardiovascular physiology and molecular genetics approach. This will hopefully help us develop diagnostic criteria to identify animals at risk for LVH and spontaneous cardiac arrest. I should mention that if we observe alterations to the QT segment, this would be particularly exciting since this is a major feature of sudden cardiac deaths in human populations, an area where large animal models are non-existent.

Thanks again for the opportunity to work with the CNPRC and I look forward to collaborating with the veterinarians in Primate Services.

Please contact me at

Personal Info

with any questions.

Sincerely,

Excluded by Requester

Excluded by Requester

DVM, PhD, Diplomate ACVIM (Cardiology)

Excluded by Requester

School of Veterinary Medicine,
 Department of Medicine and Epidemiology,
 University of California,
 2108 Tupper Hall, 258 CCAH
 Davis, CA, 95616.

Letters Of Su

Personal Info

Page 867

PRIMATE SERVICES: ANATOMIC AND CLINICAL PATHOLOGY SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
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 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Behavior Management Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
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Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename BMS_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	BMS_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	BMS_FacilitiesOtherResources.pdf
11. Equipment	BMS_Equipment.pdf

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

ABSTRACT

The primary goal of Primate Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. Animal care and research service is provided by a highly trained staff of veterinarians, Core Scientists, technicians, and administrators to meet the needs of the animals as well as the investigators using the CNPRC resource. **Behavior Management Services** is a component of the CNPRC Primate Well-being Plan that both monitors the populations and advises the Enrichment Program within Colony Management and Research Services for all of the colonies. The purpose of this service is to behaviorally monitor and socially manage the outdoor colonies using network-based approaches; systematically monitor the indoor colonies of monkeys for behavioral problems; evaluate the efficacy of current and new social and environmental enrichment; develop proactive strategies to reduce the development of behavioral problems; monitor the discharge of animals from the hospital to outdoor colonies to ensure physical and social safety; and lead a cooperative training program that emphasizes the use of positive reinforcement techniques for colony management purposes and constructive human-animal interactions. Each of these areas of emphasis is designed to proactively prevent both physical and behavioral problems. Thus, the Specific Aims for the Behavior Management Services are to: (1) Develop and implement best strategies to characterize behavioral phenotypes and provide outstanding research support by promoting social stability of the living lifespan laboratories of nonhuman primates unique to the CNPRC, (2) Scientifically assess the efficacy of current and new enrichment procedures to develop and maintain behavioral and physiological phenotypes that maximize research quality, and (3) Enhance and extend the proactive cooperative training program to utilize cost-effective management procedures.

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: A wet tissue processing laboratory and an equipment and prep room laboratory totaling 466 sq. ft. are available.

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology. See **Primate Medicine Services** and related sections.

Animal: The CNPRC currently has an animal census of ~5,000 rhesus monkeys, ~12 long-tailed monkeys, and ~86 titi monkeys. The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application.

Computer: All members of Behavior Management Services have computers and related items to perform the tasks required. These include five Dell computers equipped with a Windows 7 operating system and software for data entry and analysis which includes

Proprietary Info

Proprietary Info

Office:

Excluded by
Requester

occupies an office at the CNPRC, and the staff share office cubicles.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities, support services, and extensive expertise available as described in this application.

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

EQUIPMENT

Two Kawasaki Mules are available for rapid transit to and from the field corrals.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*	
1.	Excluded by Requester				Core Leader	Institutional Base Salary	EFFORT	0.0	0.0	28,794.00	11,484.00	40,278.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						40,278.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Technical Manager	Excluded by Requester	EFFORT		32,416.00	17,148.00	49,564.00
1	Total Number Other Personnel				Total Other Personnel		49,564.00
					Total Salary, Wages and Fringe Benefits (A+B)		89,842.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description	
List items and dollar amount for each item exceeding \$5,000	
Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,500.00
2. Foreign Travel Costs	0.00
Total Travel Cost	1,500.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	18,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	500.00
Total Other Direct Costs	18,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	109,842.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	109,842.00	24,934.00
		Total Indirect Costs	24,934.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	134,776.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester					Core Leader	Institutional Base Salary	EFFORT	0.0	0.0	29,946.00	12,637.00	42,583.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:		File Name:									Total Senior/Key Person	42,583.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Technical Manager	Excluded by Requester	EFFORT		33,713.00	18,649.00	52,362.00	
1	Total Number Other Personnel					Total Other Personnel		52,362.00
					Total Salary, Wages and Fringe Benefits (A+B)		94,945.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,545.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,545.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	18,540.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	515.00
Total Other Direct Costs	19,055.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	115,545.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	115,545.00	26,228.00
		Total Indirect Costs	26,228.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	141,773.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester				Core Leader	Institutional Base Salary	EFFORT	0.0	0.0	31,143.00	13,604.00	44,747.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person		44,747.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Technical Manager	Excluded by Requester	EFFORT		35,061.00	20,026.00	55,087.00	
1	Total Number Other Personnel					Total Other Personnel		55,087.00
					Total Salary, Wages and Fringe Benefits (A+B)		99,834.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,591.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,591.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	19,097.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	530.00
Total Other Direct Costs	19,627.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	121,052.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	121,052.00	27,479.00
		Total Indirect Costs	27,479.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	148,531.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Core Leader	Institutional Base Salary	EFFORT	0.0	0.0	32,389.00	14,570.00	46,959.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						46,959.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Technical Manager	Excluded by Requester	EFFORT		36,464.00	21,447.00	57,911.00	
1	Total Number Other Personnel					Total Other Personnel		57,911.00
					Total Salary, Wages and Fringe Benefits (A+B)		104,870.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,639.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,639.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	19,669.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	546.00
Total Other Direct Costs	20,215.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	126,724.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	126,724.00	28,766.00
		Total Indirect Costs	28,766.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	155,490.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Core Leader	Institutional Base Salary	EFFORT	0.0	0.0	33,685.00	15,619.00	49,304.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						49,304.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Technical Manager	Excluded by Requester	EFFORT		37,922.00	22,981.00	60,903.00
1	Total Number Other Personnel					Total Other Personnel	60,903.00
Total Salary, Wages and Fringe Benefits (A+B)							110,207.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,688.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,688.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	20,259.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Copying	562.00
Total Other Direct Costs	20,821.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	132,716.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	132,716.00	30,127.00
Total Indirect Costs			30,127.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	162,843.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMS_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Manager				
	Technician				
	Technician				
	Technician				
	Technician				

Individuals shown in italics are not supported by the P51 base grant; their salary support is provided by Program Income

Excluded by Requester **PhD, Core Scientist** EFFORT months % Effort Excluded by Requester Professor, Department of Population Health and Reproduction, School of Veterinary Medicine, and Core Scientist in the Brain, Mind, and Behavior Research Unit. Excluded by provides the oversight of current services, development of new services for enrichment assessment/implementation, and behavioral characterization and monitoring of the colonies. She provides expertise to CNPRC management and investigators on behavioral characterization of primate subjects and general colony animals.

Excluded by Requester **PhD, Manager** EFFORT months % Effort Excluded by Requester Oversees the scientific evaluation of current behavioral management practices and develops new practices through program specific projects under the guidance of Excluded by. She also utilizes sophisticated analytical methods to assess and enhance current enrichment and monitoring processes. In addition, prepares findings for presentation at professional meetings and submits results for publication in professional journals. Excluded by Requester

Excluded by Requester **Technician** oversees behavioral monitoring of the colony, social management of the outdoor enclosures, human-animal interactions with a focus on behavioral issues, and the cooperative training program. Excluded by is the lead social manager of the field corals, which includes animal monitoring data collection of hospital discharges, development and maintenance of hierarchies, overseeing animal selection to minimize social disruption and maintain stability, and direct supervision of staff conducting social monitoring of the colony. She is also responsible for responding when social issues arise and directing relocation of identified animals to minimize trauma and social disruption, and for allocating animal resources for new cage formations, male introductions, cage disbandment, and overseeing intensified observations during the formation time period to ensure animal safety.

Excluded by Requester **Technician** supports Behavior Management projects under the supervision of Excluded by Requester. Excluded by Requester assists with project design, communicating and coordinating with husbandry staff, scheduling data collection times, drafting protocols and ethograms, developing and testing data collection forms on handheld devices, project data collection and upload, database management, and data manipulation. Excluded by Requester conducts database management and data manipulation for both colony behavioral monitoring data and behavioral management project data.

Excluded by Requester **Technician** oversees the behavioral management of the ≥40 Specific Animal Location social groups. The tasks related to this function include coordinating and conducting behavioral observations in order to assess social interactions and abnormal behavior, recording and maintaining computerized records of these behavioral observations in order to synthesize sociometric reports, monitoring animals returning to their social group, and making strategic decisions about animal removal in order to ensure continued social stability of groups. Excluded by Requester is responsible for strategizing allocation of animals to new group formations, male introductions, and south colony cage disbandment, as well as socially monitoring these formations. Minor

duties include assisting with data collection on behavioral management projects and with positive reinforcement training

Excluded by
Requester

Technician [redacted] is the Human-Animal Interactions Coordinator and provides behavioral education to new and current staff about primate behavior and positive human-animal interactions. She also provides positive reinforcement training services for colony management purposes and by investigator request (see Behavior Research Services Core). She is responsible for responding to specific human-animal interaction issues in the colony to minimize aggression and ensure staff safety. She also maintains records on animal training in a database to monitor and assess effective training practices.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None

TRAVEL

\$1,500 is requested (1 x \$1,500) to attend a professional meeting annually. These funds are used to expose staff to science-based behavioral management approaches, such as those offered by the M.D. Anderson Cancer Center in Bastrup, Texas on enrichment and positive reinforcement training of nonhuman primates. These funds may also be used for staff to visit other NPRCs and conferences offered by the American Society of Primatologists (ASP), International Primatological Society, or AALAS to allow staff to participate in workshops and training that will expose them to research studies on primate behavior, animal management, and environmental enrichment for enhancing skill set development.

SUPPLIES

\$10,000 is requested for enrichment supplies including new enrichment testing supplies, and cooperative training supplies. Evaluation of new enrichment devices is conducted annually for potential use on a colony-wide basis, which requires testing of a substantial number of animals to accurately assess efficacy.

\$5,000 is requested for data collection supplies, such as handheld and tablet devices, digital voice recorders, stopwatches, and binoculars.

\$3,000 is requested for training supplies, such as treat reinforcers, treat dispensers, and training tools (bridges and targets) for developing and implementing positive reinforcement training.

OTHER EXPENSES

None

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		223,871.00
Section B, Other Personnel		275,827.00
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		499,698.00
Section C, Equipment		0.00
Section D, Travel		7,963.00
1. Domestic	7,963.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		98,218.00
1. Materials and Supplies	95,565.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	2,653.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		605,879.00
Section H, Indirect Costs		137,534.00
Section I, Total Direct and Indirect Costs (G + H)		743,413.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

Excluded by
Requester**2. Human Subjects**

Clinical Trial?

☒ No ☐ Yes

Agency-Defined Phase III Clinical Trial?*

☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***

Is program income anticipated during the periods for which the grant support is requested?

☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*

Anticipated Amount (\$)*

Source(s)*

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PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

BMS_SpecificAims.pdf

3. Research Strategy*

BMS_ResearchStrategy.pdf

4. Progress Report Publication List

BMS_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

BMS_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

BMS_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

SPECIFIC AIMS

Behavior Management Services monitors the populations and advises the Enrichment Program within Colony Management and Research Services. The purpose of this component is to: (1) behaviorally monitor and socially manage the outdoor colonies using network-based approaches, (2) systematically monitor the indoor colonies of monkeys for behavioral problems, (3) evaluate the efficacy of current and new social and environmental enrichment, (4) develop proactive strategies to reduce the development of behavioral problems, (5) monitor the discharge of animals from the hospital to outdoor colonies to ensure physical and social safety, and (6) lead a cooperative training program that emphasizes the use of positive reinforcement techniques for colony management purposes and constructive human-animal interactions. Each of these areas of emphasis is designed to proactively prevent both physical and behavioral problems.

Specific Aim 1. Develop and implement best strategies to characterize behavioral phenotypes and provide outstanding research support by promoting social stability of the living lifespan laboratories of nonhuman primates unique to the CNPRC.

Plan. Studies conducted at the California National Primate Research Center (CNPRC) have revealed that key behavioral phenotypes and critical social processes contribute to the physiological health and stability of large matrilineal-based rhesus macaque social groups. The plan is for Behavior Management Services and Colony Management and Research Services staff to implement and assess management procedures based upon these key phenotypes and processes (e.g., natal male removal, matriline fragmentation reduction, unrelated adult male introduction) along with new and more extensive monitoring protocols that focus on behavioral characterization and evaluation of the keystone power structure (known as peaceful subordination) in rhesus groups. This approach will ensure that social stability and the health and well-being of individuals are maximized for all groups in the outdoor colonies.

Specific Aim 2. Scientifically assess the efficacy of current and new enrichment procedures to develop and maintain behavioral and physiological phenotypes that maximize research quality.

Plan. Ongoing research by the Behavior Management Services team evaluates the efficacy of current and potential enrichment items/devices (e.g., produce, foraging devices, coconuts) to enhance animal health and well-being in indoor- and outdoor-housed colonies. The plan is to continue to identify the effectiveness of current and new devices as well as the evaluation of pairing introduction techniques and pair compatibility metrics, such as individual differences in temperament. The goal is to reduce behavioral problems and potential veterinary-related costs.

Specific Aim 3. Enhance and extend the proactive cooperative training program to utilize cost-effective management procedures.

Plan. The Behavior Management Services team has successfully developed a cooperative training program based upon internally based experimentation and external literature reviews to educate Primate Services staff on the use of positive reinforcement training and constructive human-animal interactions for enhancing primate health and well-being. This proactive approach is cost-effective as evident by the infant fostering program, which has resulted in significant cost reductions due to the near complete elimination of peer nursery-rearing for management purposes. The plan is to extend this approach to other routine management practices, such as blood collection, injections, and swabs. Cooperative training is offered in Behavior Management Services for animal husbandry and colony management.

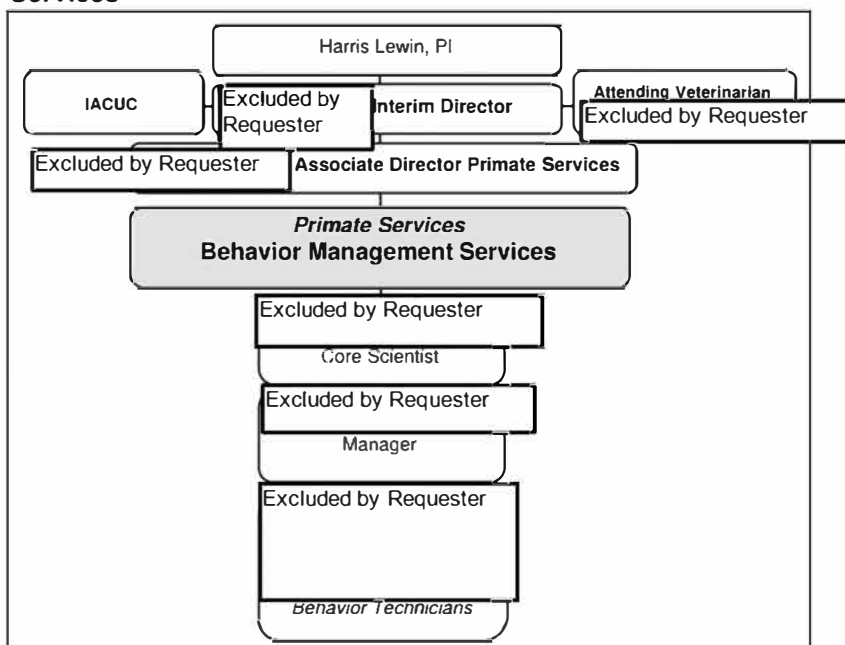
PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

RESEARCH STRATEGY

INTRODUCTION

Behavior Management Services staff (Figure 1) monitor the nonhuman primate populations and advise the Enrichment Program within Colony Management and Research Services (see **Colony Management and Research Services** section) on new and ongoing enrichment items and activities. The purpose of this program is to: (1) behaviorally monitor and socially manage the outdoor colonies, (2) behaviorally monitor the indoor colonies of monkeys for behavioral problems, (3) evaluate the efficacy of current and new social and environmental enrichment, (4) develop strategies to reduce behavioral problems, (5) monitor the discharge of animals from the hospital to outdoor colonies, and (6) lead a cooperative training program that emphasizes the use of positive reinforcement training (PRT) for colony management and constructive human-animal interactions.

Figure 1. Organizational Chart: Behavior Management Services



Members of Behavior Management Services are shown in Table 1 and the sources of support in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 1. Behavior Management Services Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Population Health and Reproduction, School of Veterinary Medicine	Core Scientist
	CNPRC	Manager
	CNPRC	Behavior Technician
	CNPRC	Behavior Technician
	CNPRC	Behavior Technician
	CNPRC	Behavior Technician

Table 2. Support for Behavior Management Services

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$105,346	\$109,842
Program Income from P51	\$0	\$0
Other Sources	\$349,485*	\$368,105*
*R24 funding TOTAL	\$454,831	\$477,947

Response to Summary Statement.

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE**Progress and Major Accomplishments: Contributions to the CNPRC Mission**

Behavior Management Services is primary to the CNPRC's mission and commitment to the well-being of the nonhuman primate colonies. This service provides critical input on enhancing the physical and psychological well-being of the animals. The Behavior Management Services team approach is central to developing and implementing the most efficient approaches for promoting well-being and thus maximizing the utility of nonhuman primates for biomedical research. The nonhuman primate populations at the CNPRC are behaviorally and socially characterized. This unique resource is due in large part to the considerable effort of Behavior Management Services staff to maintain detailed scientifically based observational records on the entire colony, and particularly unique sets of large socially complex matrilineal-based rhesus monkey groups. Significant input by behavioral staff using a comprehensive and unique knowledge base is conducted on a daily basis. This input ranges from support of investigator-initiated research in the form of animal selections to preserve social group stability while identifying behavioral phenotypes for projects, to assisting Colony Management and Primate Medicine staff in identifying animals in need of veterinary attention, or monitoring returns of previously hospitalized individuals, to providing training and educational services to investigators and

animal care staff. Extensive training and experience are stressed as a salient component for Behavior Management Services staff to conduct their work, and to provide the experienced oversight central to the overall well-being of the animals. Because stable social units are essential for enabling successful breeding populations, Behavior Management Services remains a critical CNPRC component that is central to many research studies conducted at the CNPRC. Overall, the service provides a proactive and preventive approach with the potential for significant cost reduction while maintaining a high quality nonhuman primate colony.

In the last base grant renewal, six major areas were outlined, each of which have been addressed. The first three areas have been combined as noted below due to their close relationship and will be updated together.

1. **Developed an active and adaptive enrichment program that promotes positive well-being for indoor-housed macaques.**
2. **Further evaluated efficacy of the current enrichment program emphasizing prevention and early detection of behavioral problems.**
3. **Developed and tested new enrichment devices/strategies that require cognitive effort as well as control over and feedback for the animals.**

The Behavior Management Services team has made substantial progress on several projects focused on developing an active and adaptive enrichment program for indoor-housed rhesus monkeys. The feasibility and efficacy of several new and established enrichment items have been tested including coconuts, various forage board materials, and cognitive puzzles. Recommendations have been made to the senior management on the types of enrichment to implement based upon these pilot studies. In collaboration with Core Scientists and other service functions in Primate Services, further development of the titi monkey enrichment program also includes testing and recommendations for implementation and enrichment items, such as coconuts, forage board materials, wooden perches, mealworm enrichment, and basket feeder devices. As a focus on prevention and early detection, Behavior Management Services staff members have evaluated some of the significant risk factors associated with self-injurious behavior (SIB) and the role of supplemental enrichment in reducing the potential for occurrence. Examples include socialization and experiences outdoors. Behavior Management Services staff have also conducted studies addressing the role of sophisticated surrogates for improving nursery-rearing strategies for experimental nurseries (Figure 2) and strategies for reducing stress in indoor mother-reared infants during the weaning process using desensitization and socialization techniques (Figure 3). The management team has also worked with the veterinarians in **Primate Medicine Services** for endpoint criteria for early detection procedures to address SIB cases. Studies on promoting animal behavioral motivation and well-being continue to be explored, particularly those addressing the importance of temporal and signaled predictability in husbandry practices by reducing behavioral problems (Figure 4), and the importance of cognitively challenging enrichment (e.g., solving puzzles).



Figure 2.
Nursery infant with surrogate for self-feeding.

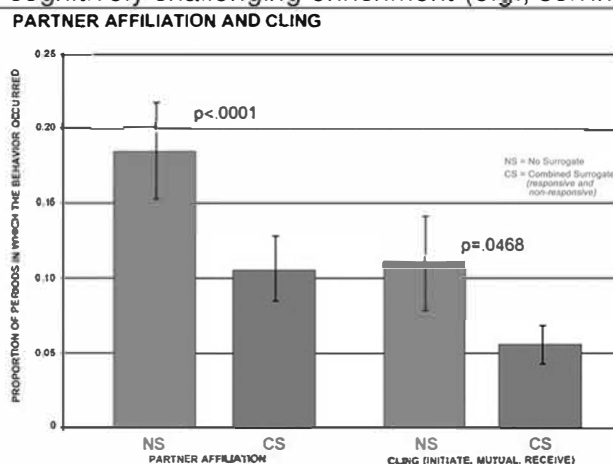


Figure 3. Proportion of periods in which infants engaged in partner affiliation and clinging. Note that surrogate-reared infants exhibited less partner affiliation and clinging than control peer-reared infants indicating that surrogates provided infants with an effective attachment figure during critical periods of development (manuscript submitted).

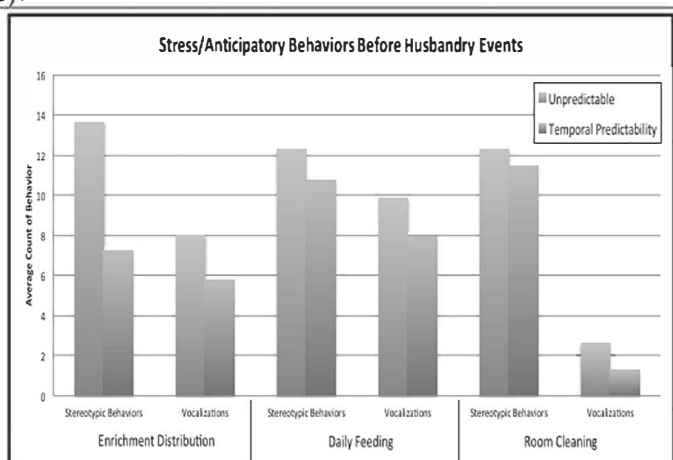


Figure 4. Predicted rates of stereotypical and anticipatory behaviors under unpredictable and temporally predicted events of enrichment, feeding and cleaning. Note that temporal predictability significantly reduces rates of stress-related behaviors for indoor-housed animals (Excluded by Requester et al., 2013).

To further promote well-being through human-animal interactions, the Behavior Management Services staff have developed a lecture series and hands-on workshop on behavior and behavioral management for new and existing employees who work directly with animals. The staff members regularly update a comprehensive manual on Behavior Management Services and Enrichment for staff professional development/outreach and a program of cross-training with other Primate Services components to foster communication, knowledge, and understanding of behavior-related aspects of colony management. Behavior Management Services staff has also established a cooperative animal training service using PRT that includes participation of staff from Behavior Management Services and **Colony Management and Research Services** to enhance animal well-being during routine husbandry practices and upon investigator request through the **Behavior Research Services Core** (see Core description).

4. Continued the development of a program in PRT for management and enrichment purposes.

Behavior Management Services staff has made good progress toward establishing a program that uses PRT. Pilot studies have been conducted that addressed four major evaluative aspects for developing a program using PRT: (1) evaluated areas in which PRT within a cooperative animal training service could be implemented most effectively, (2) conducted feasibility studies for training specific types of behaviors using PRT including difficulty and duration of training, (3) evaluated animal responses to the use of PRT, and (4) evaluated feasibility of training technical crew and other animal care and research staff to use PRT methods. Toward this end, studies conducted by Behavior Management Services staff on the use of PRT to reduce aggression in hyper-aggressive animals have been conducted, as well as studies that evaluated how personality might influence the efficacy of using PRT, and assessed the temporal feasibility of training basic behaviors such as targeting as a basis for more complex husbandry and research procedures. Case studies have been conducted on PRT training when Colony Management and Research Services or specific investigators have requested these services. Such cases included training for animal moves, injections, blood sample collection, among others. A highly successful cross-fostering program has also been implemented with orphaned infants using PRT techniques, which has substantially reduced the costs associated with nursery peer rearing. Finally, a pilot project has been completed on training technical crew and other CNPRC staff to learn new techniques necessary to use PRT in husbandry and research procedures (Figure 5), which includes both lectures and hands-on training. This pilot project has garnered high grass-roots interest in PRT techniques by a diversity of the CNPRC staff.



Figure 5. Use of PRT in nursery-housed infant.

5. Developed an adaptive social management program for the outdoor colony enclosures including design of efficacious group formation and maintenance protocols that promote social stability and minimize aggression in macaque groups.



Figure 6. Left panel shows monkeys in large ½-acre enclosures. Right panel shows a corn crib with smaller social groups of monkeys.

Excellent progress has been made in developing an adaptive social management program for outdoor colony enclosures (see Figure 6). Based on a series of studies conducted by [Excluded by] research staff (#R24-RR024396 [Excluded by] PI), the Behavior Requester

Management Services team is directly addressing the problem of social instability in large breeding groups, identifying risk factors such as natal male retention, and matriline fragmentation that exacerbate deleterious aggression and wounding in rhesus groups. Two webinars and two face-to-face meetings with personnel from other NPRCs within the Consortium (see **NPRC Consortium**) have been conducted as part of the goal to promote cross-

consortium outreach (e.g., behavioral management, colony management, veterinary services) and to discuss findings on social instability in these large groups. A major study is also in progress on group formations to establish best management practices for successful large-scale group formations in rhesus macaques. Several smaller studies conducted by Behavior Management Services staff and interns are in progress on the effect of vasectomies on female aggression and breeding behavior, the impact of blunting adult male canines on

patterns of aggression, new strategies for introducing unrelated adult males into large social groups, and evaluating factors leading to reintroduction success in a group when individuals must be temporarily removed for health treatments.

6. Developed a comprehensive video manual exhibiting macaque normal and abnormal behaviors to facilitate personnel and student training.

A comprehensive video manual (ethogram) for abnormal behaviors in macaques has been developed, and staff continues to work on this manual in order to include normal social behaviors from both the indoor and outdoor populations.

Other accomplishments include the following:

- Monthly reports to **Primate Medicine Services** and **Colony Management and Research Services** staff on the behavioral status of animals exhibiting alopecia and SIB.
- Quarterly investigator reports to inform on the behavioral status of project animals.
- Update and maintain the CNPRC Primate Well-being Plan and CNPRC "Exemption from Enrichment" form for the Institutional Animal Care and Use Committee (IACUC).
- Update and maintain the Behavior Management Manual to educate and inform investigators, CNPRC personnel, NIH, and USDA on the protocols, responsibilities, and services offered by Behavior Management Services, and to provide background on the natural history and behavior of the species housed at the CNPRC.
- Develop and update lectures and presentations on primate behavior and primate behavioral management for animal care staff, research staff, and Core and Affiliate Scientists.
- Serve on the Colony Management Advisory Committee to develop and discuss best management strategies.
- Participate in the Behavior Management Consortium Working Group to promote data and information sharing and enhance collaboration and cooperation across NPRCs (see **NPRC Consortium**).
- Provide undergraduate, graduate, and postdoctoral training opportunities (see Table 3).

Table 3. Undergraduate Student Interns (May 1, 2010 to April 30, 2014)

Undergraduate	Years of Participation	Current Status
Excluded by Requester	2	Unknown
	2	Unknown
	2	Employed by Private Source
	3	Undergraduate, UC Davis
	3	Employed by Private Source
	3	Employed, CNPRC Colony Management and Research Services
	1	Unknown
	2	Unknown
	2	Employed, CNPRC Anatomic and Clinical Pathology Services
	2	Employed Private Source
	3	Graduate Student with Excluded by Requester
	2	Unknown
	3	Employed Private Source

INNOVATION

Behavior Management Services is highly innovative due to the application of advanced computational methods including hierarchical models, model selection, and network-based statistics to understand complex physical and behavioral processes that improve health and well-being. The service is committed to using the most modern and effective approaches for evaluating social, structural, and foraging enrichment approaches guiding enrichment activities for the animals to be provided with high quality management procedures to enhance their overall physical and psychological health and well-being. This approach underscores the significant value of translational insights brought by studies in nonhuman primates.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Develop and implement best strategies to characterize behavioral phenotypes and provide outstanding research support by promoting social stability of the living lifespan laboratories of nonhuman primates unique to the CNPRC.

This process will include expanded behavioral characterization of outdoor breeding for the development of efficacious group formations and male introduction strategies including pre-group formation male assessment and selection (Figure 7). Evaluation of canine blunting on individual risk for injury and social group dynamics, testing the effects of contraception approaches for population management of social group dynamics, development of best management strategies for health check strategies, and feeding protocols will be explored among other projects. Metrics will include evaluation of behavioral and physiological changes in response to modifications to management approach (e.g., canine blunting, contraception, health checks, feeding protocols) such as rates of wounding and social relocations, rates of contact aggression and chronic physiological stress as measured by hair cortisol.

Figure 7. Successful adult male tenure promotes grooming within and among matriline, which in turn enhances social stability in large matrilineal-based social groups.



Specific Aim 2. Scientifically assess the efficacy of current and new enrichment procedures to develop and maintain behavioral and physiological phenotypes that maximize research quality.

The plan is to promote evidence-based practices on current and potentially new enrichment devices and procedures as well as the evaluation of pairing introduction techniques and pair compatibility metrics using network approaches. These include measures of temperament to enhance the overall health and well-being of primate colonies. Assessment will include systematic evaluation of pairing introduction practices in leading to long-term pair compatibility, the importance of intra-pair affiliation in maintaining long-term pairs and the efficacy of greater socialization through small indoor social group housing for enhancing social experience for experimental subjects. The results will be used to advise the Enrichment Program in Colony Management and Research Services that oversees all enrichment activities for indoor-housed animals and the Behavior Management Services that oversees the enrichment activities of the outdoor colony. Other areas of emphasis will include the utility of behaviorally relevant sounds/videos for use in the indoor colony. For each of these areas, both behavioral and physical/physiological health using standardized ethological approaches as well as new customized network approaches will be evaluated in collaboration with Enrichment to assess the efficacy of these approaches.

Specific Aim 3. Enhance and extend the proactive cooperative training program to utilize cost-effective management procedures.

The Behavior Management team will continue to develop the cooperative training program by expanding the education program to a broader group of staff members to ensure that personnel are available to perform PRT techniques as use is expanded across the CNPRC for colony management and husbandry procedures. This will involve a certification program that includes both lectures and a hands-on laboratory component. The Behavior Management Services team will also continue to train basic and gateway behaviors (e.g., target, body-part present) (Figure 8) to a wide variety of colony animals to provide a firm basis upon which other more complex behaviors (e.g., blood collection, present for injections, chair training) can be trained.

Figure 8. Female rhesus monkey in corn-crib targets to receive treat through PRT.



The Behavior Management Services team will also continue to provide a cooperative training service through the **Behavior Research Services Core** on an investigator-requested fee-for-service basis. For continued effort on emphasizing positive human-animal interaction, the team will continue to provide basic courses in primate behavior and behavioral management and plan to develop more advanced courses on primate behavior management that includes substantial cross-training in these services with staff members from other services at the CNPRC.

Developing a certification course on primate behavior that is analogous to the training certification program described in Colony Management and Research Services is also under consideration. Metrics of success will include the percentage of students that successfully complete the certification programs as well as the degree to which PRT techniques become incorporated into daily husbandry routines. Current successes include the development of a PRT service for the Behavioral Research Services Core and, most importantly, our cooperative training-based infant fostering program, which has successfully eliminated for all practical purposes the peer-rearing nursery program for field cage animals at the CNPRC.

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

PUBLICATIONS (May 1, 2010 to April 30 2014)

- Excluded by Requester Effects of natal male alliances on aggression and power dynamics in groups of rhesus macaques. *Am J Primatol* 73:790-801, 2011. PMID: PMC3058123
- Excluded by Requester Detecting instability in animal social networks: Genetic fragmentation is associated with social instability in rhesus macaques. *PLoS One* 6:e16365, 2011. PMID: PMC3027651
- Excluded by Requester Sex ratio, conflict dynamics and wounding in rhesus macaques. *Appl Anim Behav Sci* 137:137-147, 2012. PMID: PMC3357203
- Excluded by Requester Policing in nonhuman primates: partial interventions serve a prosocial conflict management function in rhesus macaques. *PLoS One* 8:e77369. doi:10.1371/journal.pone.0077369, 2013. PMID: PMC3805604
- Excluded by Requester Signaling context modulates social function of silent bared-teeth displays in rhesus macaques (*Macaca mulatta*). *Am J Primatol* 76:111-121, 2014. PMID: PMC391945
- Excluded by Requester Joint modeling of multiple social networks to elucidate primate social dynamics: I. Maximum entropy principle and network-based interactions. *PLoS One* 8:e51903. doi:10.1371/journal.pone.0051903, 2013. PMID: PMC3585323
- Excluded by Requester Ranking network of a captive rhesus macaque society: a sophisticated corporative kingdom. *PLoS One* 6:e17817. doi: 10.1371/journal.pone.0017817, 2011. PMID: PMC3058001
- Excluded by Requester Risk factors for stereotypy and self-abusive behavior in rhesus macaques (*Macaca mulatta*); animal's history, current environment, and personality. *Am J Primatol* 75:995-1008, 2013. PMID: PMC3973020
- Excluded by Requester The effects of predictability in daily husbandry routines on captive rhesus macaques (*Macaca mulatta*). *Appl Anim Behav Sci* 143:117-127, 2013. PMID: PMC3578712
- Excluded by Requester Efficacy of 3 types of foraging enrichment for rhesus macaques (*Macaca mulatta*). *J Am Assoc Lab Anim Sci* 50:888-894, 2011. PMID: PMC3228926
- Excluded by Requester Network stability is a balancing act of personality, power, and conflict dynamics in rhesus macaque societies. *PLoS One* 6:e22350. doi:10.1371/journal.pone.0022350, 2011. PMID: PMC3153932
- Excluded by Requester Human-directed contra-aggression training using positive reinforcement with single and multiple trainers for indoor-housed rhesus macaques. *Appl Anim Behav Sci* 132:178-186, 2011. PMID: PMC3100413
- Excluded by Requester Early social experience affects behavioral and physiological responsiveness to stressful conditions in infant rhesus macaques (*Macaca mulatta*). *Am J Primatol* 73:692-702, 2011. PMID: PMC3100413
- Excluded by Requester Early rearing interacts with temperament and housing to influence the risk for motor stereotypy in rhesus monkeys (*Macaca mulatta*). *Appl Anim Behav Sci* 132:81-89, 2011. PMID: PMC3084485

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review (2014) of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian and the IACUC.

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [redacted] of indoor animal space. The outdoor animal housing area includes [redacted] field corrals, [redacted] corn cribs, and [redacted] outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLTV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols. The activities described in this section are specific to the species, and the number of animals is based on a power analysis when analyzing new enrichment or related items.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian), [redacted] Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem.

and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Environmental Enrichment. The Environmental Enrichment program is part of the Colony Management and Research Services component of Primate Services, is integrated with Behavior Management Services, and includes all animals, with emphasis placed on indoor-housed animals on research projects. Indoor cages are outfitted with a variety of enrichment options including manipulation mirrors (allowing the animal to view adjacent animals), and cage toys. Perches are present in all indoor cages. Low caloric items, such as forage, are provided on forage boards located on each cage. Animals also receive fruit or vegetables twice weekly. Non-food enrichment is also emphasized. One example of such enrichment is the placement of televisions, which provide visual stimulus to colony animals. Socialization can provide substantial benefit to the animals and is generally accomplished within the limitations of research protocols and daily management practices. Cages have been retrofitted or purchased with sliding partitions to allow pairing. The current strategy is to pair animals during the day and separate them at night to facilitate the assessment of physical signs each morning. Animals are paired early in the morning when animal care staff members begin daily animal care activities, animals are then separated at night when there are limited personnel available to monitor for potential aggressive interactions. The ability to observe each animal's individual daily physical signs is essential to many research programs and overall clinical care. Behavior Management Services staff members view every animal in the colony during morning health rounds and ensure they receive daily enrichment items targeting their specific behavior aberration. All indoor animals are also assessed monthly to identify any abnormal behaviors; these animals receive a detailed behavioral assessment monthly to monitor their status and progress.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** The procedures employed in Behavior Management Services are noninvasive and do not typically incorporate the need for sedation or analgesics. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Euthanasia is not an activity conducted in Behavior Management Services. When required, animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

BIBLIOGRAPHY AND REFERENCES CITED

Excluded by Requester

The effects of predictability in daily husbandry routines on captive rhesus macaques (*Macaca mulatta*). Appl Anim Behav Sci 143:117-127, 2013. PMCID: PMC3578712

PRIMATE SERVICES: BEHAVIOR MANAGEMENT SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Genetics Management Services

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename GEN_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	Gen_BibliographReferencesCited.pdf
10. Facilities & Other Resources	GEN_FacilitiesOtherResources.pdf
11. Equipment	GEN_Equipment.pdf

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

ABSTRACT

The primary goal of Primate Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. Animal care and research service is provided by a highly trained staff of veterinarians, Core Scientists, technicians, and administrators to meet the needs of the animals as well as the investigators using the CNPRC resource. The primary mission of the CNPRC **Genetics Management Services** is to provide genetics related support and resources for colony management and banking of DNA and other samples for investigators. The Specific Aims for Genetics Management Services include: (1) Genetic management of the animal colonies, (2) Provide genetic resources to investigators, and (3) Manage the CNPRC DNA Bank and participate in the National Primate Research Centers (NPRC) Consortium. Genetic management to preserve maximum variability among colony animals is achieved by integrating several fundamental population genetic approaches. Retaining genetic variability is a principal goal of captive genetic management of nonhuman primates. The service has identified 5,000-6,000 high quality Single-Nucleotide Polymorphisms (SNPs) in macaques, developed panels of 96 genetic management SNPs, and 96 ancestry informative SNP markers for rhesus and long-tailed macaques. The CNPRC's DNA Bank is part of the National Nonhuman Primate DNA Bank network in the NPRC Consortium that has a goal of standardizing resources across the NPRCs.

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

FACILITIES AND OTHER RESOURCES

Laboratories: A 250 sq. ft. laboratory is equipped with two Dell Optiplex desktops. This laboratory includes a fume hood and has automated DNA extraction capability to isolate high quantity (5.74-8.40 µg), and high quality (A260/280: 1.71-1.92) DNA from blood samples.

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology.

Animal: The CNPRC currently has an animal census of ~5,000 rhesus monkeys, ~12 long-tailed monkeys, and ~83 titi monkeys. The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, and infectious animal housing. The outdoor animal housing area includes half-acre corrals and corncribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted above. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, also described in other sections.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and Information Technology Services provides desktop support, and other related services. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are available.

Office: Excluded by Requester occupy an office at the CNPRC. Staff share office space.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities, support services available, and extensive expertise available.

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

EQUIPMENT

Eppendorf EpMotion 5075 TMX automated DNA extraction and sample tracking barcode system, a $\leq -20^{\circ}\text{C}$ freezer and a refrigerator. The liquid handler is connected to a Dell Optiplex Gx280 desktop. There is one Dell laptop computer for data analysis and sample databasing via WebVitals.

The Molecular Anthropology Laboratory is fully equipped for molecular analyses with electrophoresis cells, high voltage power supplies, autoclaves, $\leq -80^{\circ}\text{C}$ freezers, refrigerators, standard chest freezers, 12 thermal cyclers including, platform shakers, UV transilluminators, incubators, a spectrophotometer and fluorometer, speed vac lypholyzer, ISO 2000 imaging system, an ABI 7300 4 dye real-time qPCR machine, an ABI 7500 Fast qPCR machine, and an ABI 3130xl genetic analyzer with 16 capillaries.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT			34,670.00	5,894.00	40,564.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					40,564.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	EFFORT			23,251.00	9,273.00	32,524.00
1	Technical Manager				3,338.00	1,766.00	5,104.00
2	Total Number Other Personnel				Total Other Personnel		37,628.00
					Total Salary, Wages and Fringe Benefits (A+B)		78,192.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

3,000.00

2. Foreign Travel Costs

0.00

Total Travel Cost 3,000.00**E. Participant/Trainee Support Costs**

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other:

0 Number of Participants/Trainees**Total Participant Trainee Support Costs****0.00**

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	500.00
Total Other Direct Costs	11,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	92,692.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	92,692.00	21,041.00
		Total Indirect Costs	21,041.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	113,733.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: GEN_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT			35,710.00	6,428.00	42,138.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					42,138.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	EFFORT			23,948.00	10,106.00	34,054.00
1	Technical Manager				3,438.00	1,902.00	5,340.00
2	Total Number Other Personnel				Total Other Personnel		39,394.00
Total Salary, Wages and Fringe Benefits (A+B)							81,532.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,090.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,090.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,300.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	515.00
Total Other Direct Costs	11,845.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	96,467.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	96,467.00	21,898.00
Total Indirect Costs			21,898.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	118,365.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: GEN_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT			36,781.00	6,804.00	43,585.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	43,585.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	EFFORT			24,667.00	10,775.00	35,442.00
1	Technical Manager				3,541.00	2,023.00	5,564.00
2	Total Number Other Personnel				Total Other Personnel		41,006.00
					Total Salary, Wages and Fringe Benefits (A+B)		84,591.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,183.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,183.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,609.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	530.00
Total Other Direct Costs	12,200.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	99,974.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	99,974.00	22,694.00
		Total Indirect Costs	22,694.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	122,668.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: GEN_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT			37,885.00	7,236.00	45,121.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						45,121.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	EFFORT			25,407.00	11,429.00	36,836.00
1	Technical Manager				3,647.00	2,145.00	5,792.00
2	Total Number Other Personnel				Total Other Personnel		42,628.00
					Total Salary, Wages and Fringe Benefits (A+B)		87,749.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,278.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,278.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	10,927.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	546.00
Total Other Direct Costs	12,566.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	103,593.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	103,593.00	23,516.00
		Total Indirect Costs	23,516.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	127,109.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: GEN_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT			39,021.00	7,687.00	46,708.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						46,708.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Affiliate Scientist	EFFORT			26,169.00	12,134.00	38,303.00	
1	Technical Manager				3,757.00	2,277.00	6,034.00	
2	Total Number Other Personnel					Total Other Personnel		44,337.00
					Total Salary, Wages and Fringe Benefits (A+B)		91,045.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,376.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,376.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	11,255.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Shipping	562.00
Total Other Direct Costs	12,943.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	107,364.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	107,364.00	24,372.00
		Total Indirect Costs	24,372.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	131,736.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: GEN_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Affiliate Scientist				
	Manager				
Excluded by Requester	PhD, Core Scientist	EFFORT	% Effort	Excluded by Requester	has overall responsibility for oversight of colony population genetics management. This role has been key in leading the development of the Single-Nucleotide Polymorphism (SNP) assays in use across the National Primate Research Centers (NPRCs) allowing standardized genetic data across sites. Support will continue to facilitate the adoption of the SNP panels.
Excluded by Requester	PhD, Affiliate Scientist	EFFORT	% Effort	Excluded by Requester	has extensive experience in population genetics and primate genetic management, is directly responsible for analysis of pedigree and population genetic data used in the management of both conventional and specific pathogen-free (SPF) breeding colonies, and technical development and testing of SNP panels for NPRC Consortium use.
Excluded by Requester	Manager	EFFORT	% Effort	Excluded by Requester	provides technical support for the Genetics Management Services under the guidance of Excluded by Requester

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June)

EQUIPMENT

None

TRAVEL

\$3,000 is requested (2 x \$1,500) to attend a professional meeting annually.

SUPPLIES

\$10,000 is requested for pedigree marker development.

OTHER EXPENSES

\$500 is requested for specialized shipping containers required for nonhuman primate specimens.

\$1,000 is requested for manuscript submission.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from

the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		218,116.00
Section B, Other Personnel		204,993.00
Total Number Other Personnel	10	
Total Salary, Wages and Fringe Benefits (A+B)		423,109.00
Section C, Equipment		0.00
Section D, Travel		15,927.00
1. Domestic	15,927.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		61,054.00
1. Materials and Supplies	53,091.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	2,653.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		500,090.00
Section H, Indirect Costs		113,521.00
Section I, Total Direct and Indirect Costs (G + H)		613,611.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	20,000.00	Services
2	21,100.00	Services
3	22,261.00	Services
4	23,485.00	Services
5	24,777.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

Gen_SpecificAims.pdf

3. Research Strategy*

GEN_ResearchStrategy.pdf

4. Progress Report Publication List

GEN_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

GEN_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

GEN_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

SPECIFIC AIMS

The primary goal of Primate Services is to ensure the highest quality animal care and husbandry for the California National Primate Research Center (CNPRC) nonhuman primate colonies. Primate Services encompasses Colony Management and Research Services, the National Institute on Aging Colony, Primate Medicine Services, Anatomic and Clinical Pathology Services, Behavior Management Services, and Genetics Management Services. Animal care and research service is provided by a highly trained staff of veterinarians, Core Scientists, technicians, and administrators to meet the needs of the animals as well as the investigators using the CNPRC resource. The primary mission of **Genetics Management Services** is to provide genetics-related support and resources for colony management, and banking of DNA and other samples for investigators.

Specific Aim 1. Genetic management of the animal colonies.

Plan. Genetic management to preserve maximum variability among colony animals is achieved by integrating several fundamental population genetic approaches. Retaining genetic variability is a principal goal of captive genetic management of nonhuman primates. This not only ensures each animal's value in terms of maintaining biomedical potential but also guarantees the entire population's survivability and productivities by increasing heterozygosity and correspondingly reducing the probability of homozygosity for deleterious alleles. Additional goals include a genetic management plan for the titi monkey colony.

Specific Aim 2. Provide genetic resources to investigators.

Plan. Single-Nucleotide Polymorphism (SNP)-based typing and analysis and ABO phenotyping currently represents major areas of service. The objective is to continue to genotype nonhuman primates at the CNPRC using SNPs to provide parentage assessment, ancestry/admixture testing, and genetic management services on a fee-for-service basis. The service has identified 5,000-6,000 high quality SNPs in macaques and developed panels of 96 genetic management SNPs and 96 ancestry informative SNP markers for rhesus and long-tailed macaques.

Specific Aim 3. Manage the CNPRC DNA Bank and participate in the National Primate Research Centers (NPRC) Consortium

Plan. The DNA Bank provides archived and banked samples and functions as a clearinghouse for the CNPRC. DNA and other biological samples from this bank are made available to investigators at a variety of research institutions once a proposal is reviewed and approved by the CNPRC Research Advisory Committee. Efforts to create an automated sample tracking system are underway in conjunction with the CNPRC Information Technology Services staff to ensure optimal organization and to improve access. The CNPRC's DNA Bank is part of the National Nonhuman Primate DNA Bank network in the NPRC Consortium that has a goal of standardizing resources across the NPRCs.

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

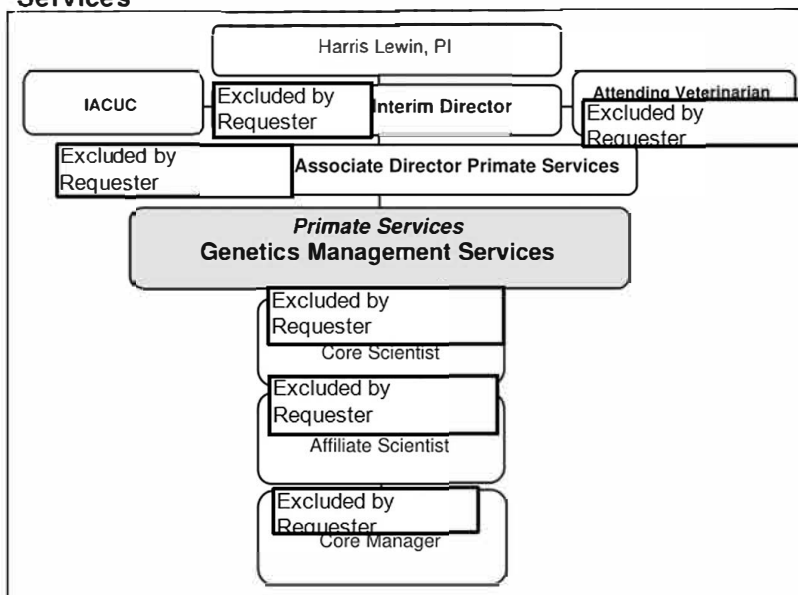
RESEARCH STRATEGY

INTRODUCTION

Genetics Management Services includes two geneticists and a Manager (Figure 1, Table 1) and is located at the California National Primate Research Center (CNPRC). This service is integrated with the activities of the Molecular Anthropology Laboratory in the College of Biological Sciences, and the UC Davis Veterinary Genetics Laboratory in the School of Veterinary Medicine. Genetics Management Services performs analyses for the purpose of genetic management of the CNPRC colonies, and provides services on a recharge basis to investigators interested in incorporating genetics-based techniques in their research programs. The service manages the DNA Bank, which has established a basic repository of DNA and other samples from animals in the colony to enhance access to these resources. The P51 base grant and extramural grants (#R24-PH005090 and #R24-OD011173, [redacted] PI)

Excluded by Requester

Figure 1. Organizational Chart: Genetics Management Services



have been the primary sources of support. Table 2 shows support for Genetics Management Services in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA.

Table 1. Genetics Management Services Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Excluded by Requester	Department of Anthropology, College of Biological Sciences	Core Scientist
	Department of Environmental Toxicology, College of Agricultural and Environmental Sciences	Affiliate Scientist
	CNPRC	Manager

Table 2. Support for Genetics Management Services

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$88,540	\$92,692
Program Income from P51	\$10,000	\$20,000
Other Sources	\$13,024	\$0
TOTAL	\$111,564	\$112,692

Response to Summary Statement

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

Genetics Management Services performed a large scale study based on a broad genomic analysis of 2,808 SNPs in 400 random rhesus macaques from the CNPRC conventional, and Levels 1 and 2 Specific Pathogen Free (SPF) colonies to ensure that only animals estimated to be of pure Indian or Chinese ancestry, based on both demographic and genetic information, are being used as a source of infants for derivation and expansion of the CNPRC's Level 2 colony. As reference samples for the analysis, pure Chinese and Indian rhesus macaques and hybrids were used. The study showed that genetic variation based on SNPs is actually slightly higher in Indian than in Chinese rhesus macaques (contrary to results of analyses using STRs and mitochondrial DNA) and that the Chinese rhesus macaque colony is far less differentiated from their founders compared to the Indian-origin animals, likely because the Chinese rhesus colony was founded more recently and with fewer founders than the Indian rhesus colony.

To both demonstrate the value of the SNP genotyping approach and begin the transition from STR to SNP-based testing for routine parentage, ancestry estimation, and genetic management across the NPRCs, funds were obtained through an R24 and the **NPRC Consortium** to SNP-type 1,600 rhesus macaques from the 7 NPRCs as well as the Caribbean Primate Research Center's populations. Participating centers selected up to 200 individuals (preferably breeding adults, or a mixture of current breeders and specific sire-dam-offspring trios) each and submitted the animal's DNA to either the CNPRC or Oregon NPRC for SNP-typing on the AIMs and genetic management panels. To ease the transition from STRs to SNPs for parentage and ancestry testing, this SNP-typing service was provided to the participating NPRCs at no cost. In terms of benefits from this transition, the standardized panels of SNPs will facilitate a unified, highly informative, efficient, and low-cost approach to providing all the information concerning pedigree relationships, ancestry estimation, and genetic management comparable to that of STR-based testing. Moreover, the SNP data is more readily integrated into the nationwide portal for shared bioinformatics resources including vital statistics, genotype, genomic, and population data that are being developed by the NPRC Consortium Working Group (see **NPRC Consortium**). Therefore, standardized testing and uniform data type across NPRCs will advance the exchange, analysis, and comparison of genetic data across NPRCs, improve efforts to combine data for various purposes, enable the exchange of useful and comparable genetic information about individuals or sets of individuals, and foster greater collaboration among researchers.

Excluded by Requester

Excluded by Requester were tasked to conduct SNP analysis for the California, Southwest, and Yerkes NPRCs, as well as the Caribbean Primate Center, while colleagues from the Oregon NPRC performed the analysis for the remaining NPRCs. For SNP testing, the respective colony managers from the NPRCs and the Caribbean Center selected animals for testing, and sent 200 μ l aliquots of DNA. The SNP genotypes are currently being compared to those based on STRs. Excluded by Requester will assist colony managers and other staff in interpreting the SNP genotype results and using this information to inform specific colony management decisions. The results of the SNP typing of breeders is based on the STRUCTURE analysis where sample outcomes are identified by 100% Chinese animals, 25% Indian animals, 50% Indian, 75% Indian, 100% Indian animals, and animals of unknown ancestry. The Caribbean Center's animals were estimated to be of pure blood Indian stock, and the degree of Indian ancestry was found to be among the highest that has been calculated across several NPRCs. The CNPRC and Yerkes NPRC populations

contained hybrid animals while the Southwest NPRC breeding pool consisted of both pure Chinese (i.e., those with 1-4% Indian ancestry) and hybrid stock (i.e., those with <90% Indian ancestry).

The population genetic estimates based on the 96-parentage or genetic management SNP panel are shown in Table 3. This panel will be used for both parentage and genetic management purposes when a shift from STRs to SNP-based testing is made. The estimates exhibited by most of these markers suggest that they are suitable for both of these purposes.

Table 3. Estimates of Genetic Variation and Differentiation among Four NPRCs

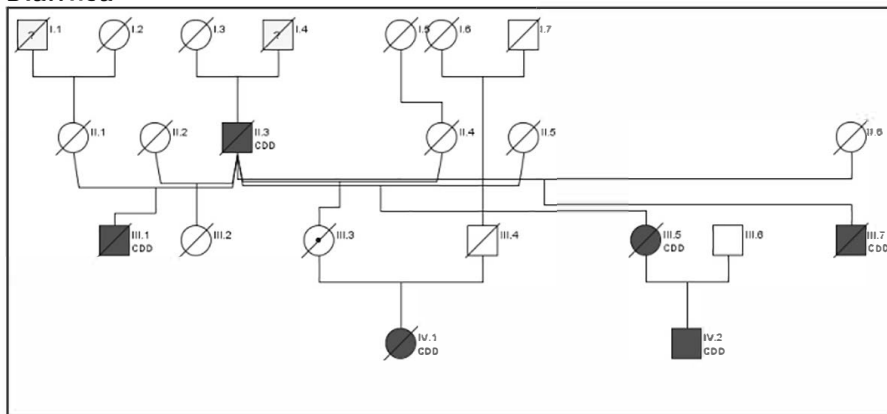
Genetic Variation	Caribbean	CNPRC	Southwest	Yerkes
Mean Observed Heterozygosity	0.44487	0.46207	0.4625972	0.47239
Standard deviation	0.09078	0.06485	0.0651983	0.06372
Mean Expected Heterozygosity	0.44554	0.46272	0.4627127	0.47247
Standard deviation	0.09058	0.06464	0.0650365	0.0638
Mean Minor Allele Frequencies	0.43849	0.4546	0.454137	0.46473
Pairwise Fst				
CNPRC	0.0559			
Southwest NPRC	0.05084	0.01198		
Yerkes NPRC	0.05299	0.01359	0.01019	

Ideopathic Chronic Diarrhea (ICD) and Left Ventricular Hypertrophy. Two recent publications

[et al., 2013; 2014] provide evidence that two issues identified in captive bred colonies of rhesus macaques, ICD and hypertrophic cardiomyopathy, are strongly influenced by genes.

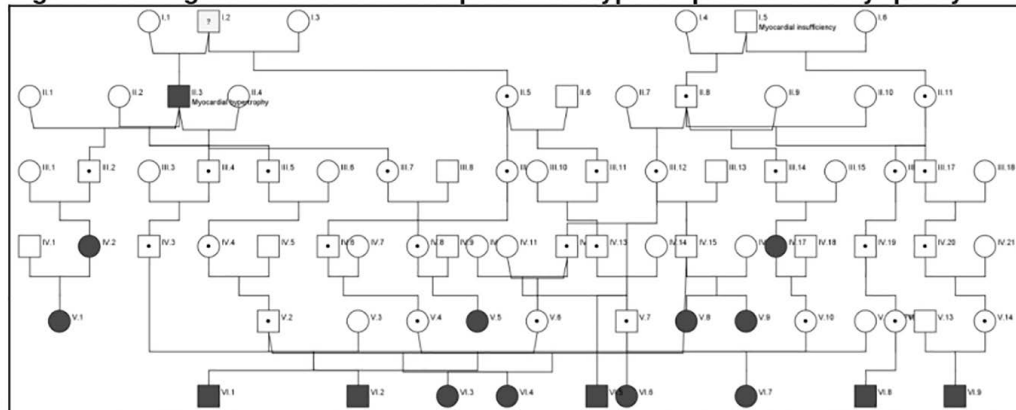
identified 175 rhesus macaques with chronic diarrhea and estimated its incidence at approximately 2% in the colony. The disease strongly clustered in eight multi-generation pedigrees (see Figure 2). Inspection of the pedigrees, segregation analysis, and heritability estimate of chronic diarrhea suggest that susceptibility to the disease is under strong genetic control.

Figure 2. Pedigree of Rhesus Macaques with Ideopathic Chronic Diarrhea



Hypertrophic cardiomyopathy is the abnormal thickening of the ventricles of the heart and an increase in cardiac mass. Analyses of 108 rhesus macaque probands revealed a strong genetic predisposition to this disease (Figure 3). The results from these pedigree analyses provide an opportunity to further study the disease in captive colonies if SNPs

Figure 3. Pedigree of Rhesus Macaques with Hypertrophic Cardiomyopathy



linked to susceptibility genes can be identified by whole genome association studies. Identification of the locations of susceptibility genes in the rhesus macaque genome could facilitate the identification of their frequency in captive breeding facilities.

Services Offered. The following are examples of services that are provided to investigators (see Table 4):

- Custom DNA extraction, purification, and quantitative PCR (qPCR) based DNA quantification.
- Development of new genotyping assays based on conventional fragment size analysis (including STRs and restriction fragment length polymorphisms, RFLPs), Sanger sequencing, copy number variation (CNV), SNP, and real-time PCR or qPCR techniques.
- Genetic and bioinformatics analysis based on the gene-by-gene approach and high-throughput genome-wide analyses, comparative genomic and phenotype-based studies, mapping and annotating rhesus genes, and analyzing the structure and expression of rhesus genes and its genome.
- Genetic management analysis, including country of origin and parentage testing and other related phylogenetic, phylogeographic, population genetic, and pedigree analyses.
- Implementation of rhesus and long-tailed macaque ABO phenotyping and species testing.
- Analyzing genealogical and demographic data including kinship assessment, pedigree validation, management of selective breeding, and development of informative pedigrees for investigators.

DNA Bank. Genetics Management Services have participated in the development and implementation of resources produced by the Working Group including the National DNA Bank and Information Technology (IT) resources. As part of the National DNA Bank, the CNPRC serves as the bank for samples of pure Indian and Chinese rhesus macaque and titi monkey tissues and DNA. Genetics Management Services have provided banking since 2011, and these activities include:

- DNA extractions of archived blood and other tissue samples with a current total of 16 batches of extractions (N=1,500). Currently, there are 26,381 biomaterial samples that include 3,626 plasma samples, 277 red blood cell samples, 2,640 buffy coats, 7,919 DNA samples, and 3,467 whole blood samples. These were obtained from 5,554 rhesus macaques, 167 long-tailed macaques, and 389 titi monkeys.
- DNA extraction and repository of samples from CNPRC newborns born in the field corrals since 2011 (~600 individuals per year).
- Samples from newborns extracted within 2 to 3 days of collection, and processing completed in one day.
- Established a Material Transfer Agreement and price breakdown (based on the National Nonhuman Primate DNA Bank rates).
- Administered the National Nonhuman primate DNA Bank.
- Converted existing databases at the CNPRC to the caLIMs-enabled environment for large-scale data tracking, including the Animal Research Management System (ARMS) and barcode system in cooperation with the IT staff.

Collaborative research in primate genetics to develop new techniques/methods for enhancing genetic management approaches at the CNPRC and other NPRCs has also been initiated. Among these activities are:

- Population analysis including estimating genetic diversity, genetic subdivisions, and inbreeding and kinship coefficients.
- Pedigree analysis based on genetic markers and PEDSYS.
- Ancestry estimation and country of origin testing.
- Advise the Director and **Colony Management and Research Services** staff on selection of animals for sale, purchase, and cage/enclosure composition.
- Advise Core and Affiliate Scientists on the selection of genetic markers for studying phenotypes of interest.

Table 4. Genetics Management Services (May 1, 2010 to April 30, 2014)

Client	Service	Data	N	Recharge (\$)
Private Source	SNP Discovery	Sequence	>20	Collaboration*
	Relatedness	STRs	2	Collaboration
	Genetic Management	STRs	54	
	ABO Blood Test	qPCR	47	1,616
	Kinship	STRs	30	1,590
	Origin	STRs	30	1,590
CNPRC	Ancestry Testing	SNPs	278	2,226
	Genetic Management	STRs and Pedigree	5,200	
	Genotyping	qPCR, SNP	>500	
	Gene Expression	qPCR, SNP	>500	
Private Source	Ancestry Testing	SNPs	150	Collaboration
	ABO Blood Test	qPCR	48	766
	Origin	STRs and Sequence	72	
	Kinship	STRs	10	610
	ABO Blood Test	qPCR	10	130
	Origin	STRs	19	1,007
	ABO Blood Test	qPCR	19	247
	SNP Discovery	RRL, SNP	25	31,968
	Twin Study	STRs	3	Collaboration
	ABO Blood Test	qPCR	10	210
Naval Medical Research Center	Genetic Characterization (Vervet)	STRs	6	378
	ABO Blood Test	qPCR	32	542
New England NPRC	Paternity	STRs	18	Collaboration
Private Source	Genetic Management (Marmoset)	Pedigree	300	Collaboration
	Origin	SNPs	30	1590
	SNP Discovery	Sequence	20	Collaboration
	SNP discovery	RRLs	25	Collaboration
	ABO Blood Test	qPCR	85	1,418
	Origin	SNPs	96	2,49
	Kinship	SNPs	96	2,897
	Genetic Management	STRs	103	Collaboration
	Origin	SNPs	400	Collaboration
Southwest NPRC	Ancestry	SNPs	200	18,000
Tulane NPRC	Paternity	STRs	>200	Collaboration
University of Maryland	Origin	STRs	46	1,484
	Genetic Characterization	STRs	46	1,484
	Kinship	STRs	46	1,431
	ABO Blood Test	qPCR	14	182
University of Oklahoma	Genetic Management (Baboon)	STRs	500	Collaboration
University of Pennsylvania	ABO Blood Test	qPCR	33	467
University of Wisconsin-Madison	Origin	STRs	12	Collaboration
Private Source	Origin	STRs	45	Collaboration
Washington NPRC	Genetic Management (Pigtail)	STRs and Pedigree	~5,000	Collaboration
	ABO Blood Test	qPCR	15	
Private Source	ABO Blood Test	qPCR	67	1,564
	Genotyping	STRs	24	Collaboration
Yerkes NPRC	Ancestry Testing	SNPs	584	26,256
				\$99,902

*Collaboration projects with non-NPRC clients (e.g., private sector, academic institutions, government laboratories) were supported by Excluded by Req R24 grants noted above. NPRCs paid for services from their P51 base grants; CNPRC P51 funds used for labor and supplies in some cases.

INNOVATION

The pedigrees of over 10,000 rhesus macaques at the CNPRC have been constructed including some founders that were introduced into the colony in the 1960s. Achieved through collaborative efforts between Dr. Excluded by Requester and the IT Services group, the pedigrees were established through DNA analysis using STRs,

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colony records, and the use of the PEDSYS program [1999]. The kinds of analyses that can be performed using this remarkable deep multigenerational pedigree information afforded by colony records and genetic data at the CNPRC include testing the familial aggregation of ICD and hypertrophic cardiomyopathy as noted above.

An innovative aspect is the implementation of 96 highly derived ancestry informative SNPs (AIMs panel) with high Δ MAF values (differences in minor allele frequency between Indian and Chinese rhesus macaques) for identifying levels of intra-species admixture and SNPs with high minor allele frequency values in all populations for use in parentage analysis and estimating parameters useful for genetic management (GM panel). The AIMs panels has been demonstrated to be capable of distinguishing purebred Chinese-origin from purebred Indian-origin rhesus macaques as well as their hybrids of more than 15% admixture with great reliability [et al., 2014]. An empirical comparison of STRs or microsatellites and SNPs revealed that both marker types provided comparable levels of predictions of relatedness in rhesus macaques [et al., 2013]. Efforts to identify even more effective SNPs for these purposes are underway.

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Of particular significance are the key leadership roles played by [Excluded by Requester] in achieving the high-priority goals of the Genetics and Genomics Working Group of the **NPRC Consortium**. Activities include the following:

- Development, testing, and validation of a molecular genetic assay that uses 96 SNPs for parentage testing in rhesus macaques.
- Validation of a second genetic assay that uses 96 SNPs to determine the ancestry (Indian- vs. Chinese-origin) of individual rhesus macaques.
- Conducted SNP genotyping using the parentage panel on 3,890 rhesus macaques from six NPRCs and the Caribbean Center, resulting in the adoption of one or both of the SNP panels at six NPRCs. Access to a standard panels of SNP markers for parentage and ancestry testing, which allows all NPRCs to produce standardized genetic information for colony management, thus facilitating the accumulation of comparable genetic data across centers.
- As a result of these developments, the Working Group communicates regularly with the Breeding Colony Managers Working Group with the goal of establishing practical, ready-to-implement recommendations and best practices for monitoring and managing the genetic composition of NPRC breeding colonies.
- Consultation and testing of the Parentage analysis tool, currently in use at five NPRCs.

An additional goal of the Genetics and Genomics Working Group in which [Excluded by Requester] play a significant role is to re-evaluate the panel of AIMs and genetic management markers as additional markers are identified and either modify or increase the size of the panels to be more effective in estimating proportions of mixed ancestry and kinship, respectively. The latter option was adopted because some NPRCs have initiated use of the original SNP panels. Currently, assignment of ancestry using the AIMs panel of the Working Group must assume that animals assigned to either subspecies (Indian or Chinese) with less than 15% or greater than 85% probability are unmixed; admixture cannot be detected in a rhesus monkey with 7 Indian and 1 Chinese great-grandparents, and all hybrids with 25% or 75% Chinese admixture cannot be discretely differentiated from those with 50% Chinese ancestry. This type of genetic test could, in principle, also be developed for different regional populations of baboons, African green monkeys, squirrel monkeys, titi monkeys, or any other primate species that exhibits substantial genetic variation among its natural regional populations.

The Genetics Management Services team represents a specialized group for management of genetic, pedigree, and demographic data at the CNPRC to facilitate continued efforts to supply investigators with a sufficient quantity of healthy and genetically well-characterized nonhuman primates for research. Based on the National Scientific Advisory Board recommendations, the activities of the service have been integrated into the function of Primate Services. A centralized genetics service is necessary in light of new genetics resources now available for nonhuman primates, to address relevant aspects of animal husbandry, health, production, and maintenance, and to satisfy the increasing number and complexity of research projects at the CNPRC.

Through the CNPRC IT LIMS, the Genetics Management Services team has enabled efficient access to common DNA Bank resources, vital statistics, genotype data, and population genetic analyses across the CNPRC. In conjunction with the other NPRC-based groups, these services and the IT resources will upload

genetic and genomics data to allow the cross-NPRC centralized information access and improved storage and sharing of genetic materials and information across the NPRCs. The IT resources at the CNPRC will be particularly crucial for the storage and analysis of whole genomic sequences generated in collaboration with, for example, BGI@UCDavis (see **Overview**).

APPROACH

Plans for the Next Funding Period

Core Scientist [Excluded by Requester] leads the Molecular Anthropology Laboratory located on the main UC Davis campus [Excluded by Requester] a population geneticist who trained under [Excluded by Requester] was hired in 2003 to bolster the overall genetic management of the CNPRC nonhuman primate colony. [Excluded by Requester] reports to the Director of the CNPRC and [Excluded by Requester] who is a member of the CNPRC Colony Management Advisory Committee. [Excluded by Requester] have been working together for almost two decades on the genetic management of the CNPRC and several other NPRC colonies and have been PI and co-PI, respectively, on two separate grants (#R24-RR005090 and #R24-RR025871). Both grants generated information and resources upon which the success of the genetics and genomics initiatives at the CNPRC was founded. Prior to the formation of the Genetic Management Services, the Molecular Anthropology Laboratory conducted genetic analyses for the purpose of genetic management for over three decades. The program initially involved paternity exclusion analysis and baseline population genetic assessments of three species of macaques housed in outdoor field corrals, including measurements of heterozygosity, kinship, and genetic subdivision. The early genetic analyses were initially performed using protein and blood group polymorphisms. In 1994, DNA variants such as STRs and mitochondrial DNA based assays replaced the protein polymorphisms as the markers of choice for the genetic testing. Based on these analyses, genetic management policies including country of origin testing, maximizing founder representation, and infant cross-fostering were developed and implemented to maintain genetic diversity within the rhesus macaque breeding groups at the CNPRC. Selective removal or redistribution of females has ensured that no matriline becomes over-represented in the breeding population. Cross-fostering of infants between breeding corrals, a technique pioneered at the CNPRC in the mid-1980s, has promoted gene flow and minimized inbreeding and genetic subdivision and has since been implemented at numerous breeding facilities throughout the U.S. Estimates of inbreeding from available field cage data demonstrate that these genetic management practices have been effective in maximizing genetic diversity. Genetic management has been employed, along with behavior, reproductive, and other colony data to facilitate the maintenance of the size and production of the conventional colony including splitting overpopulated corrals, forming new ones, and expanding the SPF and indoor colonies.

As the scope of colony genetics increases to include whole genome and target region linkage, association analyses, and the evaluation of candidate genes, novel technologies with improved analytical capabilities, database structures, algorithms for management of colony genetic data, including genome-wide bioinformatics resources, conventional genetic testing based on STRs and mitochondrial DNA, are poised to be replaced by SNPs. Despite the fact that STRs and mitochondrial DNA are still currently widely used for genetic management, particularly because of the degree of information they convey concerning an individual's profile or haplotype, or a pedigree's genetic composition or taxonomic status, these markers cannot provide a map of sufficient density to conduct whole genome association studies to map genes that influence risk of disease. SNPs are far more abundant than STRs, and therefore, more closely linked to functional genes. Additionally, their genotyping and analysis are easier to automate and interface with new bioinformatics tools. Because orthologous SNPs are neither as homoplasious as STRs, nor their transmission as gender biased as the sex-limited mitochondrial DNA, they have become the new marker of choice to address issues of genetic management.

One of the goals for the next funding period is to expand the use of the genetic management SNP panel. This panel will replace the current STR microsatellite marker panel for genetic analysis for colony management. The expansion of SNP discovery efforts and use of expanded SNP panels to accelerate candidate gene discovery and disease association studies will be expanded, as will the inventory of DNA in the CNPRC bank. The staff will facilitate the development of the nonhuman primate genetics portal for a nationalized bioinformatics resource. The caLIMS portal, under appropriate security controls, will enable efficient data acquisition and query capabilities of the CNPRC's DNA Bank, SNP and other genotype databases, results of colony-wide population genetic analyses, pathology imaging data, breeding colony management information, and behavioral data. Finally, the Genetics Management Services will assist in the design and distribution of the new

Working Group web portal-based information system with improved database structures, and algorithms for management of colony data including genetic information.

Specific Aim 1. Genetic management of the animal colonies.

Genetic management of captive bred research subjects to minimize inbreeding and genetic subdivision and retain genetic diversity is essential for sustaining the supply of nonhuman primates for biomedical research [Williams-Blangero et al., 2002]. The genetics of an individual is central to the biological response during experimentation. The inherent biological variability of colony-raised outbred rhesus macaques may increase variability and impact, for example, vaccine development, pathogenesis, and behavioral studies. Similarly, the limited numbers of wild-caught animals in conjunction with less than ideal management of these resources has resulted in inbreeding of captive populations [Excluded by Requester 1982]. This recognition has resulted in the production of animals with known genealogy and geographic origins [Excluded by Requester 2002; 2004]. With this purpose and without compromising overall production goals, colony managers can facilitate the establishment of defined pedigrees for formulating specific research objectives and also promote conservation of allele diversity within candidate genes that govern phenotypes of adaptive and biomedical significance.

Indian-derived animals predominate among the rhesus macaques at the CNPRC, representing nearly 3,800 of the total rhesus census of 5,000 animals. Chinese-Indian hybrids comprise the remainder of the rhesus colony. Thus, the genetic differences between the Chinese and Indian rhesus macaques compel genomic studies of Chinese-Indian hybrid rhesus since these synthetic hybrid populations will be included in the ~10% reduction in colony census during the next funding period (see **Colony Management and Research Services**). As a result, quantifying the degree of admixture in these animals using genetic methods and characterizing the genetic properties of hybrid populations have become areas of great importance. Furthermore, since inadvertent and unacknowledged crossing between Indian and Chinese rhesus macaques could otherwise increase in frequency among the other NPRCs [Unpublished

[Unpublished unpublished data), the intentionally mixed colony at the CNPRC provides the opportunities to study the success of methodologies to estimate levels of admixture between the two sub-species and its consequences as an invaluable tool in colony management.

The major strategies of within-colony genetic characterization and management are to:

- Establish or confirm the geographic origin of all animals.
- Work with Colony Management and Research Services to make informed decisions about maintaining overall genetic diversity while implementing a reduction in the proportion of Chinese-Indian hybrids within the breeding population.
- Equalize the representation of founding matriline and patriline to ensure that maximal genetic diversity is retained in all captive populations.
- Complete and validate pedigrees by identifying paternity and confirm maternity.
- Monitor and manage kinship and inbreeding levels to prevent accidental inbreeding and unknown relationships among animals that can bias results of experimental protocols, which typically assume experimental subjects are genetically unrelated.
- Estimate and maintain a relatively high average value of gene diversity using a panel of highly informative nuclear genetic markers.
- Minimize genetic subdivision by minimizing random genetic drift (by maximizing effective population size) and continuing the infant foster program in which newborns are exchanged between dams in each breeding group, effectively rendering the breeding colony a single random mating population.
- Advance genetic analyses of colony and/or biomedical interest (e.g., ICD and Left Ventricular Hypertrophy) to better inform about the potential genetic etiologies of these conditions.

The current panel of STRs for parentage assessment and genetic characterization of colony rhesus monkeys is a "consensus" panel of markers adopted after collaborative evaluation by the CNPRC Genetics Management Services and the Veterinary Genetics Laboratory. This panel of STRs retains the strengths of the previous panel for parentage assessment, allowing for continuity of past and future pedigree data on colony animals. In addition, the revised panel includes additional markers that are better suited for estimating specific population genetic parameters useful for "genetic management" of the CNPRC rhesus colony. Criteria for selection of the STR loci included the following: (1) a tetranucleotide motif, (2) a high level of gene diversity (to minimize allele sharing), (3) a high effective allele number (to ensure a low sampling variance in parameter estimation), and

(4) absence of linkage to other loci in the panel. More recently, in line with the efforts by the NPRC Consortium Working Group, the Genetics Management Services team is preparing for the transition from STRs to SNPs for parentage determination (pedigree construction) and genetic characterization using a panel of 24 STRs, to be replaced by the end of the calendar year by a 192 marker SNP panels comprising 96 AIMS and 96 genetic management SNPs. The Veterinary Genetics Laboratory remains responsible for the high throughput genetic testing of CNPRC animals using STRs and this data is then made available to CNPRC population geneticists for analysis to insure this primary objective of colony management is being achieved.

Specific Aim 2. Provide genetic resources to investigators.

The Genetics Management Services team employs a wide-range of genotyping, phenotyping, and haplotyping applications on different platforms (qPCR, genetic analyzer) and handles hundreds of samples on a daily basis. Services are equipped for STR analysis, single SNP typing, copy-number variation analysis [Excluded by et al., 2012], mitochondrial DNA typing and sequencing, and single specific primer (SSP)-PCR [Excluded by Requester et al., 2011; 2012]. Through the UC Davis Genome Center, the CNPRC has access to large-scale SNP typing to discover additional more informative SNPs using highly parallel sequencing of reduced-representation libraries (RRLs). The panels are run on the Fluidigm platform in single or multiple 96-well plate formats, and as such are more optimal than the Illumina platform previously used for analyzing smaller batches. Therefore, in the proposed funding period, the panels will be optimized to accommodate smaller batches of samples and employ the services of the BGI@UCDavis facility for high throughput whole genome sequencing. Assays developed are also routinely used to quantify rhesus and long-tailed-specific DNA templates more accurately using qPCR techniques [Excluded by Requester 2011], and this assay has successfully identified rhesus-long-tailed macaque hybrids from Indochina, a location from which many rhesus and long-tailed macaques imported into the U.S. originate. On a fee-for-service basis, analysis of genealogical and demographic data including kinship assessment, pedigree validation, and the management of selective breeding and development of informative pedigrees for nonhuman primates other than rhesus and long-tailed macaques can be performed.

Specific Aim 3. Manage the CNPRC DNA Bank and participate in the NPRC Consortium

The DNA Bank serves as a repository for all biological samples including DNA from CNPRC colony animals. The DNA Bank, which is managed by the Genetic Management Services staff, benefits the CNPRC by establishing a basic repository of DNA and other samples and enhancing access to these resources. Access to these samples requires a signed MTA and review and approval from the Research Advisory Committee. A mechanism for international distribution that requires CITES permits has also been instituted. One of the goals of the Genetics and Genomics Working Group is to facilitate the distribution of nonhuman primate genetic material to the biomedical research community. The NPRC Consortium Working Groups have provided the impetus to share data and information across NPRCs and in many cases with the extended nonhuman primate community. The available "Animal Locator", National DNA Bank, and Primate Pathology Image Database are examples of cross-center sharing via the NPRC Consortium Working Groups. Expanded access to external participants has resulted in a distribution of over 1,000 DNA samples.

With the work collectively performed through Specific Aims 2 and 3, there is a value added to colony management of the rhesus populations at the CNPRC and development of more robust applications of the genetic data. While the data will be used in conjunction with **Colony Management and Research Services** to make better-informed decisions related to genetic diversity within the rhesus population, the approaches, methodologies, and reagents generated will be made available to the broader NPRC and research communities. Working with the **NPRC Consortium**, information about the availability of technological advances and biological samples will be disseminated to the other NPRCs to advance initiatives strongly supported by the NIH and the Office of Research Infrastructure Programs (ORIP). **Genetic Manage Services** will work jointly with **Information Technology Services** to develop a system to track distribution of samples with a long-term metric of success of increasing use of these samples over time.

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES**PUBLICATIONS (May 1, 2010 to April 30, 2014)**

Excluded by Requester A rapid quantitative real-time PCR-based DNA quantification assay coupled with species--assignment capabilities for two hybridizing *Macaca* species. *Folia Primatol* (Basel) 82:71-80, 2011. PMID: PMC3221255

Excluded by Requester Familial aggregation of chronic diarrhea disease (CDD) in rhesus macaques (*Macaca mulatta*). *Am J Primatol* 76:262-270, 2014. PMC Journal-in-Progress

Excluded by Requester Development and validation of a SNP-based assay for inferring the genetic ancestry of rhesus macaques (*Macaca mulatta*). *Am J Primatol* (in press, a)

In Press

Excluded by Requester A simple multiplex polymerase chain reaction to determine ABO blood types of rhesus macaques (*Macaca mulatta*). *Tissue Antigens* 77:584-588, 2011. PMC Journal-in-Progress

Excluded by Requester Molecular ABO phenotyping in cynomolgus macaques using real-time quantitative PCR. *Tissue Antigens* 80:363-367, 2012. PMID: PMC3470802

Excluded by Requester Expression levels of 10 candidate genes in lung tissue of vaccinated and TB-infected cynomolgus macaques. *J Med Primatol* 42:161-164, 2013. PMC Journal-in-Progress

Excluded by Requester An empirical comparison of short tandem repeats (STRs) and single nucleotide polymorphisms (SNPs) for relatedness estimation in chinese rhesus macaques (*Macaca mulatta*). *Am J Primatol* 76:313-324, 2014. PMC Journal-in-Progress

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PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC. [Excluded by Requester]

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Excluded by Requester] of indoor animal space. The outdoor animal housing area includes [Specific Animal Location] field corrals, [Excluded by Requester] corn cribs, [Excluded by Requester] [Specific Animal Location] The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester] Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem

and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

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Excluded by Requester [redacted] Familial aggregation of chronic diarrhea disease (CDD) in rhesus macaques (*Macaca mulatta*). *Am J Primatol* 76:262-270, 2014. PMC Journal-in-Progress

Excluded by Requester [redacted]

Excluded by Requester [redacted] Development of a Chinese-Indian hybrid (Chindian) rhesus macaque colony at the California National Primate Research Center by introgression. *J Med Primatol* 38:86-96, 2009b. PMID: PMC2664393

In Press [redacted]

In Press [redacted]

Excluded by Requester [redacted] Interspecies hybridization and the stratification of nuclear genetic variation of rhesus (*Macaca mulatta*) and long-tailed macaques (*Macaca fascicularis*). *Int J Primatol* 29:1295-1311, 2008. PMID: PMC2583101

Excluded by Requester [redacted] Assessment of genetic management at three specific-pathogen-free rhesus macaque (*Macaca mulatta*) colonies. *Comp Med* 52:414-423, 2002.

Excluded by Requester [redacted] Effects of geographic origin on captive *Macaca mulatta* mitochondrial DNA variation. *Comp Med* 54:193-201, 2004.

Excluded by Requester [redacted] SIVmac pathogenesis in rhesus macaques of Chinese and Indian origin compared with primary HIV infections in humans. *AIDS* 16:1489-1496, 2002. PMC Journal-in-Progress

Excluded by Requester [redacted] Performance comparison of benchtop high-throughput sequencing platforms. *Nat Biotech* 30:434-439, 2012. PMC Journal-in-Progress

Excluded by Requester [redacted] A simple multiplex polymerase chain reaction to determine ABO blood types of rhesus macaques (*Macaca mulatta*). *Tissue Antigens* 77:584-588, 2011. PMC Journal-in-Progress

Excluded by Requester [redacted] Molecular ABO phenotyping in cynomolgus macaques using real-time quantitative PCR. *Tissue Antigens* 80:363-367, 2012. PMID: PMC3470802

Research Resources Reporter. Rhesus breeding colonies provide alternative to primate importation. NIH Bulletin II-9-11, 1978

Excluded by Requester

Expression levels of 10 candidate genes in lung tissue of vaccinated and TB-infected cynomolgus macaques. J Med Primatol 42:161-164, 2013. PMC Journal-in-Progress

Excluded by Requester

et al. (2013). An empirical comparison of short tandem repeats (STRs) and single nucleotide polymorphisms (SNPs) for relatedness estimation in chinese rhesus macaques (*Macaca mulatta*). Am J Primatol 76:313-324, 2014. PMC Journal-in-Progress

Excluded by Requester

2012. Variation in CCL3L1 copy number in rhesus macaques (*Macaca mulatta*). Comp Med 62:218-224, 2012. PMCID: PMC3364972

Excluded by Requester

Genetic management of nonhuman primates. J Med Primatol 31:1-11, 2002.

Excluded by Requester Primates of the World: Distribution, Abundance, and Conservation. Seattle: University of Washington Press, 1983.

Excluded by Requester

Distribution of macaques (*Macaca*) in China. Acta Theriologica 11:171-185, 1991.

PRIMATE SERVICES: GENETICS MANAGEMENT SERVICES

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Behavior Research Services Core

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename BRSC_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	BRSC_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	BRSC_FacilitiesOtherResources.pdf
11. Equipment	BRSC_Equipment.pdf

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

ABSTRACT

The California National Primate Research Center (CNPRC) **Behavior Research Services Core** is an efficient, low cost resource unique among the National Primate Research Centers. The Core was developed as a mechanism for experienced behavioral scientists to contribute on a recharge basis to meet investigator needs on a local to national level. Specialization in nonhuman primate behavior has long been an area of strength at the CNPRC. Three types of services are offered: (1) *standardized behavioral assessments* using protocols and equipment located at the CNPRC, (2) *cooperative training and behavior* of monkeys to facilitate research procedures using positive reinforcement techniques, and (3) *biobehavioral assessment* of animals of all ages, based upon procedures developed as part of the infant BioBehavioral Assessment (BBA) program, and comparison of investigator data with data from CNPRC's historical BBA database. In addition, off-site training and consultation services are available for studies conducted at other sites.

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

FACILITIES AND OTHER RESOURCES

Laboratories: The Behavior Research Services Core at the CNPRC comprises the laboratories of [Excluded by Requester] and contains space in the Brain, Mind and Behavior Research Unit for behavioral testing of live primates, as well as facilities for scoring behavior from videotapes generated either on- or off-site. Available space is modest, inasmuch as the majority of the behavioral assessments are done in the animals' own home cages. This is especially relevant for the Behavior and Training services. A separate testing space is available in one of the CNPRC Animal Wings for the Golub laboratory to conduct assessments outside of the home cage, such as in the [Proprietary Info] [Excluded by Requester] laboratory includes a storehouse of materials and equipment used for morphometric, physiological, and behavioral evaluation of infant to adult rhesus, including supplies for neurobehavioral assessments, gross motor observations, cognitive testing, and social interaction assessments. Dedicated animal housing and testing space is available for the BBA. [Excluded by Requester] has bench top space in the Childhood Health Building Laboratory for sample processing for BBA.

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology. See Primate Services sections for more details.

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See **Primate Services** sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and Information Technology Services provides desktop support and other related services (see other sections of the application). Staff in the Behavior Research Services Core each have desktop PCs with word processing and statistical software as well as computers running The Observer software program for scoring of videorecorded behavior. All individuals have access to the CNPRC file server for backups.

Office: Office space and administrative support is provided for the faculty and staff within the Behavior Research Services Core.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities, support services, and extensive expertise available as described in this application. Support services available on campus and at the CNPRC include a storehouse for purchase of commonly used supplies, multi-user instruments that are available on a recharge basis, and other Core laboratories offering assays and testing on a recharge basis. A shop for equipment fabrication and repair is located at the CNPRC.

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

EQUIPMENT

The following equipment is available for Standardized Behavioral Testing through the Behavior Research Services Core. Four mobile Proprietary Info (Lafayette Instruments) with the Windows-based software Proprietary Info and with touchscreen and automated reward dispensing capabilities, are available for behavior testing in the home room. These four stations were purchased through the Core. Other legacy equipment (equipment purchased by Investigators without base grant funding and available for use through the Core) includes a Bravo System (Nicolet Biomedical, Madison, Wisconsin) with dedicated PC computer that is available for brain response testing. Eight ActiTrac activity monitors (IM Systems) can be used for sleep-wake cycle assessment and general activity measures. Two small-scale Proprietary Info with test accessories for developmental and cognitive testing and a Proprietary Info test apparatus are available for rhesus testing. Custom made "puzzle boxes" and commercial puzzle mazes (Primate Products, Inc.) can be used for cognitive testing as well as enrichment purposes. Observational data can be collected on two laptop computers utilizing The Observer software (Noldus Information Technology, The Netherlands) either live or via a digital video camera.

The BBA testing protocol includes the use of all appropriate legacy equipment in Excluded by Requester laboratory to complete the testing including: Specially constructed cages for the Human Intruder, Video Playback, and Preferential Look tests; Video equipment (low-light cameras, DVD player for presenting stimuli to the animals, DVD recorder for recording animals' behavioral responses, viewing monitors (for the monkeys and for the technicians), digital mixers, and microphones); specially constructed novel objects that each contain an Actical Activity monitor; computers for recording behavior live and from videotape. In addition, equipment in the wet laboratory that is used for the BBA program includes a gamma counter, vortex, balance, pH meter, stirrers, and water baths.

The Cooperative Training and Behavior component does not utilize equipment to conduct their services.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*	
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	14,397.00	5,742.00	20,139.00
2.					Core Scientist		0.0	0.0	7,630.00	3,043.00	10,673.00	
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					30,812.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester		EFFORT	7,698.00	239.00	7,937.00
1	Core Manager	Excluded by Requester			5,674.00	3,002.00	8,676.00
2	Core Technical Support	Excluded by Requester			5,652.00	2,990.00	8,642.00
4	Total Number Other Personnel						Total Other Personnel
							25,255.00
					Total Salary, Wages and Fringe Benefits (A+B)		56,067.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,500.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,500.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	5,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	6,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	63,567.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	63,567.00	14,430.00
Total Indirect Costs			14,430.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	77,997.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BRSC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	14,829.00	6,258.00	21,087.00
2.						Core Scientist			0.0	0.0	7,859.00	3,316.00	11,175.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:											Total Senior/Key Person		32,262.00
File Name:													

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		7,929.00	246.00	8,175.00
1	Core Manager	Excluded by Requester			5,844.00	3,233.00	9,077.00
2	Core Technical Support	Excluded by			5,821.00	3,220.00	9,041.00
		Excluded by Requester					
4	Total Number Other Personnel				Total Other Personnel		26,293.00
					Total Salary, Wages and Fringe Benefits (A+B)		58,555.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,545.00
2. Foreign Travel Costs	0.00
Total Travel Cost	1,545.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	5,150.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	6,180.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	66,280.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	66,280.00	15,046.00
Total Indirect Costs			15,046.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	81,326.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BRSC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	15,274.00	6,672.00	21,946.00
2.					Core Scientist			0.0	0.0	8,095.00	3,536.00	11,631.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						33,577.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		8,167.00	260.00	8,427.00
1	Core Manager	Excluded by Requester			6,020.00	3,438.00	9,458.00
2	Core Technical Support	Excluded by Requester			5,996.00	3,425.00	9,421.00
	Excluded by Requester						
4	Total Number Other Personnel					Total Other Personnel	27,306.00
Total Salary, Wages and Fringe Benefits (A+B)							60,883.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,591.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,591.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	5,305.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	6,366.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	68,840.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	68,840.00	15,627.00
Total Indirect Costs			15,627.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	84,467.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BRSC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	15,732.00	7,077.00	22,809.00
2.					Core Scientist			0.0	0.0	8,337.00	3,750.00	12,087.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						34,896.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		8,412.00	276.00	8,688.00
1	Core Manager:				6,200.00	3,647.00	9,847.00
2	Core Technical Support	Excluded by Requester			6,176.00	3,632.00	9,808.00
		Excluded by Requester					
4	Total Number Other Personnel				Total Other Personnel		28,343.00
					Total Salary, Wages and Fringe Benefits (A+B)		63,239.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,639.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,639.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	5,464.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	6,557.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	71,435.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	71,435.00	16,216.00
Total Indirect Costs			16,216.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	87,651.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BRSC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	16,204.00	7,513.00	23,717.00
2.						Core Scientist		0.0	0.0	8,588.00	3,982.00	12,570.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						36,287.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Affiliate Scientist	Excluded by Requester	EFFORT		8,664.00	293.00	8,957.00	
1	Core Manager	Excluded by Requester			6,386.00	3,870.00	10,256.00	
2	Core Technical Support	Excluded by			6,361.00	3,855.00	10,216.00	
	Excluded by Requester							
4	Total Number Other Personnel					Total Other Personnel		29,429.00
					Total Salary, Wages and Fringe Benefits (A+B)		65,716.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,688.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,688.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	5,628.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	6,754.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	74,158.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	74,158.00	16,834.00
Total Indirect Costs			16,834.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	90,992.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BRSC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE**BUDGET JUSTIFICATION**

All funds requested in the Core are for developmental and administrative activities only. Services provided to users are fully charged to those activities based upon approved rates. Salaries recovered through Core recharge activities are dependent on actual effort on Core services. With the addition of two new Core service divisions (BioBehavioral Assessment and Cooperative Training) during the current funding period, administrative responsibilities have been reorganized as described below.

PERSONNEL

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel		Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Affiliate Scientist				
	Core Scientist				
	Core Manager				
	Technician				
	Technician				
Excluded by Requester	PhD, Core Scientist	EFFORT	months	% Effort	As Core Lead, Excluded by Requester
represents the Core within the administrative structure of the CNPRC. She attends meetings and participates in strategic initiatives to integrate the Core. Excluded by Requester will oversee the cooperative training and behavior services for the Core.					
Excluded by Requester	PhD, Affiliate Scientist	EFFORT	months	% Effort	Excluded by Requester will communicate with scientists requesting Core services and advise on the most appropriate assessments for project specific goals, supervise standardized behavioral testing, provide data quality assurance, review the literature, and attend scientific meetings relevant to the Core services to advertise the unique capabilities in the Core. Excluded by Requester supervises
in planning and executing Core management.					
Excluded by Requester	PhD, Core Scientist	EFFORT	months	% Effort	Excluded by Requester will oversee the BioBehavioral Assessment services. He will consult with investigators in the initial planning stages, as well as at the point when data are delivered, to aid in interpretation of the results.
Excluded by Requester	Core Manager	EFFORT	months	% Effort	The Core Manager will track and manage Core billing and budget expenditures and establish and maintain the Client Tracking database. She will identify and direct requests for Core Services to the appropriate leads for these services. Excluded by Requester prepares and distributes information about Core services within and outside the CNPRC, and aids with grant submissions that include budgetary information related to Core services. In managing the Standardized Behavioral Assessment services, she will write, update, and maintain working protocols, CNPRC standard operating procedures (SOPs), and Institutional Animal Care and Use Committee (IACUC) protocols for approval for all tests; train investigators, students assistants, and postdoctoral fellows in the conduct of these assessments; establish and maintain a normative database with control data from the tests for comparison to experimental data; establish and maintain a website with information on the testing and other services offered; maintain health and environmental surveillance for all animals undergoing testing through the Core laboratory logs; write work orders relevant to behavioral testing; prepare and update university recharge documents and billing for Core services; prepare budget estimates and monitor budgets for requested services; and prepare power estimates and statistical analysis strategies for use with the tests.
Excluded by Requester	Cooperative Training Technician	EFFORT	months	% Effort	Excluded by Requester will manage all investigator requests for cooperative animal training including providing quotes, conducting entrance interviews, communication with the research group, staff training, animal training, billing, and follow-up. Ms.

Excluded by
Requester

will be responsible for the actual animal training and manage day-to-day activities related to animal training for research procedures.

Excluded by
Requester**Biobehavioral Assessment Technician**

EFFORT

months

%
EffortExcluded by
Requester

is the principal technician for [Excluded by] BioBehavioral Assessment program. Her Core-related duties will be to provide budgets to interested investigators, to schedule the testing of investigator animals, and to answer questions pertaining to the conduct of the assessments.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are listed in the **Facilities Improvement** section.

During the first year of the proposed funding period, Core personnel will consult with prospective users to identify the most flexible and responsive approach to establishing the eye tracking service. The Core will then develop appropriate protocols for offering eye tracking as a service on-site to interested investigators.

Excluded by
Requester

[Excluded by] an experienced nonhuman primate eye-tracking researcher, will consult with the Core to establish this service (see letter of support). In Year 2, planning will be at the point that equipment can be purchased. This will allow the Core to take advantage of any technical updates that occur close to the time of final implementation of the Core service.

TRAVEL

\$1,500 is requested to attend one professional meeting annually to advertise the Core services to the greater research community. Core Leaders and/or [Excluded by] travel to the American Society of Primatologists (ASP) annual meeting, or another relevant scientific society meeting. ASP is a large society of primate researchers and is a potential source of useful information regarding new techniques and tests for behavioral research. Scientific meetings are also an opportunity to network with fellow researchers and publicize the goals of the Behavior Research Services Core as well as present results from Core projects.

Excluded by
Requester**SUPPLIES**

\$5,000 is requested for general Core supplies for development of new testing regimens, including disposable items such as food rewards, purchase of materials for fabrication of new testing setups, and repair of existing testing equipment.

OTHER EXPENSES

\$1,000 is requested for manuscript preparation and submission to address new testing techniques.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		167,834.00
Section B, Other Personnel		136,626.00
Total Number Other Personnel	20	
Total Salary, Wages and Fringe Benefits (A+B)		304,460.00
Section C, Equipment		0.00
Section D, Travel		7,963.00
1. Domestic	7,963.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		31,857.00
1. Materials and Supplies	26,547.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		344,280.00
Section H, Indirect Costs		78,153.00
Section I, Total Direct and Indirect Costs (G + H)		422,433.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	40,000.00	Services
2	42,200.00	Services
3	44,521.00	Services
4	46,970.00	Services
5	49,553.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

BRSC_SpecificAims.pdf

3. Research Strategy*

BRSC_ResearchStrategy.pdf

4. Progress Report Publication List

BRSC_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

BRSC_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

BRSC_Letters.pdf

13. Resource Sharing Plan(s)

BRSC_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

SPECIFIC AIMS

The Behavior Research Services Core leverages the technical and research experience of three CNPRC behavioral researchers to provide rapid, economical behavior research services to investigators at the CNPRC and other institutions. Although nonhuman primate behavior continues to be an important specialty for translational research in areas including psychiatric disease, neurodegenerative disease, and childhood behavior disorders, a nonhuman primate behavior Core is not currently available at any of the other National Primate Research Centers (NPRCs). Services are currently offered on-site in three areas: (1) *standardized behavioral assessments* to evaluate a range of brain functions, (2) *cooperative training and behavior* of monkeys to facilitate research procedures using positive reinforcement techniques, and (3) *biobehavioral assessment* of animals of all ages, based upon procedures developed as part of the infant BioBehavioral Assessment (BBA) program and optimized by comparison to historical databases. In addition, off-site training and consultation services are available for studies conducted at other locations. The Specific Aims have been developed to strengthen the services offered and increase awareness of potential clients.

Specific Aim 1. Use contemporary state-of-the-art science to develop and enhance the range of services: testing, observation, training, and consultation.

Plan. Behavioral assessments and training methods continue to evolve in the literature to better serve translational needs and links to underlying brain circuits. Automated eye tracking for assessment of cognitive and social/emotional responsiveness and information processing is a major technical tool proposed for the proposed funding period. Additional services will be added to the Core based on procedures currently under development by Core and Affiliate Scientists.

Specific Aim 2. Increase the number of service clients at the regional and national levels by enhancing the client interface.

Plan. The approaches proposed include the establishment of a client tracking database, enhancing presence in online social networking for scientists (LinkedIn, Research Gate), increasing poster displays in high traffic areas at national meetings, and offering workshops on cooperative training methodology.

Specific Aim 3. Share unique CNPRC behavioral data to support nonhuman primate research, management, and care.

Plan. Databases compiled by [Excluded by Requester] with non-P51 base grant funding are used in their respective basic and collaborative research within and outside the CNPRC. These data can also be used independently by human clinical researchers with a wide variety of interests to test specific population-based hypotheses, and by veterinary researchers working with other species to extend evolutionary and comparative findings. Based on ongoing experiences within the scientific community, the Core in collaboration with the Information Technology Services will develop procedures specifically tailored for behavioral data to share these resources.

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

RESEARCH STRATEGY

INTRODUCTION

The California National Primate Research Center (CNPRC) Behavior Research Services Core is an efficient, low cost resource unique among the National Primate Research Centers (NPRCs). The Core was originally developed at the suggestion of the CNPRC National Scientific Advisory Board as a mechanism for experienced behavioral scientists to contribute on a recharge basis to investigations conducted at the CNPRC and other institutions on a regional to national level. The Core includes Affiliate Scientist [Excluded by Requester] who has conducted NIH-funded research at the CNPRC for over 30 years (Figure 1). Her research program assesses the effects of drugs, toxicants, and nutrition on brain development and uses structured, standardized behavioral assessments that directly parallel psychological and behavioral tests used in human infants and children. These tests were the original services offered by the Core, and were supplemented with services developed by [Excluded by Requester] during the current funding period (Table 1). All services are appropriate for rhesus and other macaque species.

Three types of services are offered based on the specialization of the three participating scientists: (1) *standardized behavioral assessments*, (2) *cooperative training and behavior*, (3) *biobehavioral assessment*. The sources of support for the Behavior Research Services Core in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Figure 1. Organizational Chart: Behavior Research Services Core

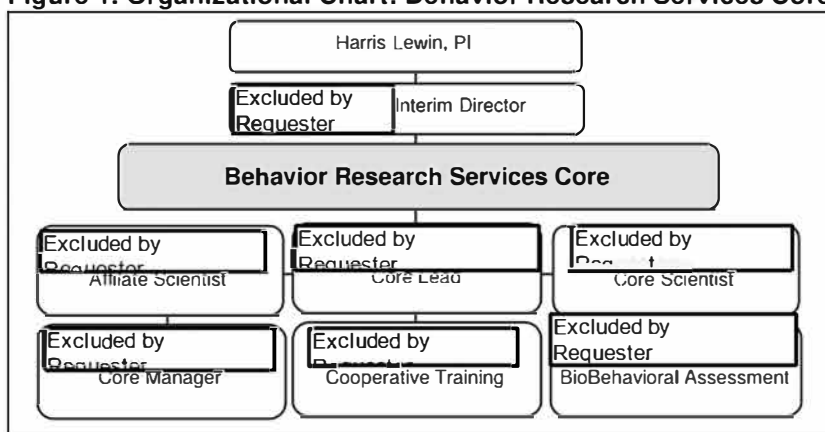


Table 1. Behavior Research Services Core Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
[Excluded by Requester]	Department of Population Health and Reproduction, School of Veterinary Medicine	Core Scientist, Lead
	Department of Environmental Toxicology, College of Agricultural and Environmental Sciences	Affiliate Scientist
	Department of Psychology, College of Letters and Science	Core Scientist
	CNPRC	Core Manager
	CNPRC	Technician
	CNPRC	Technician

Table 2. Support for the Behavior Research Services Core

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$60,930	\$63,567
Program Income from P51	\$20,000	\$40,000
Other Sources	\$0	\$0
TOTAL	\$80,930	\$103,567

Response to Summary Statement.

reviewers' comments

reviewers' comments

Progress and Major Accomplishments: Contributions to the CNPRC Mission

Two new services were successfully added to the Core during the current funding period, the BBA under the leadership of [Excluded by Requester] and Cooperative Training and Behavior under the leadership of [Excluded by Requester]. Laboratory personnel and the Core Manager worked with the CNPRC Business Office to establish recharge rates for both services. Rates for the BBA service were complex to calculate, inasmuch as the full BBA program involves not only labor, but supplies, as well as recharge activity through other CNPRC and campus services and Cores. A rate was developed to reflect a comprehensive per animal cost for the 25-hour assessment period, with different rates for animals from various housing situations with differing labor and supplies costs (e.g., nursery housing versus field cage housing, Specific Pathogen Free, SPF, versus conventional animals). Quotes can now easily be provided to investigators based on the number of animals on the study for BBA testing, as well as estimates for associated work order costs and optional assay costs. One study that assessed 14 infants for a Project Scientist in the **Brain, Mind, and Behavior Research Unit** (Dr. [Excluded by Requester]) has been completed, and estimates have been provided for five grant proposals involving BBA testing.

The Cooperative Training and Behavior team has established recharge rates for services including Target Training, training for entry into the "Box Chair" (a specialized restraint chair used for behavioral testing), Jump Box Training, Spotting for Capture in outdoor field corrals, and Group Formations. Rates are based on hourly labor rates for personnel conducting the training. During the current funding period, and following establishment of recharge rates, three CNPRC investigators used these services to facilitate research protocols including spotting services for relocation of animals from field corrals. Two additional investigators plan to use Cooperative Training and Behavior services in the upcoming year. For one study, up to 30 animals will be trained for voluntary blood collection, and a second study plans to use 8-24 animals that will need box chair training and desensitization to a nebulizer. Spotting services will also be used during the upcoming BBA testing period.

Four new [Proprietary Info] stations were purchased with P51 support during the current funding period to replace outdated and poorly functioning legacy systems. The new systems will allow the Core to respond to requests for automated cognitive testing across the lifespan with reliable and modern technology. Individual tasks within the testing software are more customizable than the old system; this provides flexibility in testing parameters and allows tailoring of tests to project specific goals. Testing programs and protocols were set-up to mimic old system parameters, an important component for continuity of testing for certain studies. Data processing systems were set-up to summarize and transfer data electronically from the [Proprietary Info] to Excel. Paper recording of results, and subsequent data entry by hand, were eliminated with the new system.

Twelve infants were evaluated from birth through 4 months of age for CNPRC Core Scientist [Excluded by Requester] for a study on the efficacy of novel surrogates for nursery-reared animals. A neurobehavioral assessment of reflex and basic development was conducted at four time points; visual novelty preference, an early test of cognitive development, was assessed; and gross motor maturation was measured in weekly observation sessions in a custom cage for 14 weeks. These animals were also assessed in the BBA Program at 3-4 months of age.

A study evaluating the effects on offspring of binge drinking of alcohol prior to establishing pregnancy was conducted for CNPRC Core Scientist [Excluded by Requester]. Ten infants were assessed from the day of birth through 4 months of age on three standardized assessments: neurobehavioral test battery, visual novelty preference, and mother-infant interaction. For mother-infant interaction, five 30-minute videos were recorded for each pair, and the videos were scored using The Observer software for the number and quality of reunions, separations and interactions. All behavioral data were analyzed and interpreted by [Excluded by Requester]. Results were presented at the Neurobehavioral Teratology Society Annual Meeting and also recently published [Excluded by Requester] et al., 2014].

[Excluded by Requester] UC San Diego, utilized the services of the Core for nine months to conduct three-to-four day a week [Proprietary Info] of adult monkeys. This testing was a continuation of services from the previous project period, where the Core conducted 2+ years of behavioral testing for the study (not shown in Table 3).

Off-site training and consultation services were provided to two contract research organizations (CROs). Dr. [Excluded by Requester] provided consultation on study design and behavioral testing methods and protocols for SNBL, Inc. and MPI Research. [Excluded by Requester] provided on-site training for a one-week period for MPI Research staff at a

primate breeding facility in South Carolina. This allowed hands-on training on a neurobehavioral assessment in newborn monkeys for MPI staff unfamiliar with behavioral testing methodology.

A variety of NIH-targeted research areas were represented in client funded research projects: substance abuse, toxicology, neurodegenerative disease, child and maternal health, and brain circuit analysis. Clients included CNPRC investigators, other UC Davis investigators, academic scientists from national institutions outside of UC Davis including the UC system, and commercial CROs (Table 4). In regards to the latter, there is a rise in the development of biological therapeutics with immune-based targeting whose safety and efficacy cannot be tested in rodent models. Manufacture of biological pharmaceuticals for neurodegenerative diseases will increasingly turn to nonhuman primates for preclinical work. The Core, which includes a board-certified toxicologist Excluded by Requester is prepared to support and conduct these types of studies.

Table 4. Number and Affiliation of Users

Type of Service	Affiliation of User	# Users	# Labor Hours
Standardized Behavioral Assessments	CNPRC	3	281
	CRO	2	62
Infant Biobehavioral Assessment	CNPRC	1	100
Behavior and Training	CNPRC	3	52

CRO=Contract Research Organization

The Behavior Research Services Core was featured as a resource in over 11 research proposals and grant submissions (May 1, 2010 to April 30, 2014; not funded or pending review). Other investigators have discussed their study needs with Behavior Research Services Core personnel. The proposed client database will supply more material regarding the Behavior Research Services Core activities that precede funded projects.

A distinguishing feature of the Core is that the assays are performed on live animals. This greatly restricts the physical strategy for providing services off-site. The practice of shipping biological samples for assays, commonly used in other Cores, is not relevant. One initial approach to addressing this was to offer behavioral scoring of videotapes so that behavioral assessment could be provided to investigators off-site. A second approach is to provide consultation and training with off-site visits of Core personnel. A third approach, proposed here, is to provide access to population-based behavioral data already collected through the research programs of Excluded by Requester. With this range of approaches the Core hopes to be able to provide a positive response to requests from anywhere in the nation to support nonhuman primate behavioral research.

INNOVATION

Unique Services and Research Opportunities Provided to the Nonhuman Primate Research Community

Outsourcing to Core facilities continues to be an important component of contemporary research that allows rapid expansion and enhanced productivity of research programs. Most academic and commercial research organizations have rodent behavior service cores. However, the Behavior Research Services Core at the CNPRC is the only such Service Core for nonhuman primates. The Wisconsin NPRC has an infant nursery with a strong behavior focus and several NPRCs have Neuroscience Cores but none offer a range of behavior assessment and training services as proposed here. Similarly, CROs specializing in nonhuman primates (SNBL, MPI, Covance, Charles River) have only very limited behavioral testing facilities and no in-house professional expertise. Translational nonhuman primate research based on naturally occurring, functionally parallel gene polymorphisms is a rapidly advancing area. As investigators seek to ground their brain disease models in functional phenotypes and endophenotypes, the Core will be able to provide domain-specific assessments that parallel human assessments through an extensive list of standardized tests. These same functional phenotypes can serve as the basis for therapeutic intervention research. No other NPRC or commercial laboratory can offer genetic phenotyping services at the behavioral level for nonhuman primates.

Because of their range of collaborative experiences, Behavior Research Services Core Scientists are able to transfer to the Core not only behavioral methodology but also effective techniques for interacting with funding agencies, preventing inefficient and ineffective experiments, responding to grant preparation requests, and supporting clients through the publication process or submission of preclinical research reports. Because Core and Affiliate Scientists participate in basic research, translational research, and applied research, the services

described here target the needs of a broad client range and provide competitive and state-of-the-art methodology.

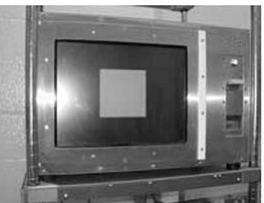



APPROACH



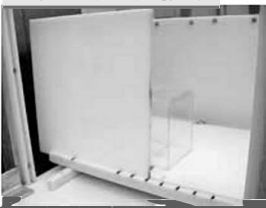
Plans for the Next Funding Period

Specific Aim 1. Use contemporary state-of-the-art science to develop and enhance the range of services: testing, observation, training, and consultation.

Tables 5 and 6 show currently available Core services with projected additions and updates for the next funding period. Additions are based on assessments and procedures currently under development that will be formalized for offering through the Core. Tests and equipment listed in **bolded italics** are **new services**.

Table 5. Standardized Behavioral Assessments. New services are shown in bolded italics.

Testing Domain	Specific Tests	Description
Cognitive Testing 	Proprietary Info Testing with Proprietary Info Proprietary Info (12 months+)	Touchscreen system with automatic reward dispenser assesses cognitive function including tests of memory and short-term learning (Delayed (Non-) Match to Sample, <i>Paired-Associates Learning</i>), attention (Continuous Performance Task, Fixed Interval), visual discrimination and set shifting (<i>Intra-Extra Dimensional Shift</i>), and spatial memory (Self-Ordered Spatial Search). Test platform has been used to assess cognitive function in human adults and children.
	 Novelty Preference (1-2 months)	Based on the human version of the Proprietary Info of Infant Intelligence, looking frequencies and durations are measured using abstract black and white pairs of stimuli.
	Object Permanence, A-Not-B Task (1-4 months)	The ability to recognize the existence of a hidden object or reward indicates maturation of the dopamine system. Perseverative error in the A-Not-B task, where a reward previously hidden under "A" is hidden under "B", but "A" is still chosen, is another assessment of cognitive development. Tasks are conducted in the Proprietary Info
	 Discrimination Tasks (8 months+)	Many tasks conducted in the Proprietary Info assess learning, memory, and visual discrimination (Reversal Learning, Concurrent Object Discrimination, Delayed (Non) Match to Sample, Hamilton Search, Parallel Strings).
	 Cognitive puzzles (12 months+)	A self-initiated home cage puzzle series involves pushing a food reward along pathways of varying complexity to a retrieval area and opening latches and clasps on a box containing food rewards.
	<i>Eye Tracking</i> (various ages)	A noninvasive eye tracking system commonly used in humans assesses cognitive function through detailed measurement of looking durations, frequencies and patterns to various visual stimuli. This system may also be used for attention and social/emotional responsiveness to visual stimuli.
Neurodevelopment	Neurobehavioral Test Battery (1-14 days)	Modeled after the Proprietary Info of Neonatal Behavior in humans, this test assesses age-appropriate muscle tone,

		reflexes, and simple elicited behavior patterns.
	Auditory Brainstem Response	A noninvasive, standardized assessment of the event-related potential (ERP) to an auditory stimulus.
<i>Motor Development</i> 	Gross Motor Development (1-14 weeks)	A specially designed cage evaluates maturation of posture and spontaneous motor patterns such as walking, climbing and manual dexterity.
	Reach and Retrieve, Fine Motor (1-3 months)	The ability to reach, grasp and retrieve depends on the myelination of corticospinal pathways, as does the development of the precision grasp (finger-thumb opposition).
<i>General Development</i>	Mother-Infant Interaction (3-4 months)	Mother-infant pairs are videorecorded in their home cage to <u>assess the maturational level</u> of the relationship by scoring, using Proprietary Info program , the number of separations and reunions with qualifiers for who initiated the behavior and the outcome of the interaction, along with the amount of synchronous behavior.
	Activity Monitoring (various ages)	A small actimeter is adapted for use in monkeys to evaluate the rest-activity cycle, hyper/hypo activity, and abnormal patterns of "naps" or waking.
	Heart Rate Variability (1-7 days)	A small, wireless heart monitor is attached via stick-on electrodes to monitor ECG, heart rate, and heart rate variability in neonates housed in the nursery.
<i>Affective Behavior</i> 	Impulsivity (various ages)	The ability to <u>inhibit a response</u> in order to receive a food reward is measured in this Proprietary Info test.
	Mood/Temperament Scoring (various ages)	Temperament and behavior during Proprietary Info sessions are rated in categories including object orientation, distractibility, activity, irritability.
<i>Social Behavior</i>	Social Dyad Observations (various ages)	Social partners are observed for the quality and quantity of interactions using Proprietary Info program . Incidences of play, affiliative behavior, aggression, grooming, and nonsocial interactions are recorded.
	Social Buffering (various ages)	The ability of a social partner to mediate behavior and stress response (cortisol) during an unfamiliar or slightly stressful situation is <u>assessed in this</u> task. Behavior is videorecorded for later scoring Proprietary Info and blood samples collected during sessions with and without the social partner.

All of the supplies and equipment needed for the tests listed above are currently available for Core use except for the eye tracking system. Funds are noted in the **Facilities Improvement** section for the purchase of the **Proprietary Info** package of monitor, eye tracker, and software. Eye tracking offers a noninvasive, data rich technique for assessing brain function that is widely used in human research and marketing. It has been enthusiastically adopted by nonhuman primate investigators and will be developed as a service with consultation from **Excluded by Requester** who has used this technique for over 5 years at the CNPRC (see letter of support). Adaptation to the eye tracking equipment will be facilitated by training protocols from the Cooperative Training staff (see **Behavior Management Services**).

Table 6 describes existing and proposed services of the Cooperative Training and Behavior team. Cooperative Training is an expanded version of the PRT previously established by [Excluded by Requester] group. It is a flexible approach to shaping, or training successive approximations, of a desired behavior. The Social Group Services are based on [Excluded by Requester] comprehensive assessment of outdoor-housed social groups in connection with her research program. This information can be used for "spotting" or identification of specific animals in large groups for capture with minimal disturbance. Social group formation for experiments conducted in a social context can benefit from the extensive information on social interaction available from Dr. [Excluded by Requester] observational databases on field cage groups.

Table 6. Cooperative Training and Behavior Services



Service Area	Specific Applications	Description
Cooperative Training		Cooperative Training is a system of animal training in which multiple operant training methods are used to encourage an animal's voluntary participation in the training session.
	Target Training	Movement of a body part to a specific location. Can include whole body movement, body part movement, or mobility training .
	Restraint Training	Voluntary movement into the box chair and presentation of head and neck for restraint. Can facilitate a wide variety of procedures with alert animals.
	Biological Sample Collection	Collection of biological samples including, but not limited to, vaginal swabs and blood collection from the cephalic vein.
	Treatment Administration	Oral, injectable, and intranasal dosing. Intranasal dosing may include nebulizer training .
	Group Separation Training	Voluntary separation from the group for treatment in home cage or jump box relocation.
	Contra-aggression Training	Case specific training to reduce human-directed aggression thereby facilitating experimental procedures.
Social Group Behavior Services	Spotting Services	Visual identification of an individual in a group setting, such as in a field cage or corn-crib.
	Social Group Formations	Selection services using colony records and/or the social histories of individual animals, and behavioral monitoring of the newly formed group to ensure social cohesion.

Table 7 describes the BBA procedure and acquired data.

Table 7. Biobehavioral Assessment (BBA) Services

Testing Domain	Specific Tests/Factors
Structured Assessments	Preferential Look, Video Playback, Human Intruder, Novel Objects
Observational Assessments	Holding Cage Observations, Temperament Rating
Stress Response Profile	Blood sampling, with dexamethasone and ACTH injections, for cortisol response
Principal Measures	Factor analysis employed to identify underlying latent traits for the Holding Cage, Human Intruder, and Temperament Rating data. These analyses are available through the <i>BBA historical database</i> .
	Holding Cage: Two factors identified: Activity and Emotionality. Factor scores calculated separately for Day 1 (response to initial separation from cage-mates and relocation to unfamiliar environment) and Day 2 (adaption to new situation).
	Human Intruder: Animals' responses across the four conditions highly correlated, so data were combined for the factor analyses. Four factors were identified: Activity, Emotionality, Aggression, and Displacement/Anxiety.
	Temperament Ratings: Four factors were found: Vigilant, Gentle, Confident, and Nervous.

The BBA is a program developed by [Excluded by Requester] with NIH R24 funding. BBA of 3-4 month-old infants in the general colony contributes to colony health and management goals. BBA of infants assigned to individual research projects is conducted through collaboration to meet the goals of those projects, and the BBA has also been extended to adults through collaboration. By offering BBA as a Core service, it becomes available to any interested investigator through the recharge mechanism. BBA is an example of a CNPRC resource that is utilized within the CNPRC and by investigators within and outside of UC Davis.

Metrics. The Core will add the new services listed in Tables 5-7.

Alternative Strategies. Interest from potential clients may result in other behavioral protocols used by Core investigators in their own research programs that will be transitioned to recharge services.

Specific Aim 2. Increase the number of service clients at the regional and national levels by enhancing the client interface.

Initiatives to enhance outreach are described below.

Client tracking database. The Core proposes to establish an Access database to track clients with interest in Core services, including dates of initial contact, type of project and testing areas of interest, affiliation of client, follow-up timeline, and outcome of contact (e.g., information only, generation of budget, grant proposal, funded project). This will allow the Core to evaluate interest and identify how clients have heard about the Core services, as well as to provide timely follow-up on initial inquiries. A central database will also better integrate the services within the Core. Due to the specific expertise within each group with regards to services provided and the appropriateness of those services for specific project goals, each group provides quotes (using a standardized Core quote form) and subsequent scheduling and conduct of testing. All billing is submitted to the Core Manager monthly for compilation before submission to the Business Office. A database will allow all three components of the Core to document contact with potential clients, provide follow-up on inquiries, and track the outcome of interest in Core services.

Scientific Social Networking. Behavior Research Services Core scientists and staff will expand profiles on LinkedIn and ResearchGate to include the Behavior Research Services Core as an aspect of their profile and nonhuman primate behavior as an area of expertise. They will obtain and provide recommendations for expertise in nonhuman primate behavior methodology on these sites and participate in online forums around this area. These activities will expand the online presence of the Core and professional networks.

Advertising to External Scientists. The CNPRC website has been updated with new information and research opportunities specific to the Behavior Research Services Core and direct contact information for the Core Manager. The Core has adapted a poster for advertising use and brochures that are brought to national meetings for display.

Cooperative Training Workshops. These workshops are currently offered to technicians in Primate Services and will be advertised annually on the CNPRC website for attendance by external investigators with interest in learning more about the Core services. These workshops review the theory and history behind behavioral modification as well as application to common needs of investigators.

Metrics. Success of this aim will be reflected in a year-to-year increase in clients contacting the Core and in projects resulting in recharge

Alternative Strategies. UC Davis is currently increasing the student body and faculty size and there is institutional commitment to new Core Scientists in the Scientific Research Units (see **Overview**). This will present opportunities to interface with newly recruited faculty about use of the Core.

Specific Aim 3. Share unique CNPRC behavioral data to support nonhuman primate research, management, and care.

Two sets of data compiled by [Excluded by Requester] with non-P51 base grant funding are shown in Table 8. These data are used in [Excluded by Requester] basic and collaborative research within and

outside the CNPRC. For example, [Excluded by Requester] has used the hematology data from the BBA in a publication on environmental influences on infant hematology [Excluded by Requester] 2013]. Combined use of the data is illustrated in several joint publications [Excluded by Requester] 2013; [Excluded by Requester] 2011; [Excluded by Requester] 2011]. The data can also be used independently by researchers with a wide variety of interests to test specific population-based hypotheses, and by veterinary researchers working with other species to extend evolutionary and comparative findings.

Table 8. Description of Behavioral Data for Proposed Core-Based Sharing

Data Characteristics	Group Housing Social Observations Data	BioBehavioral Assessment Data
Data acquisition	Data collection software: [Proprietary Info] Data collection hardware: hand held devices [Proprietary Info]	Data collection software: [Proprietary Info] Data collection hardware: Laptop and desktop computers [Proprietary Info]
Data storage	Program: [Proprietary Info] Site: CNPRC server [Proprietary Info]	Program: [Proprietary Info] Site: Computer, with backups on three different servers
Data object (number)	Dyadic interaction (>100,000)	Animal assessed by 5 digit ID (>3600)
Classifiers	Age, sex, cage of origin, MAOA, and 5HTTLPR genotype, pedigree, degree of Chinese ancestry, body condition scoring	Age, sex, cage of origin, MAOA and 5HTTLPR genotype, pedigree, degree of Chinese ancestry, weight, rearing condition
Metadata	Date:time, cage location, weather, observer, observer reliabilities	Date, cage of origin, SPF status, dam reproductive history
Variables/Summary Variables (number)	~115	12 factor analyzed scales (behavioral responsiveness (4), temperament (4), responses to human intruder challenge (4)); 21 variables from CBCs and flow cytometry; 4 plasma cortisol

Resource sharing, cross-site composite databases, and interactive online databases are a cutting-edge feature of contemporary science. While the Core renewal is very modest, larger projects provide framework for establishing this shared resource through the Core with the following sequence of goals during the next funding period:

1. Identification of portions of the data appropriate for sharing and the mechanism(s) required.
2. Development of materials describing the data including codebooks and data
3. Development of a [Proprietary Info] tool for screening and consultation with clients on feasibility and value of a proposed project using the data.
4. Formatting of confidentiality and acknowledgment agreements through the UC Davis campus Technology Transfer services (see **Administration Overview**)
5. Establishing procedures for the CNPRC Research Advisory Committee consultation.
6. Developing materials describing the resource for public distribution and posting as pdfs on the website.

With this resource-sharing project, the CNPRC will join nonhuman primate field sites and other nonhuman primate research facilities that are beginning to accumulate and share population-based behavioral data as well as health and genetics data.

Metrics. Success of this aim will be demonstrated by the final version of the data sharing materials available on the CNPRC website.

Alternative Strategies. Portions of the BBA data may be incorporated into other population databases at the CNPRC.

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

CORE PUBLICATIONS (May 1, 2010 to April 30, 2014)

- Excluded by Requester Policing in nonhuman primates: partial interventions serve a prosocial conflict management function in rhesus macaques. PLoS One 8:e77369. doi:10.1371/journal.pone.0077369, 2013. PMID: PMC3805604
- Excluded by Requester Behavioral effects of prenatal ketamine exposure in rhesus macaques are dependent on MAOA genotype. Exp Clin Psychopharmacol 20:173-180, 2012. PMID: PMC3481859
- Excluded by Requester Nervous temperament in infant monkeys is associated with reduced sensitivity of leukocytes to cortisol's influence on trafficking. Brain Behav Immun 25:151-159, 2011. PMID: PMC2991489
- Excluded by Requester Prenatal iron deficiency and monoamine oxidase A (MAOA) polymorphisms: combined risk for later cognitive performance in rhesus monkeys. Genes and Nutr 9:381, doi: 10.1007/s12263-013-0381-3, 2014. PMID: PMC3968295
- Excluded by Requester Influence of prenatal iron deficiency and MAOA genotype on response to social challenge in rhesus monkey infants. Genes Brain Behavior 11:278-290. PMID: PMC3511847.
- Excluded by Requester Binge drinking prior to pregnancy detection in a nonhuman primate: Behavioral evaluation of offspring. Alcohol Clin Exp Res 38:551-556, 2014. PMC Journal-in-Progress
- Excluded by Requester Latent variables affecting behavioral response to the human intruder test in infant rhesus monkeys (*Macaca mulatta*). Am J Primatol 75:314-323, 2013. PMID: PMC3581725
- Excluded by Requester The effects of predictability in daily husbandry routines on captive rhesus macaques (*Macaca mulatta*). Appl Anim Behav Sci 143:117-127, 2013. PMID: PMC3578712
- Excluded by Requester Degree of Chinese ancestry affects behavioral characteristics of infant rhesus monkeys (*Macaca mulatta*). J Med Primatol 42:20-27, 2013. PMID: PMC3632404
- Excluded by Requester Enhancing genotyping of MAOA-LPR and 5-HTT-LPR in rhesus macaques (*Macaca mulatta*). J Med Primatol 41:407-411, 2012. PMID: PMC3492537
- Excluded by Requester Object discrimination and reversal learning in infant and juvenile non-human primates in a non-clinical laboratory. J Med Primatol 42:147-157, 2013. PMC Journal-in-Progress Data for this publication was obtained through Core services

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VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, and the IACUC.

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- 1. Proposed Use of the Animals.** Male and female rhesus monkeys (*Macaca mulatta*) from newborn to aged will be used for Behavior Research Services Core (assessments. The exact age, sex, number, and specific assessment(s) will be determined by the research study utilizing the services of the Core. CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a face mask; full coverage eye goggles or face shields; and gloves. All work conducted is according to the Primate Center employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures, and related facility and laboratory training documents required for employment.

Many of the Standardized Behavioral Assessments employ the use of reward-based testing following training and adaptation periods. [Proprietary Info] takes place in the animal's home cage where a computer cart is rolled to the front of the cage for test sessions. A touchscreen monitor presents various cognitive tests, and rewards are automatically dispensed for correct responses. A series of puzzle boxes and mazes are also administered in the home cage and require the animal to manipulate latches and locks to retrieve food rewards or to push food rewards along pathways to a retrieval area. Tasks in the [Proprietary Info] involve transfer to a test room in a custom designed transfer cage that also serves as the test cage. Tasks are presented in a trial-based fashion on a test board usually requiring displacement or manipulation of objects for a food reward.

Proprietary Info

Other non-invasive standardized tests include a neurobehavioral test battery, modeled after human infant neurobehavioral assessments, for assessment of age-appropriate reflexes, muscle tone and simple elicited behavior patterns; an observation cage constructed of semi-rigid mesh netting for evaluation of infant motor development; activity monitoring through the use of a small actimeter worn on a harness; heart rate variability in neonates via a small, wireless heart monitor; assessment of mother-infant interaction and social dyad interaction through home cage observations; and visual novelty preference where infants are hand-held and swaddled in a soft cloth for recording of frequency and duration of looking at abstract black and white pairs of stimuli. The social buffering assessment evaluates the ability of a social partner to mitigate the effects of a stressful situation (transfer to an unfamiliar room, alone or with the partner). Sessions are recorded for later scoring of behavior, and following each session an armpull blood sample is collected for cortisol measurement. For the noninvasive Auditory Brainstem Response (ABR) measurements, animals are sedated with ketamine (5-10 mg/kg IM), and as needed dexmedetomidine (0.04 mg/kg IM; followed by atipamezole for reversal), small needle electrodes are placed subdermally, and an auditory stimulus is presented through a headphone in the ear. Event related potentials to the auditory stimulus are recorded through a software program.

Cooperative Training and Behavior Management Services utilizes the concept of cooperative training and shaping ("progressive approximations") through positive reinforcement techniques to elicit a desired behavior. All training is conducted in a step-wise fashion, with each part of the procedure established and reinforced before moving to the next step. Depending on the project, animals may be trained in their home cages or in other restraint devices. Alternately, the training may be to adapt animals to a restraint device. Hand-held target wands may be used to cue animals to desired positions, with reinforcement administered

through the use of a clicker and/or food treat. For spotting services in large social groups, animals will be identified by a trained observer and captured according to CNPRC standard operating procedures.

For the Biobehavioral Assessment, three- to four-month old monkeys (or other ages, depending on the research project) will be removed from their living cages and separated from their mothers (and/or peers) for a 25-hour period, and will be transferred to a testing suite that includes a housing area and a testing area. During the 25-hour period, animals will be individually housed and given a towel and stuffed toy to cling to. Each animal will be observed for a 5-minute period, and behavior recorded, while in its temporary living cage (holding cage observations). On three occasions, each animal will be moved between the holding cage and a specially constructed test cage located in the testing area for the following tests: (a) a preferential look test, in which animals will view pre-recorded pictures of unfamiliar rhesus monkeys; (b) a video playback test, in which animals will view a pre-recorded videotape of an unfamiliar adult male alternating aggressive and nonsocial behavior; and (c) a human intruder test, in which an adult human presents her profile and frontal view of her face from both a distant (36") or close (12-18") location. Animals will also have blood samples drawn on four occasions during this period while under brief physical restraint, and will receive single injections of dexamethasone (500 µg/kg) and adrenocorticotrophic hormone (ACTH) (2.5 IU). At the end of the 25-hour testing period, animals will be returned to their mothers and then to their living cages.

2. **Justification of Animal Use, Species Choice, and Numbers.** The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel available. The use of nonhuman primates is crucial for the study of human health and disease. The assessments conducted through the Behavior Research Services Core are specifically designed for rhesus macaques. Rhesus are commonly used as an animal model for human health related research and are especially useful for behavioral research due to the close correspondence in stages of development. Monkey models help bridge the gap between rodent research and humans and also provide an advantage over human studies with tightly controlled environmental conditions. The numbers used will depend on the research project and the power calculations of the PI. For Standardized Behavioral Assessments, group sizes of 10-12 are recommended for hypothesis testing if there is no other basis for power calculations.
3. **Veterinary Care.** The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian). Excluded by Requester Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.
4. **Provisions to Minimize Discomfort, Pain, and Injury.** All procedures will be conducted in a manner to minimize distress. No painful procedures are intentionally included; noninvasive and nonmanipulatory methods are used as much as possible. The majority of the Standardized Behavioral Assessments take place after extensive training and adaptation, and many tests utilize positive reinforcement in the form of a food reward. Food deprivation is not used, although some feedings may be rescheduled to induce appetite for food-rewarded tasks. Many assessments, such as Proprietary cognitive puzzles, dyadic observations, and activity monitoring, take place in the home cage. Transport, if necessary, takes place in a modified jump

box or a modified incubator for infants, which are familiar to animals from routine colony husbandry practices. This jump box is also used as the test box for some assessments. ABR testing takes place under ketamine and dexmedetomidine and uses small subdermal needle electrodes, with respiratory rate, oxygen saturation, and temperature continually monitored throughout the procedure. The heart rate variability testing requires animals to be separated from their mother for up to 24 hours (if they are not nursery reared) which may cause some distress. However, monitoring sessions are generally scheduled at least 1-2 days following birth to allow mother-infant bonding. Experience from a previous project has demonstrated no problems reuniting the mother and infant following a 24-hour separation. Animals may experience some stress during the social buffering test, however the observation sessions are short and one of the two sessions is conducted with a familiar buddy. Armpull blood draws are performed by experienced animal technicians. Some neonatal assessments, such as novelty preference and eye tracking, are conducted with the animal hand-held and swaddled in a soft cloth by experienced Core personnel. Other assessments such as the observation cage are limited to 10-minute sessions.

Cooperative training and behavior by definition employs methods that reduce discomfort and distress to the animal. The goal of the training is to encourage the animal's voluntary participation in the desired behavior or situation. Positive reinforcement techniques are used, and sessions are generally short in duration.

During BBA testing, care will be taken to insure that the animals suffer minimal distress. Separation from the dam (which is necessary for this testing) is likely to result in some emotional distress; testing is limited to a 25-hour period to minimize. Also provided are a stuffed toy and a towel to which the animals may cling for comfort. The amount of time each animal participates in the assessments (e.g., the human intruder test) is kept to as short a time as possible. Animals will be manually restrained briefly on four occasions in order to draw blood samples from a femoral vein. During blood sampling, procedures such as keeping the lights low, speaking softly, and handling the animals gently, are employed which seems very effective in reducing the distress from the manual restraint.

5. **Methods of Euthanasia.** Euthanasia is not an endpoint for any Behavior Research Services Core assessments. In general, animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

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CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

LETTERS OF SUPPORT

Letters of support from the individuals named below are provided on the pages that follow.

1.

Excluded by Requester

 PhD, Assistant Professor, Department of Psychiatry and Behavioral Sciences, University of California, Davis
2.

Excluded by Requester

 PhD, Assistant Professor, Department of Psychiatry, Stanford University



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SANTA BARBARA • SANTA CRUZ

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June 18, 2014

Dear [Excluded by Requester]

Thank you very much for your invitation to act as a Consultant on the P51 application you are currently preparing. I would be delighted to lend my expertise to the establishment of an eye-tracking program within the Behavior Research Services Core at the California National Primate Research Center. Non-invasive video eye-tracking provides a wealth of high-resolution, empirical data regarding nonhuman primate visual attention, perception, and motivation. It is also an ideal modality for the animals to make operant choices in decision-making tasks. Modern eye-tracking systems also require very little training and little or no head or body restraint, which means that high-throughput data can be collected with little or no psychosocial stress on the animals.

I have been conducting eye-tracking experiments with juvenile and adult rhesus monkeys for 6 years. I have published 2 peer-reviewed journal articles to date that use eye-tracking with rhesus monkeys. One additional paper is currently under revision and several more are still in preparation. I would be willing to lend my expertise to 1) choice of the most ideal eye-tracking system for nonhuman primates, 2) set-up and quality-control testing of this new system, 3) design of protocols for animal training and data collection, 4) establishment of methods for various forms of data analyses that investigators could follow once the data are acquired, and 5) provide a data analysis and interpretation service for investigators on a freelance basis (as needed). I am open to other forms of assistance at your request.

[Personal Info]

[Personal Info]

I will provide this assistance through in-person meetings on Fridays as needed, or through virtual Skype meetings at any time that is convenient for yourself or investigators interested in utilizing this core eye-tracking service. I would also like to offer you and any interested investigator access to my large library of video stimuli for eye-tracking experiments with rhesus monkeys, including 300 30-second videos showing species-typical social behavior and 300 30-second control videos showing other species engaged in social behaviors.

Please let me know if there is any other way I could be of assistance with this exciting, new core service at the CNPRC. Good luck with your application.

Sincerely,

[Excluded by Requester]

Department of Psychiatry and Behavioral Sciences
University of California, Davis

Excluded by Requester

STANFORD
UNIVERSITY



Excluded by Requester

May 28, 2014

Re: Introducing eye tracking services at CNPRC

Dear Colleagues,

I am writing to support the proposed purchase of eye tracking equipment as part of the CNPRC base grant renewal. My clinical research program at Stanford focuses on identification of biomarkers of social impairments in autism spectrum disorder, with the goal of developing novel pharmacotherapies that enhance social functioning in these children.

I recently established a translational research program at CNPRC to aid in this endeavor. The Biobehavioral Assessment program has been key to identifying the low-Sociable phenotype that is central to this translational work. In looking forward to selecting appropriate endpoints for FDA clinical trials, the eye tracking methodology widely used in humans to quantify social responsiveness is an attractive possibility. Eye tracking of social visual stimuli is becoming widely used in autism research programs as a noninvasive measurement of socially-mediated brain function. The availability of this method in nonhuman primates at CNPRC could strengthen the rapid investigation and translation of therapeutics for autism to the clinical setting.

I understand that purchase of the state-of-the-art Tobii system would be accompanied by development of a protocol by the Behavior Research Services Core that would allow immediate access to this sophisticated research tool for ongoing projects. Perhaps more importantly, the feasibility of seamlessly adding this method to our monkey research with high probability of success would be much enhanced when we apply for funding.

Developmental neuroscience research is being transformed by inclusion of state-of-the-art technology. CNPRC can play a vital role in bringing these tools to affiliate scientists conducting nonhuman primate research through considered equipment purchases such as the one proposed here.

Please do not hesitate to contact me if there is any additional information that I can provide to support the proposed purchase of this important equipment.

Sincerely,

Excluded by Requester

CORE SERVICES: BEHAVIOR RESEARCH SERVICES CORE

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Endocrine Core

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename EC_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	EC_BibliographyReferenceCited.pdf
10. Facilities & Other Resources	EC_FacilitiesOtherResources.pdf
11. Equipment	EC_Equipment.pdf

CORE SERVICES: ENDOCRINE CORE

ABSTRACT

The **Endocrine Core** at the California National Primate Research Center (CNPRC) includes a state-of-the-facility that promotes scientific research focused on the use of nonhuman primate models to investigate the foundations of human health and the diagnosis and treatment of disease. The Endocrine Core continues to function as a central component and driving force in the CNPRC program, serving a spectrum of NIH-supported investigators nationwide. From inception, the Endocrine Core has been responsive to the research community in meeting NIH strategic priorities by providing high quality consultations and services. The Endocrine Core brings specialized expertise in nonhuman primate reproduction and female healthy aging that enhances the nonhuman primate colonies. These endeavors hinge on the growing productivity, emergent innovations, and strong ties with institutional and national programs that are directed to meet the needs of investigators and trainees.

CORE SERVICES: ENDOCRINE CORE

FACILITIES AND OTHER RESOURCES

Laboratories: The Core occupies two laboratories and shared equipment space in the main CNPRC laboratory building. Endocrine Core assays utilize chemiluminescent (Centaur CP), EIA/ELISA (microtiterplate colorimetric), RIAs (Gamma/Beta) and cell-mediated bioassay (luminescence) platforms.

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology. See **Primate Services** sections for more details.

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See **Primate Services** sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and **Information Technology Services** provides desktop support and other related services (see other sections of the application). Five PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are available. Three of the PCs are used to run equipment (e.g., gamma counter, plate reader, HPLC), and the others are networked for word processing, statistical analysis, sample tracking, billing, data entry, illustration preparation, and electronic mail.

Office: [Excluded by Requester] has an office at the Center for Health and the Environment and shared office space is available for [Excluded by Requester] at the CNPRC.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

CORE SERVICES: ENDOCRINE CORE

EQUIPMENT

The Endocrine Core includes biosafety cabinets (2), $\leq -80^{\circ}\text{C}$ freezers, $\leq -20^{\circ}\text{C}$ freezers, 4°C refrigerators, a refrigerated centrifuge, microcentrifuge, Sorvall superspeed centrifuge, microplate reader, microplate washer, fume hood (2), gamma counter, beta counter, HPLC with electrochemical and UV detection, Centaur CP analyzer, microtiter spectrophotometer, and celite chromatography column manifold.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	15,845.00	491.00	16,336.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						16,336.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Core Manager	Excluded by Requester	EFFORT		12,392.00	6,555.00	18,947.00	
1	Total Number Other Personnel					Total Other Personnel		18,947.00
					Total Salary, Wages and Fringe Benefits (A+B)		35,283.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,500.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,500.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	6,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Radioactive Waste Disposal	3,000.00
Total Other Direct Costs	10,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	46,783.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	46,783.00	10,620.00
		Total Indirect Costs	10,620.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	57,403.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: EC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	16,320.00	506.00	16,826.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	16,826.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Core Manager	Excluded by Requester	EFFORT		12,763.00	7,060.00	19,823.00	
1	Total Number Other Personnel					Total Other Personnel		19,823.00
					Total Salary, Wages and Fringe Benefits (A+B)		36,649.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,545.00
2. Foreign Travel Costs	0.00
Total Travel Cost	1,545.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	6,180.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Radioactive Waste Disposal	3,090.00
Total Other Direct Costs	10,300.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	48,494.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	48,494.00	11,008.00
Total Indirect Costs			11,008.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	59,502.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: EC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	16,810.00	535.00	17,345.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						17,345.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Core Manager	Excluded by Requester	EFFORT		13,146.00	7,509.00	20,655.00	
1	Total Number Other Personnel					Total Other Personnel		20,655.00
					Total Salary, Wages and Fringe Benefits (A+B)		38,000.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,591.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,591.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	6,365.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Radioactive Waste Disposal	3,183.00
Total Other Direct Costs	10,609.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	50,200.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	50,200.00	11,395.00
Total Indirect Costs			11,395.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	61,595.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: EC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	17,314.00	568.00	17,882.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						17,882.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Core Manager	Excluded by Requester	EFFORT		13,541.00	7,964.00	21,505.00	
1	Total Number Other Personnel					Total Other Personnel		21,505.00
					Total Salary, Wages and Fringe Benefits (A+B)		39,387.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description	
List items and dollar amount for each item exceeding \$5,000	
Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,639.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,639.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	6,556.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Radioactive Waste Disposal	3,278.00
Total Other Direct Costs	10,927.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	51,953.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	51,953.00	11,793.00
		Total Indirect Costs	11,793.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	63,746.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: EC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	17,834.00	603.00	18,437.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						18,437.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Core Manager	Excluded by Requester	EFFORT		13,947.00	8,452.00	22,399.00	
1	Total Number Other Personnel					Total Other Personnel		22,399.00
					Total Salary, Wages and Fringe Benefits (A+B)		40,836.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,688.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,688.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	6,753.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Radioactive Waste Disposal	3,376.00
Total Other Direct Costs	11,255.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	53,779.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	53,779.00	12,208.00
Total Indirect Costs			12,208.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	65,987.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: EC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget (F-K) (Funds Requested)

CORE SERVICES: ENDOCRINE CORE

BUDGET JUSTIFICATION

All funds requested in the Core are for developmental and administrative activities only. Services provided to users are fully charged to those activities based upon approved rates.

PERSONNEL

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Core Manager				

Excluded by Requester **PhD, Core Scientist** EFFORT months % Effort Excluded by Requester is Professor in the Department of Population Health and Reproduction, School of Veterinary Medicine, and Core Scientist in the Reproductive Sciences and Regenerative Medicine Research Unit. Excluded by Requester has extensive expertise in reproductive endocrinology and aging research with human and nonhuman primates. As Endocrine Core Lead, Excluded by Requester is responsible for all administrative activities; oversees all requests for service and provides oversight for both technical and scientific activities; responds to CNPRC colony and Clinical Pathology Laboratory requests for assistance; and directs collaborative projects and the recruitment of staff.

Excluded by Requester **Core Manager** EFFORT months % Effort Excluded by Requester is the Core Manager and is responsible for the operations of the Endocrine Core. She provides day-to-day management including interaction with clients; development and maintenance of standard operating procedures (SOPs); oversight of laboratory quality assurance/quality control (QA/QC); compliance with local, state, and federal regulations; training of staff and students; and billing/tracking of all Core activities. She is also responsible for developing, validating, and optimizing assays and other specialized methods to meet the needs of Core clientele. Excluded by Requester has over 20 years research experience and extensive expertise in developing assays and specialized methods specifically related to the Endocrine Core.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are listed in the **Facilities Improvement** section.

TRAVEL

\$1,500 is requested to attend one professional meeting annually to stay abreast of new, cutting edge technology and to advertise the Core services to the greater research community.

SUPPLIES

\$6,000 is requested for general laboratory supplies, reagents, tissue culture media, and miscellaneous supplies to support the technical development of new methodologies in the Endocrine Core.

OTHER EXPENSES

\$3,000 is requested for radioactive waste disposal and miscellaneous items related to shipping and administrative functions. With the increased use of EIAs, ELISAs and chemiluminescent assays, the use of radioactivity has been reduced although radioisotope use is still required.

\$1,000 is requested for manuscript submission related to new technologies developed in the Core.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		86,826.00
Section B, Other Personnel		103,329.00
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		190,155.00
Section C, Equipment		0.00
Section D, Travel		7,963.00
1. Domestic	7,963.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		53,091.00
1. Materials and Supplies	31,854.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	15,927.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		251,209.00
Section H, Indirect Costs		57,024.00
Section I, Total Direct and Indirect Costs (G + H)		308,233.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	150,000.00	Services
2	158,250.00	Services
3	166,954.00	Services
4	176,136.00	Services
5	185,823.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

EC_SpecificAims.pdf

3. Research Strategy*

EC_ResearchStrategy.pdf

4. Progress Report Publication List

EC_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

EC_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

EC_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

CORE SERVICES: ENDOCRINE CORE

SPECIFIC AIMS

The CNPRC Endocrine Core serves to promote scientific research that focuses on the use of the nonhuman primate animal model to investigate the foundations of human health and the diagnosis and treatment of disease. The Endocrine Core continues to function as a central component in the CNPRC program, serving a spectrum of NIH-supported investigators nationwide. From inception, the Endocrine Core has been responsive and provided added value to the research community in meeting NIH strategic priorities through high quality consultations and service. The Endocrine Core brings specialized expertise in nonhuman primate reproduction and female healthy aging that enhances the breeding and aging colonies. The goals for the next funding period are reflected in the following Specific Aims that focus on providing support in research, service, training, and colony management.

Specific Aim 1. Provide the necessary research tools and advanced scientific methods to permit endocrine investigations at the highest level of competence, and to contribute to a deeper understanding of physiology and pathology of humans using the nonhuman primate model.

Plan. The primary goal is to facilitate research and ensure a supportive environment for the investigation of endocrine function and disorders, such as those related to reproduction, metabolism, growth, and development. Data from the Core provides important opportunities for collaborative research, dissemination of new information, training, as well as pilot projects to support new NIH grant submissions.

Specific Aim 2. Ensure exceptional expertise in nonhuman primate research and services are provided to investigators using nonhuman primates at the regional and national levels to advance NIH-supported research excellence.

Plan. Assays are continuously updated and reference standards renewed to ensure accurate results. While the primary focus has traditionally been placed on reproductive endocrinology, there is increased focus on metabolic hormones. The Endocrine Core works closely with the CNPRC Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services to ensure that all needs of the colony are recognized and met in-house where possible. All major equipment is maintained with service contracts and computers, with software updated on a three-year basis. A website is maintained to inform the research community of the services available. Both Excluded by Requester are available on a daily basis by electronic mail and to meet face-to-face with investigators, staff, and/or students in a timely manner.

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

Plan. The mentoring and training of new investigators in need of additional expertise in endocrinology at any career stage is an important responsibility of the Endocrine Core. All requests for training and access to critical reagents are pursued when possible. Graduate student projects where the major advisors are CNPRC Core or Affiliate Scientists are prioritized, but courtesy services are broadly provided to graduate students if their requests are within the scope of the Core and the student has expressed an interest in endocrine training. Postdoctoral fellows pursue projects in the Endocrine Core under the supervision of the Core manager.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

Plan. The Endocrine Core will continue to support all aspects of colony care including veterinary care, colony management, and research projects. The Core has recently expanded this role by promoting specific clinical inquiries and guiding junior veterinary clinicians in the development of research projects emanating from and depending on endocrine expertise. The Endocrine Core brings specialized expertise in nonhuman primate reproduction and female healthy aging to enhance the breeding program and the aging colony.

CORE SERVICES: ENDOCRINE CORE

RESEARCH STRATEGY

INTRODUCTION

The Endocrine Core provides sample analysis for CNPRC staff and the greater research community. The Core is led by [Excluded by Requester] and managed [Excluded by Requester] (Figure 1, Table 1). The main focus of this service is primate reproductive endocrinology but the Core also responds to requests for non-reproductive hormone analyses. A recharge schedule for all sample analyses is determined and maintained by the CNPRC Administration and Operations Services. The main features of the Endocrine Core include development of unique assays and validation of common assays for application to the rhesus macaque. A secondary component of the service includes consultation, training, and provision of critical reagents for the scientific community at large. New assays are developed or adapted for application to the rhesus macaque following an approved request and appropriation of development funds.

Figure 1. Organizational Chart: Endocrine Core

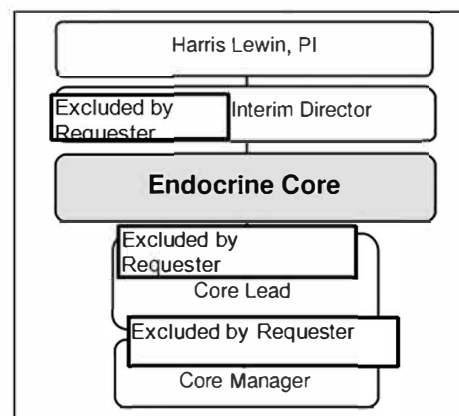


Table 1. Endocrine Core Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
[Excluded by Requester]	Department of Population Health and Reproduction, School of Veterinary Medicine	Core Scientist
[Excluded by Requester]	CNPRC	Core Manager

The sources of support for the Endocrine Core in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 2. Support for the Endocrine Core

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$44,788	\$46,783
Program Income from P51	\$150,000	\$150,000
Other Sources	\$0	\$0
TOTAL	\$194,788	\$196,783

Response to Summary Statement.

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

While over 90% of all biomedical animal use is directed to non-primate species, the critical need for nonhuman primate research activities remains. For this reason, the availability of laboratory resources that provide methods development and their application to nonhuman primate models is of critical importance. Such facilities need to be comprehensive to provide services broadly and also focused on developing trends in modern medicine. Despite the unique parallels between nonhuman primate and human reproduction, there are differences that must be understood and considered for the appropriate use and interpretation of nonhuman primate model findings. As all mammalian reproduction is mediated and controlled through endocrine processes, endocrine monitoring remains a critically needed component in most investigations of reproductive

function. Therefore, the CNPRC Endocrine Core, focused on nonhuman primate endocrinology, is a key resource for the broad research community at the national level. Examples of differences in human and nonhuman primate reproductive physiology are functional, such as the length of pregnancy, development of a fetal zone in the fetal adrenal gland, and the production of specific estrogenic compounds. Other differences are structural and include the primary structure of protein hormones such as chorionic gonadotropin (CG). Both types of differences must be understood and accounted for in providing insightful and appropriate research information when using nonhuman primates in modeling human diseases. Notably, standards for best practices for the measurement of some reproductive hormones are still being revised at the international level. This “moving target” in basic methodology requires that the broad research community have access to a limited number of laboratories that understand the needs and nuances of emerging standards. A prime example of how existing methodologies may change over time is the looming mandate that low levels of circulating estradiol and testosterone in clinical studies may require mass spectrometry for accurate determinations. Should this emerge as a mandate, it would require changes in the Endocrine Core and such adjustments are currently under consideration. A shift of this nature would be challenging for the individual investigator, further underscoring the importance and significance of a high-quality and up-to-date endocrine service to provide clinically relevant measurements to the research community.

The investigation of reproductive failure is critical for National Primate Research Centers (NPRCs) as many aspects of human reproduction can only be monitored and modeled by employing nonhuman primate resources. One of the primary goals in the establishment of NPRCs was to provide a relevant animal model that recapitulates women’s reproductive physiology to better understand human reproductive diseases and related reproductive failure. Those research endeavors are complicated in long-lived slow reproducing primate species including humans. These unique attributes add to costs and limits animal numbers in research programs. While the nonhuman primate model is essential, it also requires minimally invasive yet incisive investigative tools in providing information that can be directly compared to human physiology and diseases. In this regard the CNPRC Endocrine Core fulfills a critical role in detecting and quantifying reproductive hormone production, circulation, and mechanisms in a fashion directly mirroring human conditions. The Core maintains an endocrine service specializing in both human and nonhuman reproductive endocrinology, which permits meaningful nonhuman primate research protocols to be designed and executed.

An emerging need where the nonhuman primate model offers unique advantages is the field of healthy aging in women, where the CNPRC is an international leader. The Core has provided novel insights into the relationship between ovarian and adrenal function during the menopausal transition, a topic of growing concern in light of the results of the NIH-funded Women’s Health Initiative and the outgrowth of the “timing hypothesis” relating to the adverse effects of hormone replacement therapy. The CNPRC has been a leader in the nonhuman primate studies to model these concepts, largely because of the unique services available through the Endocrine Core. These services have been provided widely to a broad clientele underscoring the value added by the conduct of research in nonhuman primates.

The CNPRC Endocrine Core provides service in four important ways. *First*, it responds to the specific needs of the CNPRC in providing consultations and assay service to CNPRC veterinarians, colony managers, and research investigators. *Second*, as noted above, the Endocrine Core provides a global service to the broader research community. *Third*, the Core provides training and unique assay reagents to visiting scientists, graduate and postdoctoral students, and trainees at all levels. *Fourth*, the Core responds to requests from the **Clinical Pathology Laboratory** (within Anatomic and Clinical Pathology Services in Primate Services) in adapting and validating clinical assays that are compatible with its assay platforms. All of these service areas are facing a demand for continued growth and development in the next funding period.

The services offered through the Endocrine Core pertain to serum, urinary, and salivary hormone measurements with the reproductive hormones being the primary analytes of interest (see below), as the reproductive health of the colony is an important area of focus for the CNPRC. In addition, as primate reproductive physiology is species-specific, methods available for most other species are not necessarily appropriate for studies with the nonhuman primate model. The Endocrine Core is one of the few Cores nationally that can provide services required for nonhuman primate endocrine research. For example, monitoring pregnancy in the human clinical setting is enhanced by measurements of human CG (hCG). However, this assay is not useful for the laboratory macaque because assays for hCG do not detect macaque

CG (mCG). Only one practical mCG assay exists and is made available to all research facilities through the CNPRC Endocrine Core. Another example is estriol, the major estrogen of human pregnancy, which is a minor component of the macaque pregnancy where estrone predominates. Serum mCG and urinary estrone conjugate measurements are uniquely available through the Core on a service basis and can be critical when investigators are formulating their research strategies. Unique reagents are also made available to investigators who wish to perform their own assays.

More than one-half of the clients that requested services from the Endocrine Core during the current funding period are supported by the NIH. Most of these requests, which represent approximately 40% of all services provided by the Endocrine Core, are in response to requests from CNPRC Core or UC Davis-based Affiliate Scientists. Another ~15% of requests originate from other UC campuses. Although these requests largely involve the analysis of samples on a recharge basis, consultation and/or training is also required in many cases. It is fortunate that the CNPRC Endocrine Core is led by an active research scientist with over 35 years of NIH-supported research in human and nonhuman primate reproductive physiology. This expertise and the innovations that the Core Leader has brought to the field provide a unique service with resources that have been developed over decades and continue to proliferate.

The support of activities that directly enhance the health and streamline the management of the colony is another important aspect of the Core activities. While most veterinarians have training in primate medicine they do not have the opportunity to gain the necessary insights into aspects of the menstrual cycle to have an immediate perspective in primate reproductive medicine. Specifically, most aspects of reproductive aging are unique to primate species and are currently rapidly evolving. Since a major concern of all NPRCs is the creation and maintenance of an aged population of animals (see **National Institute on Aging Colony**), there are constant challenges to maintain the appropriate acumen in the clinical staff. The Core responds to questions relating to issues from more serious issues such as menometrorrhagia to those relating to seasonality and lactational amenorrhea. In addition, the Core Leader encourages and supports in-house clinical research projects and provides consultation and laboratory support as needed.

During the current funding period over 80 individual requests were received and fulfilled with recharge of approximately \$515,000 in direct costs (not including the non-university differential or NUD; May 1, 2010 to April 30, 2014) (Table 3). Of these requests, over 50% were from one of the ten UC campuses, with approximately two-thirds of this 50% from UC Davis primarily for assays requested for colony management issues or by Core or Affiliate Scientists. Remaining clients were represented equally from other UC campuses and non-UC campuses. Requests for services were also submitted from foundations and industry.

Table 3. Endocrine Core Use (May 1, 2010 to April 30, 2014)

Grant Year	Services Provided	Users	User Affiliation (N)	Recharge (\$)
2010 - 2011	Assays	21	Core Scientist (3), UC Davis (5), External (13)	165,665
2011 - 2012	Assays	18	Core Scientist (2), UC Davis (3), External (13)	130,945
2012 - 2013	Assays	12	Core Scientist (2), UC Davis (2), External (8)	117,641
2013 - 2014	Assays	11	Core Scientist (1), UC Davis (2), External (8)	100,474
TOTAL				\$514,745

The Endocrine Core provides a broad portfolio of services to clients that require the analyses of biological samples for the analytes shown in Table 4. All assays have been validated for application to the rhesus monkey and most have been adapted to the Centaur autoanalyzer platform.

The Endocrine Core has continued to provide a comprehensive menu of service, training, and consultations with regard to endocrine monitoring to support and maintain scientific programs at the CNPRC. In the current funding period, the Core added new equipment (Centaur) that permitted upgrading of most assays to optimize efficiency and throughput. This has not only benefited the Endocrine Core but has provided an additional avenue for the CNPRC Clinical Pathology Laboratory to expand its service by collaborating with the Core. Each year new assays are developed and old assays are adapted to the Centaur platform. Notable advancements in the current funding period include the addition of B-type natriuretic peptide, dehydroepiandrosterone sulfate, insulin, and expansion of the thyroid hormone portfolio to include free thyroxine, free triiodothyronine, and ultra-sensitive thyroid stimulating hormone. Continued growth in assay capability ensures sustainability as more services are developed and refined. An example of a service provided was a request requiring validation of a thyroid panel for the rhesus macaque [Excluded by Requester, al., 2010]. The Core

successfully completed the request and the validated assay was incorporated in the Endocrine Core's repertoire and is currently offered as a part of our routine service.

Table 4. Endocrine Core Assays

Assay Type	Analyte
Cell-based Bioassays	Androgen receptor ligand load Estrogen receptor ligand load Luteinizing hormone (LH)/chorionic gonadotropin (CG)
Serum Assays	Androstendione B-type natriuretic peptide (EDTA plasma) CG (human and macaque) Cortisol Dehydroepiandrosterone and Dehydroepiandrosterone sulfate Estradiol, Estrone, Estriol Ferritin Follicle stimulating hormone (FSH) Insulin Levonorgestrel LH Progesterone Prolactin Sex hormone binding globulin Testosterone Triiodothyronine (free and total) Thyroid stimulating hormone (conventional and ultra-sensitive) Thyroxine (free and total)
Urinary Assays	Cortisol CG (human and macaque) Estrone conjugates (E1C) Follicle stimulating hormone (β subunit) Pregnanediol-3-glucuronide (PdG)

The primary strength of the Endocrine Core is its broad experience with nonhuman primate species [Excluded by Requester] has expertise with not only the macaque species but has research experience with prosimians, African Old World monkey species, great apes, and New World monkeys. This broad experience along with information presented on the Core's web page has guided non-NPRC research laboratories to contact the Endocrine Core for information, reagents, consultations, and services. Examples of this type of collaboration include a publication that supports a research team investigating South American species as parallel captive and free-ranging animal models [Excluded by Requester] al., 2011] and the use of Vervet monkeys for metabolic research [Excluded by Requester] al., 2013]. Experimental data from such collaborations are archived and can be used for advising primate facilities, zoos, and wild animal parks that have an interest in captive propagation.

The secondary strength of the Endocrine Core is its simultaneous and parallel interest and activities in both human and nonhuman primate reproduction. During the current funding period, research findings first described in the nonhuman primate were shown to have significant impact in women's healthy aging [Excluded by Requester] et al., 2009]. This descriptive study was followed by three population-based studies that redefined the endocrine foundation of the menopausal transition in women [Excluded by Requester] 2011; 2012 [Excluded by Requester] et al., 2012]. Ultimately, experimental studies were performed using the nonhuman primate that provided a mechanistic basis for findings described in women [Excluded by Requester] al., 2013 [Excluded by Requester] al., 2013]. These Core activities have complemented [Excluded by Requester] Program Project (#P01-AG016765; see **Brain, Mind, and Behavior Research Unit**), and provide a potential mechanistic explanation for some of the surprising findings resulting from experiments with hormone replacement therapies [Excluded by Requester] al., 2013 [Excluded by Requester] 2012 (see Figure 2, below). At the present time, the Endocrine Core is collaborating with the **Multimodal Imaging Core** to describe and characterize receptors for luteinizing hormone (LH) in the adrenal cortex of female higher primates to provide additional mechanistic information.

The new information relating to women's healthy aging and the validation of the macaque model for investigating the underlying mechanisms has expanded several research programs [Excluded by Requester] has initiated an augmentation to [Excluded by Requester] Program Project to investigate the role of adrenal steroids in the preservation

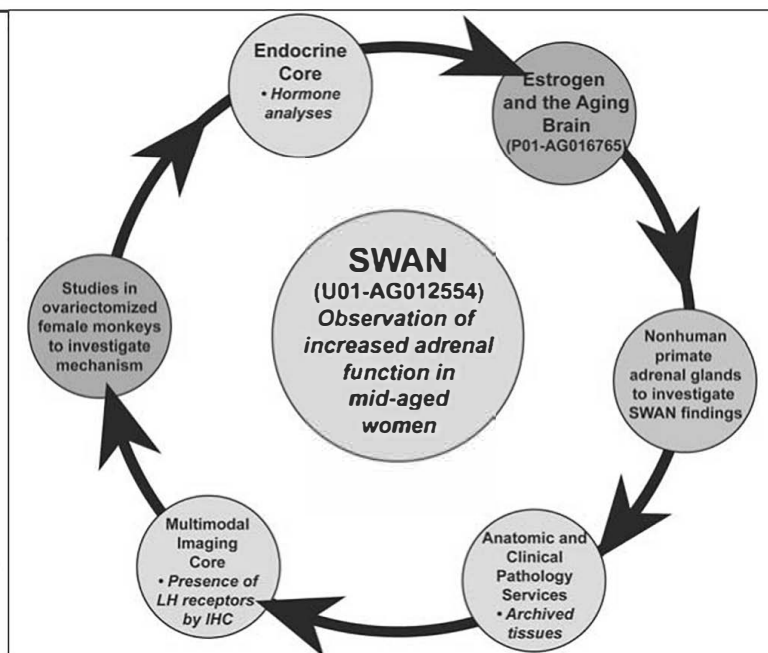
and function of dendritic spines in the frontal cortex [Excluded by Requester] graduate student [Excluded by Requester] (**Respiratory Diseases Research Unit**), is including the role of estrogen receptor beta (ER beta) ligands from the adrenal cortex in his investigation of gender differences in the aging lung. A veterinary resident [Excluded by Requester] is investigating the role of ER beta ligands as a potential intervention for endometriosis in older female macaques (see **Primate Medicine Services**). In addition, a possible case of pregnancy-induced Cushing's disease was identified by the veterinary staff. This unique case would not have been fully appreciated prior to the identification of LH receptors in the adrenal gland of virtually all female macaques.

INNOVATION

Unique Services and Research Opportunities for the Nonhuman Primate Research Community

The Endocrine Core continues to make scientific contributions to the science that is dependent upon the nonhuman primate model. This is most evident in the area of healthy aging with an emphasis on the menopausal transition. While rodent models have provided the foundations for this field it is now apparent that the species-specificity of reproductive aging and lifespan health requires modeling in the macaque. Studies in the current funding period investigated the benefits and risks of different hormone replacement regimens. In the conduct of those studies it was recognized that subtle changes in adrenal steroid production may be as important as the more apparent changes in ovarian function in terms of symptoms and health trajectories in mid-aged women (see **Reproductive Sciences and Regenerative Medicine Research Unit**). The Endocrine Core was able to characterize the relationships between age, ovarian status, and adrenal steroid production and demonstrate that inter-individual differences in adrenal steroid production were greater than changes in ovarian function. This provided for the first time a rationale for the observed wide disparity in how individual women traverse the menopausal transition. *More importantly these studies suggest that it is the combined change in ovarian function and adrenal steroid production that contributes to the individual response to the menopausal transition.* Importantly, these results also suggest that a major difference in the response to different hormone replacement therapy regimens resides in the adrenal cortex. As noted, the Endocrine Core demonstrated the presence of LH receptors in the adrenal cortex of female macaques to provide a working hypothesis for mechanism(s) involved in the modulation of the adrenal cortex as ovarian function declines and circulating LH levels rise (Figure 2).

Figure 2. Example of integration of research studies and Core services at the CNPRC. The Study of Women's Health Across the Nation (SWAN), a population-based study, found an association of increased adrenal function in mid-aged women. This observation led to ancillary investigations in a nonhuman primate experimental study (#P01-AG016765, Estrogen and the Aging Brain [Excluded by Requester] PI). This study revealed similar changes in adrenal function in ovariectomized female rhesus macaques by the Endocrine Core. These hormone results prompted examination of archived adrenal tissue through the **Anatomic and Clinical Pathology Services**. High-resolution magnification of immunohistochemically (IHC) stained tissues by the **Multimodal Imaging Core** revealed receptors for LH in the adrenal cortex. The combined efforts of multiple CNPRC services and Cores led to a new concept in women's healthy aging.



The Endocrine Core provides state of the science services in hormone measurements that are specifically directed towards primate species. As described above, a Centaur autoanalyzer (Siemens) was purchased as a part of the Analytical and Resource Core equipment budget during the current funding period. This acquisition permitted a transfer of the majority of established assays to this platform. The application of the Centaur platform is unique as it was developed specifically for human clinical use and usually requires the purchase of reagents and software from the vendor. The Endocrine Core was fortunate to obtain access to the Centaur software from Siemens to allow the installation of macaque-specific reagents for assays developed specifically

for this species. This also permitted the Core to work more closely with the CNPRC **Clinical Pathology Laboratory** and adapt assays that were previously sent out to a commercial laboratory for analysis. As more commercial assays are being developed for the chemiluminescence platform, it becomes easier and requires less time to adapt assays developed for the human clinic to be transferred to the Endocrine Core service. The Centaur assay format and quality control parallels those of human clinical laboratories thus they are attractive to investigators that would otherwise be sending samples for a more expensive service in a CLIA-approved laboratory for less macaque-specific assay results. As the Endocrine Core becomes more familiar with this relatively new technology, it becomes quicker and more economical to develop new assays. In addition, since the automated platform reduces both technician time and re-analysis of samples, there can be as much as 25-30% reduction of costs compared to conventional radioimmunoassay or enzyme-linked colorimetric assay formats that are commonly used in research with non-primate species. This sets the stage for intense outreach and marketing of the core in the proposed funding period.

Steroid hormones are non-species specific in terms of their structure and assay formats. This simplifies the validation of androgen, estrogen, progesterin, and corticoid assays for the monkey model. However, the Endocrine Society has recently indicated that low circulating levels of estradiol and testosterone in humans will require measurements by liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS) and suggests this requirement will be applied to animal models as well in the future. In an attempt to adapt to this coming change and to preserve the utility of the archived data, an ongoing collaboration with the University of Michigan will compare the results of paired Centaur and LC/MS/MS results for estradiol and testosterone from two thousand human samples that were previously determined to be below 20 and 100 pg/mL, respectively. Since the University of Michigan shares the unique Centaur estradiol and testosterone assays with the Core, and applies them to large population-based epidemiological studies, the Core is in an excellent position to validate current data by all standards using the most recent criteria. There is no doubt that changes like these will be a constantly evolving process and the Endocrine Core will continue its proactive approach to maintain this special relationship with Michigan and continue to provide reagents for urinary metabolite assays.

All protein and larger polypeptide hormone molecules have primary structure differences when comparing humans and macaques. These differences can be subtle in peptides and smaller proteins. However, this is a more pronounced problem for larger protein hormones, where many peptide differences could affect primary epitopes. In these cases, direct use of human-based assays for nonhuman primates can lead to errors and misinterpretations of results. Unfortunately, few of these molecules have been purified from the macaque to a degree sufficiently adequate to generate specific antibodies. For this reason, the Endocrine Core routinely has initiated a process to validate each assay for the macaque before it is offered as a service. This is accomplished in two ways. In some instances the Core searches for antisera that maximize analyte recognition in order to identify existing epitope-antibody pairs that permit the development of specific and sensitive assays. The unique mCG assay is an example of such an assay that exists nowhere else. This is also true for the urinary assays (PdG, E1C, FSH, and hCG). In addition, innovations by the Core include development and use of cell-based assays for bioactive LH/CG, total estrogen, and total androgenic compounds, and in particular the development and application of engineered cells as hormone assay tools. The Endocrine Core has developed stably transfected cell lines for this purpose. Each of these assays use a specific immortalized stably transfected cell line with the human LH receptor, the ER alpha receptor, or the androgen receptor inserted. These assays have become popular because it is now understood that a specific molecule is not necessarily the unique ligand that is responsible for all of the signal transduction through what was once thought to be a ligand-specific receptor.

One of the goals of the CNPRC colony managers is to enhance the quality of the aged population, especially females (see **National Institute on Aging Colony**). In this regard, the Endocrine Core is working with **Primate Medicine Services** to screen for and treat diseases that limit the survival of older females into their third decade of life. A prime example is the current investigation of bazodoxifene (BZA) to treat endometriosis. This is now a resident project Excluded by Requester that enjoys support from Private Source to determine if BZA, a potent selective ER modulator (SERM), can be used as a short-term treatment for blocking the progression of endometriosis in older females. The pilot project is underway and it is anticipated this will develop into a full research project during the next funding period.

Many outside laboratories employ Core assay methods and unique reagents and therefore the Endocrine Core provides training and consultation that are unique. mCG and the urinary estrogen and progesterone metabolite assays are prime examples. Since purified mCG is not available and excretion is highly variable, the validation of such assays must be performed empirically. These activities require the collection and characterization of hundreds of well-documented samples in order to establish normative ranges and identify pathological conditions. For these purposes, developmental funds are made available, and when the assays have clinical or colony relevance, samples are made available through the CNPRC Clinical Pathology Laboratory. This was the mechanism used for the validation of the recently developed thyroid panel.

Most requests for new assays come from individual investigators. Such requests occur several times each year. A few additional requests come from the Clinical Pathology Laboratory and these are considered a primary responsibility in support of the CNPRC Core and Affiliate Scientists. The second priority is to add assays that will provide substantial and long-standing benefit to the Core. The third priority is availability of critical reagents and the quantity of effort that would be required for validation. All requests for new assay development are referred to the Director's Office and the Research Advisory Committee for approval and allocation of funds.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Provide the necessary research tools and advanced scientific methods to permit endocrine investigations at the highest level of competence, and to contribute to a deeper understanding of physiology and pathology of humans using the nonhuman primate model.

The primary goal is to facilitate research and ensure a supportive environment for the investigation of endocrine function and disorders, such as those related to reproduction, metabolism, growth, and development. Resultant data will provide important opportunities for collaborative research, dissemination of new information, training, as well as pilot projects to support new NIH grants.

The Endocrine Core will facilitate research programs by providing updates in terms of laboratory methodology and scientific advances in the field that can promote new, improved, and more relevant research projects using the nonhuman primate animal resources. These topics will be considered for discussion at the Core Scientist meetings as appropriate. This information will also be provided as alerts to the CNPRC Research Advisory Committee and as updates to the CNPRC Endocrine Core web page. Specifically, the Endocrine Core will interact with CNPRC Core Scientists at the individual level to alert them to emerging concepts and developing research activities. The Endocrine Core will also monitor the literature to stay abreast of advances in clinical endocrinology and determine if specific methodologies can or should be adapted to nonhuman primate animal models. The Core will continue to disseminate information through publications in top-rated journals and encourage service clients to acknowledge the assistance of the Core in their publications.

Metrics. Additional and improved methods and more aggressive interactions will lead to increased collaborations and more joint publications. In addition, junior staff will be encouraged to be involved in more complex research projects and therefore produce a higher quality of research publication. Closer attention to collaborative and service activities will increase the Core's visibility by affiliations in published reports.

Alternative Strategies. For advances in methodology and assays that are not directly related to specific CNPRC projects, the Core will provide short summaries for dissemination and distribute the information through the CNPRC web page. Gaining more visibility through acknowledgements in published manuscripts will also alert research scientists to the opportunities provided in the Core.

Specific Aim 2. Ensure exceptional expertise in nonhuman primate research and services are provided to investigators using nonhuman primates at the regional and national levels to advance NIH-supported research excellence.

Assays are continuously updated and reference standards renewed to ensure accurate results. While the primary focus has traditionally been placed on reproductive endocrinology, there is a recent trend to include metabolic hormones when the need is apparent and justified. The Endocrine Core works closely with the Clinical Pathology Laboratory to ensure that all needs of the colony are recognized and met in-house where possible. All major equipment is maintained with service contracts. A website is maintained to inform the

research community of the services available. Both Excluded by Requester are available on a daily basis to meet with investigators, staff, and/or students.

New assays will continue to be developed, adapted, and validated as requested when possible. The trend to include more metabolic analytes will continue and likely expand as the Clinical Pathology Laboratory expands their analyte menu for in-house analysis. Mandates to upgrade methods will be pursued aggressively in order to maintain parity with traditional clinical laboratories. An additional technician will be added as service revenues permit. Access to mass spectrometry through the UC Davis West Coast Metabolomics Center and other entities on campus on a recharge basis will be pursued during the next funding period.

Metrics. As new methods are requested, developed, and applied both the number of clients and associated research publications will increase. As new staff and veterinarians are introduced to more challenging research projects more grants will be obtainable and better research publications will be produced.

Alternative Strategies. When traditional assay methods cannot be development or adapted to meet requests, the Endocrine Core will explore the possibility of using cell-based bioassays that have been proven to provide a solution for LH and total estrogens and androgens (see above).

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

A responsibility of the Endocrine Core is to mentor and train new investigators at all career stages that are interested in gaining expertise in endocrinology. All requests for training and access to critical reagents are supported when possible.

Metrics. The quantity of trainees exposed to Endocrine Core assays and services will increase as methods are expanded and streamlined. More importantly, the visibility of the Endocrine Core will be increased through the production of more and a higher quality of research publications.

Alternative Strategies. As an alternative, the Core will initiate the inclusion of detailed standard operating procedures (SOPs) and protocols on the web page in order to ensure adequate portability and successful adaptation of assays and reagents at other laboratories.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care.

The Endocrine Core will continue to respond to all aspects of colony care including veterinary care, colony management, and research support. The Core has recently expanded this role by promoting specific clinical inquiries and guiding junior veterinary clinicians in embarking on innovative research projects that emanate from and depend on endocrine expertise. The Endocrine Core brings specialized expertise in nonhuman primate reproduction and female healthy aging that can enhance the breeding program and expand the aging colony, which supports the CNPRC lifespan health initiative. These endeavors hinge on the growing productivity, emergent innovations, and strong ties with institutional and national programs that are directed to meet the growing needs of investigators and trainees.

Since reproductive health and fertility is a key issue in colony management, the Endocrine Core generally receives questions and requests on a weekly basis. These will continue to be addressed in a timely manner and investigative strategies encouraged when appropriate. Collaboration with the veterinary staff has grown during the current funding period and it is anticipated that this trend will continue.

Metrics. Since most of the projects initiated with colony managers relate to reproductive health and healthy aging, it is expected that the Core will be able to support an older colony over the next five years which is crucial for research studies focused on the lifespan. For example, if endometriosis can be treated successfully then the ability to develop an aged colony of reproductively sound females will be improved.

Alternative Strategies. Efforts will be made to contact NPRC colony managers to alert them to potential projects or programs that could be initiated. New developments in the scientific literature that are relevant to colony management will be considered when appropriate and discussed at the regularly scheduled Colony Management Advisory Committee Meetings that engage Core Scientists, veterinarians, and staff.

CORE SERVICES: ENDOCRINE CORE

PUBLICATIONS (May 1, 2010 to April 30, 2014)

- Excluded by Requester Multiple clinically relevant hormone therapy regimens fail to improve cognitive function in aged ovariectomized rhesus monkeys. *Neurobiol Aging* 34:1882-1890, 2013. PMID: PMC3622837
- Excluded by Requester Modulation of higher-primate adrenal androgen secretion with estrogen-alone or estrogen-plus-progesterone intervention. *Menopause* 33:223-228, 2013. PMC Journal-in-progress
- Excluded by Requester Assessment of luteal function in the vervet monkey as a means to develop a model for obesity-related reproductive phenotype. *Syst Biol Reprod Med* 59:74-81, 2013. PMC Journal-in-progress
- Excluded by Requester Dehydroepiandrosterone sulfate levels in women following bilateral salpingo-oophorectomy. *Menopause* 18:494-498, 2011. PMC Journal-in-progress
- Excluded by Requester Adrenal androgens during the menopausal transition. *Ob/Gyn Clin North Am* 38:467-475, 2012. PMID: PMC3185242
- Excluded by Requester Ovarian adrenal interactions during the menopausal transition. *Minerva Ginecol* 65:641-651, 2013. PMC Journal-in-progress
- Excluded by Requester Androstenediol complements estradiol during the menopausal transition. *Menopause* 19:657-663, 2012. PMID: PMC3366061
- Excluded by Requester Menopausal transition stage-specific changes in circulating adrenal androgens. *Menopause* 19:658-663, 2012. PMID: PMC3366025
- Excluded by Requester Dehydroepiandrosterone sulfate levels reflect endogenous luteinizing hormone production and response to human chorionic gonadotropin challenge in older female macaque (*Macaca fascicularis*). *Menopause* 20:329-335, 2013. PMID: PMC3546135
- Excluded by Requester Clinically relevant hormone treatments fail to induce spinogenesis in prefrontal cortex of aged female rhesus monkeys. *J Neurosci* 32:11700-11705, 2012. PMID: PMC3657730
- Excluded by Requester Thyroidal radioactive iodide uptake in the lactating rhesus monkey. *J Lab Anim* 44:155-158, 2010. PMC Journal-in-progress
- Excluded by Requester The use of long acting subcutaneous levonorgestrel (LNG) gel depot as an effective contraceptive option for cotton-top tamarins (*Saguinus oedipus*). *Zoo Biol* 30:498-522, 2011. PMC Journal-in-progress
- Excluded by Requester Continuously delivered ovarian steroids do not alter dendritic spine density or morphology in macaque dorsolateral prefrontal cortical neurons. *Neuroscience* 4522:841-845, 2013. PMC Journal-in-progress

CORE SERVICES: ENDOCRINE CORE

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC.

1. Description of the Proposed Use of the Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal Location] indoor animal space. The outdoor animal housing area includes [Specific Animal Location] field corrals [Specific Animal Location] corn cribs [Specific Animal Location]. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their blood, urine, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA) or Radiation Use Authorization (RUA), and related facility and laboratory training documents required for employment.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester]. Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals

housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

- 4. Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
- 5. Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

CORE SERVICES: ENDOCRINE CORE

BIBLIOGRAPHY AND REFERENCES CITED

Excluded by Requester Multiple clinically relevant hormone therapy regimens fail to improve cognitive function in aged ovariectomized rhesus monkeys. *Neurobiol Aging* 34:1882-1890, 2013. PMID: PMC3622837

Excluded by Requester Modulation of higher-primate adrenal androgen secretion with estrogen-alone or estrogen-plus-progesterone intervention. *Menopause* 33:223-228, 2013. PMC Journal-in-progress

Excluded by Requester Assessment of luteal function in the vervet monkey as a means to develop a model for obesity-related reproductive phenotype. *Syst Biol Reprod Med* 59:74-81, 2013. PMC Journal-in-progress

Excluded by Requester M. Dehydroepiandrosterone sulfate levels in women following bilateral salpingo-oophorectomy. *Menopause* 18:494-498, 2011. PMC Journal-in-progress

Excluded by Requester Adrenal androgens during the menopausal transition. *Ob/Gyn Clin North Am* 38:467-475, 2012. PMID: PMC3185242

Excluded by Requester Menopausal transition stage-specific changes in circulating adrenal androgens. *Menopause* 19:658-663, 2012. PMID: PMC3366025

Excluded by Requester Dehydroepiandrosterone sulfate levels reflect endogenous luteinizing hormone production and response to human chorionic gonadotropin challenge in older female macaque (*Macaca fascicularis*). *Menopause* 20:329-335, 2013. PMID: PMC3546135

Excluded by Requester Clinically relevant hormone treatments fail to induce spinogenesis in prefrontal cortex of aged female rhesus monkeys. *J Neurosci* 32:11700-11705, 2012. PMID: PMC3657730

Excluded by Requester Thyroidal radioactive iodide uptake in the lactating rhesus

Excluded by Requester The use of long acting subcutaneous levonorgestrel (LNG) gel depot as an effective contraceptive option for cotton-top tamarins (*Saguinus oedipus*). *Zoo Biol* 30:498-522, 2011. PMC Journal-in-progress

CORE SERVICES: ENDOCRINE CORE

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Immunology and Pathogen Detection Resources Core

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename IPDRC_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	IPDRC_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	IPDRC_FacilitiesOtherResources.pdf
11. Equipment	IPDRC_Equipment.pdf

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE

ABSTRACT

The **Immunology and Pathogen Detection Resources Core** plays a critical role in nonhuman primate research and colony management at the California National Primate Research Center (CNPRC). The Core provides routine and specialized laboratory diagnostic and research assays that address aspects of respiratory and infectious disease immunology as well as pathogen detection needs. The two Core components work cooperatively to leverage personnel and equipment used for immunology assays and pathogen detection. The Immunology component of the Core aims to provide state-of the-art assistance, from start to end, for research studies that have an immunologic component and also to spearhead the use of the nonhuman primate as a model for the human immune system. This work includes experimental design, execution, and data analysis/interpretation. The Immunology component has particular interest and expertise in evaluation of immune function throughout the primate lifespan, from gestation to old age. The Pathogen Detection component of the Core continues to be the leading reference laboratory for nonhuman primate infectious disease testing while fulfilling the mission to improve the nonhuman primate resource. The Core will remain at the forefront of scientific discovery relevant to pathogens and immune responses as well as advancements in reagents and technology leading to the development of new methods through the following Specific Aims: (1) Provide state-of-the-art research assays relevant to nonhuman primate models of human disease and nonhuman primate colony health, (2) Provide exceptional expertise and services to researchers at the regional, national, and international levels, and (3) Mentor and train the next generation of translational nonhuman primate investigators.

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE

FACILITIES AND OTHER RESOURCES

Laboratories: The Core occupies eight laboratories encompassing 1,210 sq. ft. of laboratory space. These laboratories include four BSL-2-designated spaces containing biosafety hoods appropriate to work with BSL-2 agents. The Core additionally has access to shared equipment rooms. Central facilities with autoclaves, glass washing, medical waste disposal, dry ice, and wet ice machines are available as well

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology. See **Primate Services** sections for more details.

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See **Primate Services** sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and **Information Technology Services** provides desktop support and other related services (see other sections of the application). Core faculty and staff have been provided with a computer that is appropriate to their tasks.

Office: Office space is provided to Excluded by Requester and shared space is provided for the technical staff.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities, support services, and extensive expertise available as described in this application. The Core laboratory, in particular, has ready access to all Core Scientists and other CNPRC Core laboratories. The environment allows for mutual strong intellectual support and resource sharing. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE

EQUIPMENT

Biosafety cabinets (9), fume hood (3), $\leq -80^{\circ}\text{C}$ freezers (4), $\leq -20^{\circ}\text{C}$ freezers (10), 4°C refrigerators (6), refrigerated centrifuges (6), microcentrifuges (7), microplate reader, microplate washer, microscopes (3), incubators (9), spectrophotometer, epMotion 5070 automatic pipetting station, ABI thermocyclers (2), Nanodrop ND-1000 spectrophotometer, Bioplex luminex bead reader, Quiagen Biorobot M48, balances, vortex, water baths, pH meters, heat blocks, rotating platforms, vacuum pumps.

Becton-Dickinson FACSCalibur flow cytometer with 2 lasers capable of 4-color analysis, FACSria cell sorter with 3 lasers capable of 10-color analysis and 4-way sorting, and an LSRII flow cytometer with 4 lasers capable of 13-color analysis.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	15,210.00	5,088.00	20,298.00
2.					Assoc Director for Primate Services			0.0	0.0	9,075.00	3,619.00	12,694.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	32,992.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		5,381.00	2,146.00	7,527.00
1	Core Manager	Excluded by Requester			56,967.00	30,136.00	87,103.00
1	Immunology Technical Support:				24,757.00	13,096.00	37,853.00
	Excluded by Requester						
1	Pathogen Detection Technical Support	Excluded by Requester			12,621.00	6,677.00	19,298.00
4	Total Number Other Personnel				Total Other Personnel		151,781.00
					Total Salary, Wages and Fringe Benefits (A+B)		184,773.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,000.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	30,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	31,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	218,773.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	218,773.00	49,661.00
Total Indirect Costs			49,661.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	268,434.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IPDRC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/	Institutional	EFFORT	0.0	0.0	15,667.00	5,517.00	21,184.00
					Core Scientist	Base Salary						
2.					Assoc Director			0.0	0.0	9,075.00	3,830.00	12,905.00
					for Primate							
					Services							

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

34,089.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		5,542.00	2,339.00	7,881.00
1	Core Manager	Excluded by Requester			58,675.00	32,457.00	91,132.00
1	Immunology Technical Support:	Excluded by Requester			25,500.00	14,106.00	39,606.00
1	Pathogen Detection Technical Support			Excluded by Requester		13,000.00	7,191.00
4	Total Number Other Personnel					Total Other Personnel	158,810.00
					Total Salary, Wages and Fringe Benefits (A+B)		192,899.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,090.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,090.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	30,900.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	31,930.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	227,919.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	227,919.00	51,738.00
Total Indirect Costs			51,738.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	279,657.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IPDRC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	16,137.00	5,877.00	22,014.00
2.					Assoc Director for Primate Services			0.0	0.0	9,075.00	3,964.00	13,039.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

35,053.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		5,708.00	2,493.00	8,201.00
1	Core Manager	Excluded by Requester			60,436.00	34,519.00	94,955.00
1	Immunology Technical Support:				26,265.00	15,002.00	41,267.00
	Excluded by Requester						
1	Pathogen Detection Technical Support	Excluded by Requester			13,390.00	7,648.00	21,038.00
4	Total Number Other Personnel					Total Other Personnel	165,461.00
					Total Salary, Wages and Fringe Benefits (A+B)		200,514.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,183.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,183.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	31,827.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	32,888.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	236,585.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	236,585.00	53,705.00
Total Indirect Costs			53,705.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	290,290.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IPDRC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	16,621.00	6,236.00	22,857.00
2.					Assoc Director for Primate Services			0.0	0.0	9,075.00	4,082.00	13,157.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

36,014.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester		EFFORT	5,880.00	2,645.00	8,525.00
1	Core Manager	Excluded by Requester			62,249.00	36,613.00	98,862.00
1	Immunology Technical Support:				27,053.00	15,912.00	42,965.00
	Excluded by Requester						
1	Pathogen Detection Technical Support	Excluded by Requester			13,791.00	8,111.00	21,902.00
4	Total Number Other Personnel					Total Other Personnel	172,254.00
						Total Salary, Wages and Fringe Benefits (A+B)	208,268.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,278.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,278.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	32,782.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	33,875.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	245,421.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	245,421.00	55,711.00
Total Indirect Costs			55,711.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	301,132.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IPDRC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	17,119.00	6,611.00	23,730.00
2.					Assoc Director for Primate Services			0.0	0.0	9,075.00	4,208.00	13,283.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

37,013.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		6,056.00	2,808.00	8,864.00
1	Core Manager	Excluded by Requester			64,116.00	38,854.00	102,970.00
1	Immunology Technical Support:				27,864.00	16,886.00	44,750.00
	Excluded by Requester						
1	Pathogen Detection Technical Support				14,205.00	8,608.00	22,813.00
	Excluded by Requester						
4	Total Number Other Personnel					Total Other Personnel	179,397.00
						Total Salary, Wages and Fringe Benefits (A+B)	216,410.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,376.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,376.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	33,765.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	34,891.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	254,677.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	254,677.00	57,812.00
Total Indirect Costs			57,812.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	312,489.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IPDRC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE**BUDGET JUSTIFICATION**

All funds requested in the Core are for developmental and administrative activities only. Services provided to users are fully charged to those activities based upon approved rates.

PERSONNEL

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Associate Director Primate Services				
	Affiliate Scientist				
	Core Manager				
	Technician				
	Technician				
	Technician				
	Laboratory Manager				

Excluded by Requester is the Manager, Clinical Pathology Laboratory; her support is shown in Anatomic and Clinical Pathology Services.

Excluded by Requester MD, PhD, Core Scientist EFFORT months % Effort Excluded by Requester

is Assistant Professor in the Department of Medical Microbiology and Immunology, School of Medicine. He is an expert in immune responses to agents of chronic infection, including SIV, HIV, and HCV, especially on encounter with the developing immune system. As Core Lead, Excluded by Requester will be responsible for the overall direction of the Core and for coordination of all activities. He will provide oversight of day-to-day work in the Immunology component of the Core, directing developmental activities, interfacing with clients, overseeing staff, and reviewing data before release.

Excluded by Requester DVM, DACLAM, Associate Director for Primate Services EFFORT months % Effort Dr.

Excluded by is Associate Professor in the Department of Medicine and Epidemiology, School of Veterinary Medicine. He is responsible for the clinical operations in Primate Services as well as the Specific Pathogen Free (SPF) colonies. Excluded by Requester has responsibilities for the clinical pathogen detection components of the Core.

Excluded by Requester DVM, PhD, Affiliate Scientist EFFORT months % Effort Excluded by Requester is a

Research Virologist at the CNPRC with expertise in the study of viral pathogenesis and the effects of antiviral drug treatments. Excluded by Requester has supervisory responsibility for the scientific pathogen detection components of the Core, including oversight of assay development activities, primary management of Ms. Excluded by and publication of results. In addition, he will produce SIV viral stock, which will be made available for distribution to qualified scientists on a recharge basis.

Excluded by Requester Core Manager EFFORT months % Effort Excluded by Requester is a certified Senior Clinical Laboratory Scientist and serves as the Core Manager. She has primary responsibility for maintenance of the laboratory and oversees all aspects of Quality Control and Quality Assurance for the Core. Excluded by Requester has extensive expertise in all technical aspects of Core services and has been a member of the pathogen detection services since its inception.

Excluded by Requester Technician EFFORT months % Effort Excluded by Requester provides primary technical support for serology assays. This work includes ELISAs, multiplex microbead immunoassays (Luminex), slide arrays, immunohistochemistry, western blot, and immunofluorescence.

Excluded by Requester

Technician

EFFORT

months

% Effort

Excluded by Requester

provides technical support primarily dedicated to immunology activities, including isolation of cells, preparation of nucleic acid, real time PCR, cellular immunology assays, and data collection on Core cytometers. He will also help to develop new immunology assays under the supervision of

Excluded by Requester

provides additional technical support in the Core and is supported by program income.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are listed in the **Facilities Improvement** section.

TRAVEL

\$3,000 is requested (2 x \$1,500) to attend professional meetings annually to advertise the Core services to the greater research community and update on new developments and research applications.

SUPPLIES

\$30,000 is requested for necessary laboratory supplies, reagents, and miscellaneous supplies to support the technical development of new methodologies in the Core.

OTHER EXPENSES

\$1,000 is requested for manuscript submissions related to new assays and techniques.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		175,161.00
Section B, Other Personnel		827,703.00
Total Number Other Personnel	20	
Total Salary, Wages and Fringe Benefits (A+B)		1,002,864.00
Section C, Equipment		0.00
Section D, Travel		15,927.00
1. Domestic	15,927.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		164,584.00
1. Materials and Supplies	159,274.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,183,375.00
Section H, Indirect Costs		268,627.00
Section I, Total Direct and Indirect Costs (G + H)		1,452,002.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

Excluded by Requester

2. Human Subjects

Clinical Trial? ☒ No ☐ Yes

Agency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	350,000.00	Services
2	369,250.00	Services
3	389,559.00	Services
4	410,985.00	Services
5	433,589.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

IPDRC_SpecificAims.pdf

3. Research Strategy*

IPDRC_ResearchStrategy.pdf

4. Progress Report Publication List

IPDRC_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

IPDRC_Vertebrate_Animals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

IPDRC_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE

SPECIFIC AIMS

The Immunology and Pathogen Detection Resources Core provides routine and specialized laboratory diagnostic and research assays and expertise necessary to address respiratory and infectious disease immunology and pathogen detection needs. The Core provides a unique portfolio of laboratory tests and leverages personnel and equipment used for immunology assays and pathogen detection. The Immunology component of the Core aims to provide state-of-the-art assistance, from start to end, for research studies with an immunologic component. This includes experimental design (e.g., assays, samples, costs, available control data), execution (e.g., sample processing, performance of immunology assays), and data analysis/interpretation. The Pathogen Detection component of the Core continues to be the leading reference laboratory nationally for nonhuman primate infectious disease testing while fulfilling the mission to improve the nonhuman primate resource. The Core will remain at the forefront of scientific discovery relevant to pathogens and immune responses as well as advancements in reagents and technology leading to the development of new methods.

Specific Aim 1. Provide state-of-the-art research assays relevant to nonhuman primate models of human disease and nonhuman primate colony health.

Plan. The Core will work collaboratively with investigators at the California National Primate Research Center (CNPRC) and through the National Primate Research Centers (NPRCs) program to gain further insight into the biology of infectious agents and nonhuman primate immune responses throughout life. New discoveries in immunology and infectious disease provide the impetus for the application of new technological advances in reagents, equipment, and methods to relevant, ready-to-use or custom assays for research as well as diagnostic purposes (including management of conventional and Specific Pathogen Free, SPF, colonies). Most testing is currently performed on blood or tissue samples. However, current publications have shown that with newer equipment and methods, other sample types requiring less invasive collection procedures can be used for diagnosis and research, sometimes with improved sensitivity and specificity. For example, the Immunology component of the Core has optimized methodologies to obtain immunologic information from stool samples to minimize costly and invasive biopsies. Further pursuit of this work could result in useful field assays and lower testing costs. Such approaches are particularly valuable for field studies and internationally in resource-poor areas. In addition, database management and other Information Technology improvements will facilitate delivery of sample data and validation of our techniques.

Specific Aim 2. Provide exceptional expertise and services to researchers at the regional, national, and international levels.

Plan. In addition to directly performing assays on submitted samples, the Core has a long-standing history of providing support in experimental design, assisting in data analysis/interpretation, and sharing resources (e.g., test protocols, reagents, and reference samples). The Core's service-oriented effort also includes preparation of infectious simian immunodeficiency virus (SIV) stocks for investigators and the provision of cell samples from various tissues for identification of tissue-resident immune cells. The Core and the related equipment are available for use by others once trained. Outreach in the proposed funding period will be increased via electronic mail and website enhancements.

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

Plan. Core faculty and staff provide training and consultation to both internal and external students and scientists, and regularly participate in activities at the CNPRC, the NPRC Consortium, and UC Davis campus committees and working groups to contribute their expertise in immunological and pathogen detection testing and ensure that the highest quality standards of animal care and research are met. These activities result in improved colony health and better utilization of the nonhuman primate research models of human diseases while ensuring that the highest standards for responsible conduct of research and animal care are maintained.

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE

RESEARCH STRATEGY

INTRODUCTION

The Immunology and Pathogen Detection Resources Core (Figure 1) plays a critical role in nonhuman primate research and colony management at the California National Primate Research Center (CNPRC). The Core provides specialized expertise and services necessary to support investigators and to address the rapid evolution of scientific knowledge about pathogens and immune responses. In this role, the Core serves an important function as a “go to” resource for both up-to-date testing facilities but also for guidance about types of assays needed in research and colony management. Considering the importance of immunology and pathogen detection in many disease conditions throughout the lifespan, the Core serves an essential function as a resource for other institutions nationally and internationally.

The Core provides vital support for the CNPRC through laboratory diagnostic and research assays and expertise in respiratory and infectious disease immunology and pathogen detection. The Core has a long and successful track record and has been critical to the scientific mission of the CNPRC as well as provided a rich resource to optimize the health of the colony. Continuation of this successful track record requires that we remain at the forefront of scientific discovery about pathogens as well as advancements in reagents and technology relevant to the development of new methods. The present proposal aims to set the stage to allow such a positive trajectory. Core members, shown in Table 1, are deeply committed to the scientific, service, and educational missions of the Core, and have a strong history of outreach and service to the scientific community.

Figure 1. Organizational Chart: Immunology and Pathogen Detection Resources Core

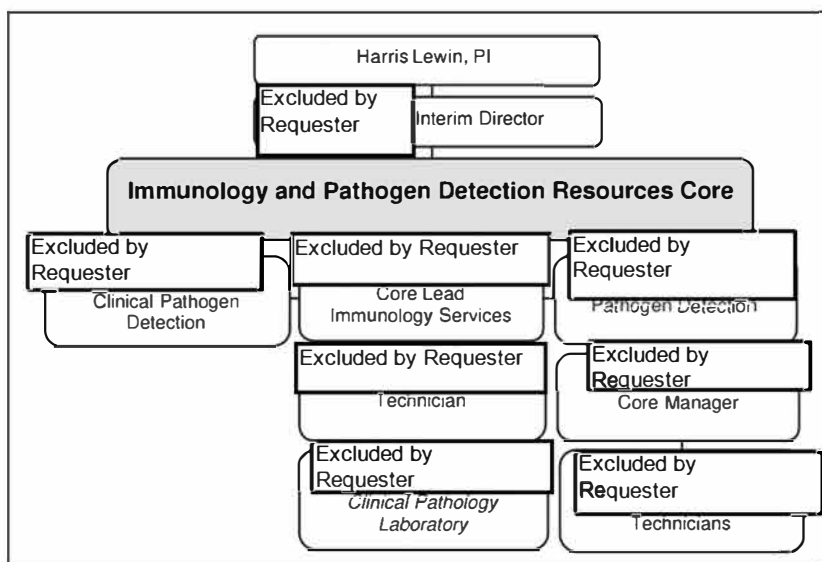


Table 1. Immunology and Pathogen Detection Resources Core Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Medical Microbiology and Immunology, School of Medicine	Core Scientist
	Department of Medicine and Epidemiology, School of Veterinary Medicine	Associate Director of Primate Services
	CNPRC	Affiliate Scientist
	CNPRC	Core Manager
	CNPRC	Technician
	CNPRC	Technician
	CNPRC	Technician
	CNPRC	Clinical Pathology Laboratory

Sources of support for the Immunology and Pathogen Detection Resources Core in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 2. Support for the Immunology and Pathogen Detection Resources Core

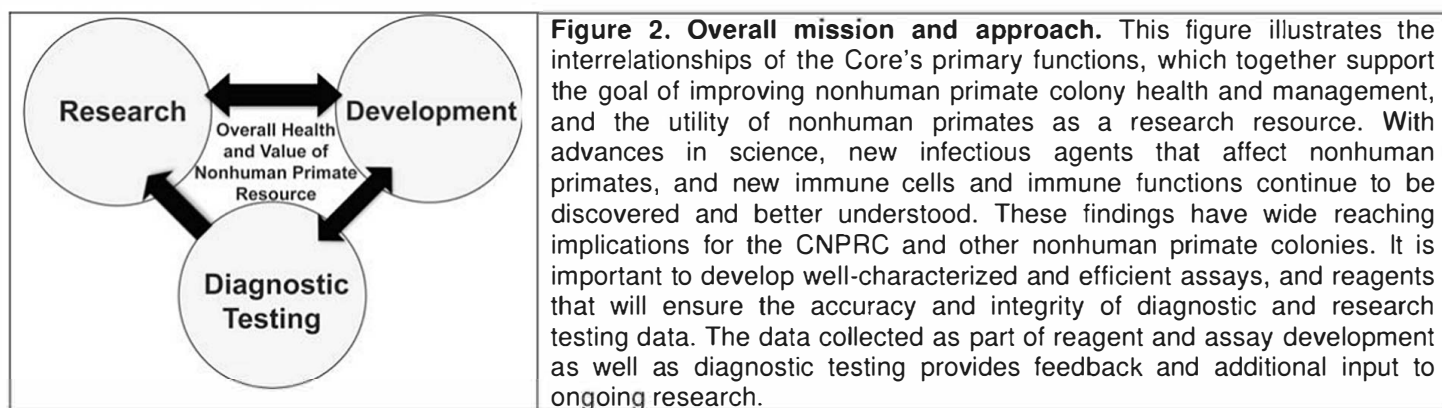
	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$202,465	\$218,773
Program Income from P51	\$305,000	\$350,000
Other Sources	\$0	\$0
TOTAL	\$507,465	\$568,773

Response to Summary Statement.

reviewers' comments

SIGNIFICANCE**Progress and Major Accomplishments: Contributions to the CNPRC Mission**

The Core is an integral component of the CNPRC and supports the overall mission of meeting the needs of local, national, and international investigators in a broad variety of areas using a combination of services, development, research, and training (Figure 2).



The Pathogen Detection Laboratory was started in 1987 as an outgrowth of the "AIDS Virus Diagnostic Laboratory", which was highly regarded for its role in applying clinical diagnostic standards to research methods in the early years of HIV diagnostic test development. Under the direction of Excluded by Requester and with funds from the NCRR, the mission was to develop and offer testing for nonhuman primates in order to develop Specific Pathogen Free (SPF) colonies and improve overall nonhuman primate colony health. From its inception the Pathogen Detection Laboratory functioned as both a research and diagnostic laboratory, and quickly became self-supporting. At that time, the service tested over 10,000 samples from more than 100 clients for up to six different agents and generated a gross income exceeding \$1 million annually. The service also played a leading role as a reference laboratory, providing training and technology transfer (via training, protocols, characterized controls and reagents, and proficiency testing) to enable other SPF colonies to set up laboratories to perform their own testing in-house. The success of these efforts has led to a decrease in routine testing volume; however, there continues to be a need to develop new and improved tests as science and technology advance, leading to the discovery of new pathogens and more sophisticated technologies that can be used to detect those pathogens.

In 2010, and in response to recommendations made prior to the last competitive base grant renewal, the Pathogen Detection Laboratory and the newly formed Infectious Diseases Immunology Core and Respiratory Diseases Immunology Core were integrated together with other Cores into the Analytical and Resource Core (ARC). In March 2013 the CNPRC National Scientific Advisory Board recommended to better define Cores and dismantle the ARC structure ("*...the Pathogen Detection Laboratory should remain as a stand-alone core because of its significant breadth and volume of activity for both Core Scientists and off campus investigators*"). In 2014 it was determined that the Pathogen Detection Laboratory would be best linked with immunology services under the umbrella of the Immunology and Pathogen Detection Resources Core because of overlap in mission and to leverage resources (including personnel and equipment). Due to changes in personnel

(including [Personal Info] in 2012). [Excluded by R equester] a virologist, took on the scientific leadership for Pathogen Detection [Excluded by R equester] Associate Director for Primate Services, assumed responsibility for the clinical Pathogen Detection services and SPF colonies, and [Excluded by R equester] immunologist, assumed leadership for the immunology section. The Flow Cytometry services, which previously was included in the Clinical Pathology Laboratory has been integrated into the Immunology component of the Core to provide synergy and efficiency of scale, and [Excluded by R equester] was selected as the Core Lead. Taking advantage of yet another effort to leverage resources, research flow cytometry assays are now made available through the Core structure using shared supervision and equipment with the Clinical Pathology Laboratory (a function served by [Excluded by Requester] see **Anatomic and Clinical Pathology Services** in Primate Services).

During the current funding period (May 1, 2010 to April 30, 2014) the Core processed and analyzed 50,481 samples for the CNPRC colonies (28,821), other NPRCs (17,091), national academic institutions (3,316), NIH-funded studies nationally (436), and other sources such as the private sector (817). Funds were primarily from end users in addition to support from the P51 base grant for Core activities (see Table 3).

Table 3. Number of Assays (May 1, 2010 to April 30, 2014)

Assay	2010-2011	2011-2012	2012-2013**	2013-2014
	# Tests [^]			
SRV PCR	4,411	3,408	2,556	1,932
STLV PCR	294	228	204	22
SIV PCR	243	217	205	19
SFV PCR	946	634	485	549
RRV PCR	946	631	393	313
Antibody Screening Panels to detect and identify ~ 10 antibodies simultaneously (i.e., 10 EIAs)	4,655	2,566	2,907	3,535
IFA (confirmatory testing for screening results)	552	364	120	64
Western Blot (confirmatory testing for screening)	251	95	279	265
Gamma-interferon Testing for TB	259	82*	130	53
Custom Tissue Culture and Cytokine/Chemokine Studies (in some cases this is the number of studies not individual samples)	13	42	74	72
Flow cytometry samples	8,060	2,749	2,685	1,973

[^]These numbers represent the number of tests reported. The actual number of tests is higher (i.e., PCR is always run in at least duplicate, and have an approximate 10% repeat rate for validation)

*Due to manufacturer problems, gamma interferon reagents were unavailable during most of 2011

**2012 numbers are low because weather forced cancellation of much of the routine CNPRC SPF colony sample collection

During this period, the Core has been highly active in:

- Support of colony management and health (both SPF and conventional colonies).
- Support of research projects and development of nonhuman primate models of human disease, including projects carried out in collaboration with the CNPRC Infectious Diseases Research Unit.
- Development and validation of new or enhanced assays.
- Performance of diagnostic and research testing.
- Consultation, technology transfer, training/mentoring, troubleshooting, and provision of reagents and protocols.

Some examples of these activities are provided below.

Service Activities. The Core provides testing services to local, regional, national, and international research colonies (both SPF and conventional), zoological collections, veterinary laboratories, commercial colonies, and veterinary practices of all sizes. Methods and reagents are validated, standardized, and controlled by in-laboratory studies and proficiency testing. The Pathogen Detection component maintains reference banks of characterized specimens. Test methods include ELISA, immunofluorescence assay (IFA), Western Blot, Multiplex Microbead Assay, Slide Array, immunohistochemistry, *in situ* hybridization, and PCR. Agents include simian betaretrovirus (SRV), simian immunodeficiency virus (SIV), simian T-cell lymphotropic virus (STLV), Herpes B virus, measles, simian foamy virus (SFV), rhesus rhadinovirus (RRV), rhesus cytomegalovirus

(RhCMV), simian parvovirus, and tuberculosis (TB). The current workload is approximately 7,500 samples and \$350,000 annually (Table 3).

Other services provided to a growing number of investigators and projects include the following:

- During 2010-2014, 28 investigators made use of the Immunology services. The number of samples analyzed expanded from ~250 to ~750 in 2012-2013. This number excludes many blood, tissue, and fluid samples that was processed by the Immunology component of the Core and then provided to investigators for further analysis, and also excludes flow cytometry samples shown in Table 3. Approximately 40% of samples processed by the Immunology component of the Core originated from CNPRC researchers (particularly the Infectious Diseases Research Unit), 20% from other UC Davis researchers, and ~40% from other collaborating academic investigator.
- During 2010-2014, a total of 1,431 vials of infectious SIV stock were provided on a recharge basis to 12 investigators/research laboratories (8 at UC Davis, 4 external); most of this virus was used for *in vivo* studies in macaques, primarily funded by the NIH. In particular, stocks of highly virulent SIVmac251 are a unique resource that an increasing number of investigators are requesting.
- The Immunology component maintains CNPRC flow cytometers, which are in nearly constant use by investigators who analyze a very large number of samples collected daily at the CNPRC. Training in the use of flow cytometers, as well as maintenance of this equipment, constitutes an important part of the service to the CNPRC and outside investigators. For example, the Immunology component of the Core has trained outside investigators in functional regulatory T-cell assays as well as flow cytometric analysis of gut tissue-derived cell populations.

Table 4. Summary of Clients

	2010-2011	2011-2012	2012-2013	2013-2014
Core Scientists	18	14	17	14
UC Davis Investigators	7	9	10	6
Other Affiliate and Visiting Scientists	52	41	40	21
Total Institutions	43	37	39	25

Developmental Activities. The Pathogen Detection component of the Core developed and validated improved panels for pathogen detection using either commercial or in-house reagents; PCR and antibody assays were reviewed and optimized to include newly discovered agents and to take advantage of new developments in technology. Currently, the need for better TB diagnostics is a major focus. Examples of specific accomplishments include the following:

- Validated selected commercially available (EMD-Millipore, Invitrogen, R&D Systems) and in-house multiplex cytokine/chemokine panels on various macaque sample types including tissue culture supernatant, plasma, saliva, and dried blood spots.
- Demonstrated the use of recombinant antigens to replace viral lysates for the routine detection of antibodies against a panel of nonhuman primate pathogens. The recombinant antigen panel is as accurate as viral lysates and is potentially safer and more economical [Excluded by Requester 2011].
- Validated SRV PCR probes and primer sets for all known serotypes including some new SRV4 isolates that have been reported since 2010. This work is ongoing as the Core continues to validate and, if needed, develop new reagents to detect newly discovered isolates [Excluded by Requester 2010].
- Re-optimized and evaluated the existing SRV PCR primers and probes on newer-generation reagents and instruments. This work is in progress but data generated thus far have shown it to be superior to the current equipment, reagents, and protocol.
- In support of a vaccine trial, adapted and optimized a microbead immunoassay using a panel of measles antigens for total and neutralizing antibody titration assays for measles virus in rhesus macaques. This work has been expanded and is continuing with other candidate vaccines.
- Outreach has been improved through a newly designed web page that provides an overview of current services including assays, reagents, consultations, and custom services. Lists of test agents, methods, and rates as well as instructions for sample submission are available. In addition, the Core sends routine electronic mail and postal mailings, presents at nonhuman primate meetings, and provides an electronic mail and voicemail contact that is answered within one business day.

The Immunology component of the Core developed and validated new functional assays and flow cytometry panels and is currently focused on developing improved assays for natural killer (NK) cell (and other innate lymphoid cell) phenotypes and activities. Other accomplishments include:

- Optimization of intracellular staining for T-bet and eomesodermin in macaque T-cells, to allow identification of exhausted T-cell subsets.
- Creation of new flow cytometry panels allowing identification of group 1 and group 2 innate lymphoid cells (ILC1s and ILC2s) in macaques.
- Installation of the ViiA7 real-time PCR system for cytokine message detection.
- Development of appropriate reference genes for quantitative PCR techniques (GAPDH, RPL13a, and RPL32).
- Addition of a service for RNA integrity testing with the Agilent Bioanalyzer microfluidics system.
- Identification of surface markers for macaque Th17 cells and establishment of correlation with functional capacity.

Research Activities. Some examples include the following:

- A sampling of publications from the current funding period demonstrates progress in understanding the transmission and pathogenesis of simian betaretrovirus, RRV, retroperitoneal fibromatosis herpesvirus, SFV, chikungunya virus, calicivirus and mycobacterium. Excluded by [redacted] 2011; Excluded by [redacted] 2010; Excluded by [redacted] 2014; Excluded by Requester [redacted] 2014; Excluded by [redacted] 2011; Excluded by [redacted] 2010; Excluded by [redacted] 2012; Excluded by [redacted] 2010; Excluded by Requester [redacted] 2014; Excluded by Requester [redacted] 2011; Excluded by [redacted] 2010]. Manuscripts presenting findings related to borna virus in neurological disease, listeria, and simian parvovirus in fetal loss, and perturbed immune system cytokine profiles in simian T-cell lymphotropic virus infection have also been published or are in preparation. Excluded by [redacted] 2013].
- One highlight is a collaborative project with investigators at the University of California, San Francisco on the identification of a novel adenovirus that correlated with a sudden high-mortality outbreak of respiratory disease in the CNPRC titi monkey colony. The putative cause was isolated and propagated in the Core. Excluded by [redacted] et al., 2010].
- Similarly, the Core and co-investigators from the Center for Infection and Immunity of Columbia University received ARRA supplemental funds to investigate the prevalence and implications of known and novel pathogens in the imported macaque population and subsequent undiagnosed respiratory disease, enteric disease, and rash or febrile illness; while also investigating the microbiome in both healthy and symptomatic macaques. Several isolates have been identified and this work continues under the direction of [redacted] at Columbia. Another continuing project is the "*Evolution, Recombination, and Emergence of Simian Retroviruses in Bangladesh*" in collaboration with [redacted] at the University of Washington. Excluded by Requester [redacted] **Infectious Diseases Research Unit** serves as the on-site PI (and PI for the subcontract) for all aspects of the work conducted in the Core.
- The Core contributed to a variety of scientific projects in the current funding period including collaborations with the **Infectious Diseases Research Unit** and **Respiratory Diseases Research Unit**. Excluded by [redacted] 2012; Excluded by [redacted] 2012; Excluded by [redacted] 2011; Excluded by Requester [redacted] 2012; 2014]. A sampling of the resulting publications demonstrates contributions to understanding reactive airway disease, influence of breast milk on immune development, SIV vaccine responses, antiviral drug therapy, tuberculosis vaccines, and mucosal integrity in SIV infection.
- A particular highlight was participation in developing assays for both circulating and gut-resident Th17 cells in SIV-infected macaques. Excluded by Requester [redacted] et al., 2012]. The work involved physical or flow cytometric sorting of cells bearing candidate surface markers; optimization of protocols for purification of functional Th17 cells from gut tissue; and assessment of the potential of flow cytometric or immunohistologic staining protocols for detecting cytokine transcription factors expressed in Th17 cells.
- Profiling immunologic differences between nursery-reared and dam-reared infants was also accomplished (manuscript in press). This work is a result of the Core's focus on lifespan health issues and has led to a new understanding of variable immune function in colony animals.

Training. From 2010 onward, the Core has trained 19 graduate students and 14 undergraduate students. The Core also provided testing, consultation, materials, and/or training to over 60 institutions, including seven other NPRCs, three NIH/PHS agencies, 26 academic institutions, eight zoological parks, and 17 others private

entities. Two veterinary medicine residents performed their residency research projects with the Core as noted below.

The Core also played an active role in conducting applied clinical research in nonhuman primate medical care. Veterinary medicine residents and veterinarians at the CNPRC have completed their residency and laboratory animal medicine board qualifying projects in collaboration with the Core. Examples include [Excluded by Requester] studies on idiopathic chronic diarrhea in colony animals and participation of clinical veterinarians in the study of SPF and conventional colony viral status and management [Excluded by Requester] [2013] [Excluded by Requester] [2012]; [Excluded by Requester] et al., 2014 [Excluded by Requester] [2013]. Their projects not only fulfilled the required research experience for the residents but also focused on a significant colony management/medical care problems and supported clinical practice in this field. The addition of [Excluded by Requester] will strengthen these efforts in the next funding period particularly for the SPF colonies.

INNOVATION

Unique Services and Research Opportunities for the Nonhuman Primate Research Community

The Core has a history of developing and improving assays and to stay current with the latest advances in pathogen detection and immunology. Through collaborative partnerships with national and international investigators, the Core will continue to remain at the forefront of scientific discovery. Examples of innovation include:

- Nonhuman primate colonies are exploring the expansion of the SPF definition to include additional agents. As the colonies determine the agents to include, the Core will be at the forefront in developing assays to detect those agents.
- New and improved assay protocols will be needed as new infectious agents or serotypes are discovered. For example, a review of published literature reveals the recent discoveries of several new simian betaretrovirus, STLV, and SFV types which could impact nonhuman primate colonies. As the current assays were formatted prior to these discoveries, it will be important to determine if they can detect these new agents or if new reagents and assays will need to be developed. The Core is in an excellent position to perform this testing and to develop new assays based on its extensive history and successes.
- The Core regularly reviews performance characteristics of all equipment and assays in relation to the latest published literature and new developments. The Core continues to explore both in-laboratory and commercial liquid and solid matrix array platforms for potential diagnostic use in nonhuman primates. Refinement of the assays is continuously ongoing and the Core remains at the research frontier of these efforts.
- Many immunology laboratories have specialized in measurement of adaptive (i.e., inflammatory) immune responses to vaccines and infectious diseases. In contrast, the Core has a longstanding expertise in other immune axes, most importantly: tolerogenic responses that can be seen in infant animals, counter-regulatory responses seen in chronic viral infections (e.g., IL-10 production, Eomes expression, and/or PD-1 expression), Th2 responses seen in allergy or helminth infection, and the innate responses to infection manifested in antigen-presenting cells and innate lymphoid cells.
- The Immunology component of the Core has a unique developmental focus, as it is frequently consulted regarding the immunologic implications of colony management practices, including feeding practices, antibiotic administration, and SPF status. These requests for consultation have resulted in an innovative emphasis on understanding the diversity of immune system ontogeny of particular importance with the CNPRC focus on lifespan health. Substantial resources have been dedicated through research collaborations and funded NIH grants to understand which immunologic parameters are most variable in nonhuman primate infants and which are most impacted by management practices. There is an accompanying newer effort to understand the aged immune system, especially those features reminiscent of the immune "exhaustion" seen in chronic viral infection.
- The Immunology component of the Core uses innovative analytic tools. Efforts to understand developmental variability has required the novel application of sophisticated bioinformatics and statistical tools to immunologic data. For example, frequency information for over 150 different immune cell phenotypes in breast- and bottle-fed infants has been accumulated. Analysis of these data required application of statistical techniques more commonly used for analysis of "-omics" data, including principal component analysis, clustering of both experimental subjects and variables, and random forest techniques. Use of these analytic tools aids in understanding the totality of the influence of colony management

practices on the immune system. This innovative approach is the result of interaction between Core staff and the UC Davis Host Microbe Systems Biology Core, led by Excluded by Requester Core Scientist, Infectious Diseases Research Unit.

APPROACH

The goals and activities of the Core are in direct alignment with the overall Specific Aims of the CNPRC through a focus on research, service, and training, which all result in improved colony health and better utilization of the nonhuman primate research resource across the lifespan.

Specific Aim 1. Provide state-of-the-art research assays relevant to nonhuman primate models of human disease and nonhuman primate colony health.

The Core must recognize important research trends and respond effectively, providing services and assays that allow continued success as the research environment changes. Newer-generation equipment and reagents need to be evaluated and adopted for various assays. There is the need to develop new PCR tests to detect new strains or new organisms discovered since current protocols were instituted. In addition, the increasing availability of recombinant and inactivated virus antigens provide improved targets for antibody detection against a growing number of nonhuman primate viruses. Similarly, ongoing advances in immunology require that new assays for newly identified cell types or immune functions be made available to investigators. New and improved assays and methods will lead to better characterization of the pathogen and immune profile of the macaque, making it a healthier, better pedigreed, better controlled research model and thus improving the nonhuman primate lifespan health resource. As part of Specific Aim 1, four goals are proposed.

Goal 1. Development and Optimization of PCR and Antibody Detection Assays. Since PCR testing is dependent on the functionality of equipment, the Core will need to replace aging equipment to ensure: (1) optimal quality, (2) cost-effectiveness, and (3) sustained service support from manufacturers. Newer-generation equipment and reagents will need to be evaluated and adopted for routine PCR testing. A review of published literature and parallel studies using current protocols demonstrates the need to develop new PCR tests which will detect strains of SRV, STLV, and SFV discovered since current protocols were instituted. In addition, the increasing availability of recombinant and inactivated virus antigens provides improved targets for antibody detection against a growing number of nonhuman primate viruses. Specific projects under consideration include:

- **SRV PCR.** The Core plans to further optimize SRV PCR testing by evaluating the BioRad and Roche systems and 3 or 4 other mastermixes before the final combination of equipment, method variables, and reagents can be determined and validated for improved efficiency at reduced cost per sample.
- **STLV PCR.** From parallel studies with other laboratories, it is known that the Core's STLV PCR assay developed in 2004 is less sensitive than some of the newer assays. The goal is to re-optimize using newer reagents and methodologies.
- **SFV PCR.** Since the assay was developed in 2005, a number of new isolates have been found, some of which still need to be sequenced. The Core will need to determine if the current assay works or if new primers and probes need to be designed to re-optimize the assay.
- **Multiplex Viral Antibody Panel.** The Core has successfully validated and incorporated recombinant and viral lysate antigens for B Virus surrogate, SRV, STLV, SIV, and Measles into the standard assay. The Core plans to also focus on a newly available inactivated B virus (not a surrogate), SV40, lymphocytic choriomeningitis virus (LCMV), new RRV recombinant, and RhCMV. In addition, the Core will evaluate the feasibility of meeting requests for additional parvoviruses, filoviruses, flavivirus, and adenovirus assays.
- **B Virus Confirmatory Test.** The National B Virus laboratory recently made inactivated antigen available for purchase. Up until now the Core has not had an assay that uses actual B Virus. This will be an important tool to confirm screening results generated from testing with surrogate markers such as HVP2 or HSV.
- **TB Antibody Testing.** Skin Testing and interferon gamma release assays like Primagam lack sensitivity (especially in latent cases). Enhancements have been proposed to these cellular immune assays and also an enhanced testing algorithm that includes humoral antibody assays to recombinant or synthetic peptides. This work continues in collaboration with several investigators opportunistically as appropriate samples and reagents become available.

- **Confirmatory RhCMV Test.** Some research methods (indirect IFA, western blot) exist but none are suitable for routine diagnostic use to confirm reactive RhCMV antibody screening results. RhCMV is one of the SPF Level 2 agents and represents an unfulfilled need for immunological detection.
- **Parechovirus Antibody Test.** Some Luminex and IFA work has been done on these agents in a research mode. Although the assays are not yet accurate or sufficiently robust for routine use, the data are sufficiently promising to prompt further development for diagnostic use. If successful this may have direct application to screening the CNPRC colony.

Goal 2. Development and Optimization of Flow Cytometry-based Immune Assays. Recent and ongoing projects in the Core include:

- **Definition of Surface Markers for Macaque Th17 Cells.** Mucosal immunology is a traditional strength at UC Davis and Th17 cells are prominent in the mucosal immune system. Investigators proposing either expansion or depletion of Th17 cells need to know if the cells can be identified based on surface markers alone, to allow sorting or depletion of live cells. The Core evaluated CCR4 and CCR6 expression on rhesus macaque Th17 cells (identified by intracellular cytokine staining) and IL-17 expression within sorted CCR4+ and CCR6+ cells, in order to determine if these chemokine receptors were reliable markers of Th17 cells. It was found that almost 100% of circulating macaque Th17 cells are CCR6+, leading to the proposal that CCR6+ cells expanded *in vitro* could be used to augment Th17 cell populations.
- **Optimization of Intracellular Eomesodermin Staining.** Eomes (eomesodermin) expression is up-regulated during chronic LCMV infection of mice and supports CD8+ T-cell exhaustion. There is accordingly tremendous interest in knowing whether Eomes expression might also be associated with other chronic viral infections, such as SIV infection. Therefore, the Core recently evaluated various permeabilization techniques and antibodies in order to define conditions that are suitable for Eomes staining in nonhuman primates.
- **NK Cell Memory Phenotyping.** Once considered purely short-lived, rapid responders, NK cells now straddle the line between innate and adaptive immunity, possessing limited antigenic specificity, an extended lifespan, and mediating enhanced recall responses. The memory capabilities of NK cells have been clearly shown in the setting of murine CMV infection but less clearly in humans. Nonetheless, the activating CD94–NKG2C receptor appears to be important in human CMV (HCMV) recognition. Human NK cells expressing NKG2C exist at a high frequency in HCMV-seropositive healthy subjects, as compared with HCMV-seronegative individuals. A unique subset of NK cells that expresses NKG2C at high levels and the maturation marker CD57 persists at an elevated frequency in HCMV-seropositive individuals and increases after HCMV reactivation. The Core is planning to work closely with Core Scientist Peter Barry (**Infectious Diseases Unit**) to determine if CD94 and/or CD57 are reasonable candidates for NK cell memory markers in RhCMV-exposed macaques. If so, then RhCMV infection of macaques would be a perfect NK cell memory model with relevance to humans.
- **Quantitation of CCR4 Expression on T-cell Subsets.** Sakaguchi and colleagues have shown that anti-CCR4 monoclonal antibody selectively depletes human effector-type FoxP3⁺CD4⁺ regulatory T cells *in vitro*, evoking antitumor immune responses [Excluded by Requester 2013]. If this were also true of macaques, then depleting anti-CCR4 antibodies might provide a route to depletion of Tregs *in vivo* and elucidation of their role in pathogenesis of various disease states. The Core will therefore measure the density of CCR4 receptors on macaque Tregs and other T-cell subsets.

Goal 3. Alternative Sample Types for Diagnostic and Research Testing. Most of the Core's testing is performed on blood or tissue samples. Current publications have shown that with newer equipment and methods, other sample types requiring less invasive collection procedures can be used for diagnosis and research, sometimes with improved sensitivity and specificity. Some successful initial attempts were made at using alternative sample types (e.g., dried blood spots, saliva, urine, feces) for PCR, antibody, and antigen capture testing. The Core is also testing the limits of immunologic information that can be obtained from stool samples so that costly biopsies can be minimized. Further pursuit of this work could result in useful field assays and lower testing costs. This work is especially applicable internationally in resource-poor areas.

Goal 4. Database Management / Information Technology (IT). Components of the Core currently use a custom LIS database with unique identifiers for each sample. The LIS is a web-based custom [Proprietary Info] database, designed by the CNPRC IT team that allows, for example, tracking of animal information, sample

information, location, investigator/project information, tests requested, results reported, and billing for every sample received. In addition, cumulative reports that track totals for services and investigators can routinely be generated. This application needs to be further enhanced to include electronic test requesting. In addition, every sample and test has a unique identifier number which will need to be replaced or supplemented by a barcode. Further enhancements will be explored to improve the overall services, including linkage to electronic health records and user accessibility.

Metrics. Our success in this aim is best measured by the number of samples tested and the number of scientific manuscripts published using Core data. These outcomes reflect the ability of Core personnel to recognize scientific developments that are important to colony management and/or clients, and to then implement effective response strategies.

Alternative Strategies. As the Core begins to produce greater volumes of information, e.g., from cytokine bead arrays and/or immune profiling approaches, then greater provision of analysis expertise may be useful to our client investigators. Often the utility of data from these approaches is limited by the capacity for proper analysis that is available. Thus, providing more analysis work could result in more publications.

Specific Aim 2. Provide exceptional expertise and services to researchers at the regional, national, and international levels.

In addition to directly performing assays on submitted samples, the Core has a long-standing history of providing technical and intellectual support as well as sharing resources (e.g., test protocols, reagents, test and reference samples) with other laboratories. The Pathogen Detection component of the Core plays a crucial role in resolving individual problem cases and also better characterizing and managing conventional and SPF colonies as a whole; the large archive of sample serves as an important resource for developing new assays and offering services not otherwise available. The Core and related equipment are also available for use by others after the necessary training. To provide optimal services and meet the needs of the research community, the Core will continue to work in close synergy with the **Infectious Diseases Research Unit** and **Respiratory Diseases Research Unit**. As part of Specific Aim 2, four goals are proposed.

Goal 1. Production of Reagents and Provision of Reference Samples. The Core will continue to provide the following opportunities to investigators:

- The Pathogen Detection component of the Core provides protocols, test reagents, reference samples, and proficiency testing to assist many laboratories at other institutions in performing their own diagnostic testing and will continue to perform this function.
- The Core will continue a long history of providing infectious SIV stocks to investigators across the nation for *in vivo* and *in vitro* experiments.
- The Immunology component of the Core will provide cell samples from various tissues for identification of tissue-resident immune cells.

Goal 2. Training on Shared Use of Equipment and Instruments. The Core will continue to provide the following training and equipment use opportunities:

- The Core has a variety of instruments for RNA/DNA and PCR-based assays, including real-time PCR systems (see Equipment for a detailed list). Training and access to automated nucleic acid extraction, ELISA, and multiplex microbead liquid array instruments (Luminex) will continue.
- The flow cytometers at the CNPRC are required for multiple immunologic investigations of all kinds, whether carried out by Core personnel or by investigators analyzing their own samples. The Core is currently equipped with a BD FACSCalibur (standard 4-color assays), a BD FACS Aria (3 lasers, for multicolor flow cytometric analysis and live cell sorting), and a BD Fortessa 5-laser flow cytometer (with a UV laser providing the capability to perform CaFlux assays and Hoechst staining). Investigators interested in using these instruments can choose to run their own assays or have their samples run by a trained technician on a recharge basis. Training in the use of the instruments is available from the Flow Cytometry Service Manager. Excluded by Cell sorting will only be performed by the Flow Cytometry Service Manager and trained technicians supervised by Excluded by. The Immunology component of the Core will perform the staining, acquisition, and analysis of standard panels or will develop new flow cytometric assays to an investigator's specifications. To ensure continued availability and efficient use of the flow

cytometers, all users will be trained and certified by Excluded by Requester before gaining access to the instruments. In addition, users will be referred to the Flow Cytometry Course offered through UC Davis which provides a broad theoretical overview and introduction to advanced techniques, including cell sorting and signaling assays. Continued education will also be accomplished through quarterly invitation of speakers that are experts in flow cytometry for the joint Center for Comparative Medicine and CNPRC Seminar Series.

Goal 3. Consultation Services. Samples from nonhuman primates are extraordinarily precious for both ethical and scientific reasons. The Core can aid investigators to make best use of these samples by providing input at all phases of an experiment.

- In the design phase, the Core provides advice and information on reasonable sampling strategies; consultation on assays achievable given limited sample amounts, particularly for tissue samples; cost information for budgeting purposes; and historical or baseline data, when available, for use in power calculations. For example, a Core Scientist recently requested advice on how best to evaluate immune function in bisphenol A (BPA)-exposed macaques. Based on the suspected spectrum of immunologic effects of BPA, as well as the chemical's known binding targets (including estrogen-related and aryl hydrocarbon receptors), the Core recommended a minimal set of assays covering macrophage activation in response to innate stimuli, T-cell polarization, and Th17 cell differentiation. The Core also provided historical data on variability of these parameters in untreated animals, which were useful for power calculations.
- In the execution phase, the Core can assist in sample processing and performance of assays to any extent desired by the Principal Investigator (PI); in some cases, the Core provides only processing and isolation of immune cells while in others the Core is responsible for every step from processing to analysis. In 2012-2013, for example, the Core participated in a large project comprising collection of more than 400 samples. In this case, the Core performed only plasma collection, peripheral blood mononuclear cell (PBMC) isolation, sample collection at necropsy, and lymphocyte isolation from lymph nodes and gut tissues. The PI chose to perform most immune assays in his laboratory.
- Finally, in the analysis phase, the Core provides both data access through a web-accessible portal and expertise on correct interpretation of the assay results. For example, raw flow cytometry files are made available via an enterprise Box account; FACS file analysis and gating are performed by Core research staff, who prepare a pdf file showing all gates for every sample; the pdf files are reviewed and approved by Excluded by Requester before any data are released. The resultant frequency data are then compiled into tables, which are made available both as CSV files on the Box account and as Heroku Postgresql databases. These tables and a summary of results are then transmitted to the PI.

Goal 4. Increased Outreach. Outreach of Core service activities will be increased via electronic mail and website enhancements. The website has been upgraded using Proprietary Info in alignment with UC Davis' adoption of this web content management system.

Metrics. The success of the Core service mission is measured by the number of tests, reagents, and protocols provided to clients, and the number of people that received training or consultation. An indirect outcome is the number of grants submitted and awarded that result from our technical and intellectual support.

Alternative Strategies. To date, our outreach to new investigators needing service has been primarily achieved through our website, regular postal and electronic mail updates (averaging quarterly), 24-hour telephone call back response, and presentations at symposia and workshops. The Core maintains a client list of over 300 (125 currently active) clients. One alternative strategy to increase services is to provide greater visibility by highlighting testing, consultation, and reference and banked samples on newer electronic platforms (e.g., mobile platforms, social media, CNPRC newsletter). Improved dissemination of information will bring more investigators to the Core. In addition, our existing outreach efforts can be intensified, e.g., through development of a new website and highlighting of Core laboratory services in NPRC Consortium working groups.

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

Core Leads and staff provide training and consultation to both internal and external students and investigators. They also actively and regularly participate in CNPRC activities and committees, the **NPRC Consortium**, and UC Davis campus committees and working groups to contribute their expertise in immunological and pathogen

detection testing and ensure that the highest quality standards of animal care and research are met. These activities will result in improved colony health and better utilization of the nonhuman primate research models of human diseases across the lifespan at the CNPRC, nationally, and internationally. The Core also provides consultation to the UC Davis Occupational Health and Safety Program in reviewing testing and treatment practices in any cases of human exposure to nonhuman primate infectious agents. Through Manager [Excluded by Requester] participation in the NPRCs Breeding Colony Manager's and the SPF Director's Consortia, the Core provides ongoing expert guidance in the establishment, validation, implementation and quality monitoring of appropriate laboratory testing assays and algorithms for management of infectious diseases. [Excluded by Requester] chairs the virus testing subgroup and co-chairs (with [Excluded by Requester] of the Wisconsin NPRC) the TB sub-group. These functions are carried out through educational lectures and panel presentations, hands-on training, protocols, control materials, proficiency testing, and data analysis.

Metrics. The best metrics for this aim include: (1) numbers of students and investigators training on-site with Core staff, and (2) number of co-written grant applications. The latter metric is important because collaboration on grant applications involves teaching collaborators regarding available assays, their best use, and limitations.

Alternative Strategies. Core personnel have provided instruction as invited presenters at various local, national, and international educational workshops, symposiums, and classes and will consider initiating courses or classes, e.g., in flow cytometry or in current markers of specific cell types to increase our contributions.

Timeline. Core priorities are set and work undertaken only in response to requirements for colony management purposes and/or demonstrated demand from clients. For example, work on Goal 1 of Aim 1 was initiated in response to new scientific knowledge indicating a need for better assays to correctly manage the colony; work on Goals 2 and 3 was initiated in response to repeated requests from internal and external Core laboratory clients. In the latter cases, developmental reagent costs are normally shared with interested clients. Thus, commitments of staff time are made only in response to scientific needs and colony management priorities, and financial expenditures are correspondingly minimized.

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VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC.

1. Description of the Proposed Use of the Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal] of indoor animal space. The outdoor animal housing area includes [Specific Animal] field corrals [Specific Animal] corn cribs [Specific Animal] Location. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester]. Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus

as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

- 4. Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
- 5. Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE

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FoxP3+CD4+ regulatory T cells, evoking antitumor immune responses in humans. Proc Natl Acad Sci USA 110:17945-17950, 2013.

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Excluded by Requester

Excluded by Requester

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Excluded by Requester

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Excluded by Requester

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Excluded by Requester

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Excluded by Requester

Excluded by Requester

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CORE SERVICES: IMMUNOLOGY AND PATHOGEN DETECTION RESOURCES CORE RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Inhalation Exposure Core

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename IEC_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	IEC_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	IEC_FacilitiesOtherResources.pdf
11. Equipment	IEC_Equipment.pdf

CORE SERVICES: INHALATION EXPOSURE CORE

ABSTRACT

The primary mission of the **Inhalation Exposure Core** is to serve as a state-of-the-art facility and educational resource for the design, completion, analysis, and interpretation of studies involving health effects of airborne materials. The Inhalation Exposure Core provides short- and long-term generation, delivery, and analysis of precisely controlled atmospheres to investigate human health effects of environmental challenges using both *in vitro* and *in vivo* laboratory animal models. In coordination with Primate Medicine Services, the Inhalation Exposure Core also provides pulmonary function testing and bronchoscopy as outcome measures for health effects as a result of exposures in nonhuman primates. With an emphasis on pulmonary toxicology and animal models of chronic respiratory disease, Inhalation Exposure Core scientists and staff provide critical intellectual expertise and technical support for investigators to conduct research projects that require evaluation of biological responses to atmospheric exposures. The Inhalation Exposure Core provides consultation for the Human Exposure Facilities housed in the UC Davis Human Performance Laboratory, and works directly with investigators in the UC Davis Air Quality Research Center. By partnerships across campus, the Inhalation Exposure Core contributes to broad programs in pulmonary medicine involving the UC Davis Schools of Medicine and Veterinary Medicine and Colleges of Biological Sciences and Engineering. The scope of these programs on the UC Davis campus is to examine the health risks associated with exposure to outdoor and indoor airborne irritants, allergens, and toxins by conducting comparative studies across multiple animal species. Embedded in this rich environment, the Inhalation Exposure Core is ideally placed to support research in acute and chronic human disease by guiding experimental design, developing methodology, executing studies, providing data analysis, and interpretation. The Inhalation Exposure Core is the only such Core facility for inhalation exposure housed within a National Primate Research Center. Through the unique infrastructure, capabilities, and expertise offered by the Inhalation Exposure Core, the California National Primate Research Center (CNPRC) provides an innovative resource to local, regional, and national investigators conducting studies in pulmonary toxicology and animal models of respiratory disease.

CORE SERVICES: INHALATION EXPOSURE CORE

FACILITIES AND OTHER RESOURCES

Laboratories: Proprietary Info

Proprietary Info

Proprietary Info

The Core has the capability to generate a broad range of test atmospheres. The Core delivers atmospheres by multiple modalities (see Equipment). The Core pulmonary function testing laboratory is a unique state-of-the-art facility with equipment to evaluate multiple lung function end-points in infant, juvenile, and adult nonhuman primates.

Exposure Facilities

Chamber or System Type	Number	Exposure Capability
Proprietary Info	8	Aerosols and gases, long-term
	4	Aerosols and gases, long-term
	2	Aerosols and gases, long-term
	2	Indirect calorimetry metabolic rate measurement of a monkey for 24 h
	3	Aerosols and gases, small animals or single monkey for short-term
Cigarette smoke room	1	House nonhuman primates
Clean air room with CBR (chemical, bacteriological and radiological) air filtration	2	House nonhuman primates in clean air
Modular clean air building with CBR (chemical, bacteriological and radiological) air filtration	1	House nonhuman primates in clean air
Concurrent flow spirometry aerosol inhalation system	1	High efficiency aerosol delivery by inhalation to a monkey with simultaneous measurement of respiratory volumes and rates for estimation of dose
Oxygen and ozone inhalation system	1	Adjustable oxygen percentage with or without ozone delivered to a monkey via nasal cannula and tracheal tube
Inhaled steroid delivery system	6	Deliver steroid or other aerosols by mask to awake infant monkeys for 5 to 10 minute dosing periods
PennCentury™ MicroSprayer™	1	Administer liquid spray with droplet size of 16 to 22 µm directly into the lung through a bronchoscope
<i>In vitro</i> exposure system	1	Expose cell culture or explant preparations simultaneously to as many as three levels of ozone or nitrogen dioxide
Isolated-perfused lung exposure system	1	<i>In vitro</i> exposure of isolated and perfused lungs to ozone and other gases
TSE Cigarette Smoke Generator	1	Automatically smokes cigarettes to produce smoke for inhalation exposure purposes
Face Mask Aerosol Delivery System	1	System for delivery of aerosols of diagnostic or treatment compounds in sedated, spontaneously breathing monkeys

Clinical: Clinical care and related procedures in the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology. See Primate Services sections for more details.

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in

other sections of the application. See Primate Services sections for more details.

The chambers and caging were designed in accordance with AAALAC standards. While undergoing exposure, monkeys are housed in stainless steel, open mesh cages. Prior to exposure, animals are given an appropriate period to become acclimated to the chamber environment. Automatic watering systems are used, and the exposure chambers are equipped with spray rings to facilitate daily cleaning. Chamber loading is normally held to an animal volume of less than 1% of the chamber volume. A single level array of cages is used. The chambers are well ventilated with clean air, and daily cleaning. Young monkeys can be housed in small, socialized groups. For long periods in the chambers, adult monkeys are housed in specially designed pair cages for enrichment. These have a removable panel between two cages. Identical chambers in the same room are used for the exposed groups and for the filtered air control groups.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and Information Technology Services provides desktop support and other related services (see other sections of the application). All aspects of the inhalation facility are computer linked and controlled by a central computer using LabView software. Each of the five pulmonary function data acquisition stations has a dedicated computer. Another computer is available for analysis of pulmonary function data.

Office: Four offices (total 577 sq. ft.) house the Core Manager and technical personnel, including the Pulmonary Function Testing technical personnel.

Other: The Primate Center provides the optimal environment for studies with nonhuman primates based on the facilities, support services, and extensive expertise available as described in this application. The facility is also equipped with a shop for instrument repair/fabrication and animal holding rooms for housing animals on ongoing studies. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

CORE SERVICES: INHALATION EXPOSURE CORE**EQUIPMENT*****Major Gaseous Pollutant Monitoring Equipment***

Equipment	Function
9 Teledyne-API ultraviolet ozone analyzers	Continuous analyzers
2 Dasibi ultraviolet ozone monitors	Continuous analyzers
Dasibi oxides of nitrogen analyzer	Continuous analyzer
Teledyne-API dynamic dilution calibrator	Manual or automatic calibration of ozone, oxides of nitrogen, carbon monoxide and sulfur analyzers; absolute ozone photometer; gas phase titration of ozone and nitric oxide
Dasibi programmable multi-gas calibrator	Manual or automatic calibration of ozone, oxides of nitrogen, carbon monoxide and sulfur analyzers; absolute ozone photometer; gas phase titration of ozone and nitric oxide
4 Meloy sulfur analyzers	Continuous analyzers for sulfur dioxide and other sulfur compounds
2 Teledyne-API carbon monoxide analyzer	Continuous analyzer
MiniRAE volatile organic compound (VOC) detector	Continuous analyzer (from AQRC, UCD College of Engineering)
10 Proportional controller systems	Extremely precise (<1%) feedback control of chamber ozone concentration
4 Multiple chamber gas samplers	Sequentially samples up to four chambers with a single monitor
Dell Optiplex 960 computer with LabView software and National Instruments hardware data acquisition system	Logs exposure concentrations, temperatures and other parameters for exposure data reports or emergency alarm notification

Aerosol Characterization Equipment

Method	Comments
Total filter	Mass determination of all particle sizes in conjunction with chemical or gravimetric analyses; a variety of fiber and membrane filters are used depending on the analysis. A microbalance with filter weighing chamber can be used. Filters can be examined by microscopy.
Inertial impaction	7-stage, Mercer-type single jet cascade impactors with an after filter; effective cut-off aerodynamic diameter (ECAD) of final stage is 0.3 μm . For aerodynamic size determination, used in conjunction with chemical analyses; Sierra ambient cascade impactor for gravimetric or chemical determinations; Berkeley Controls quartz crystal microbalance cascade impactor for automated measurement of aerodynamic size.
Ion chromatograph	Dionex unit for the chemical separation and determination of anionic and cationic constituents of aerosol samples
Photometer	TSI DustTrak™ light scattering aerosol monitors; continuous monitor of particle concentrations from 0.001 to 100 mg/m^3
Scanning Mobility Particle Sizer (SMPS)	TSI system for continuous measurement of particle size distributions from 0.004 to 0.9 μm and number concentration (from AQRC, UCD College of Engineering)
Optical particle counter	Climet single particle light-scattering counter for number concentration and optical equivalent size distribution; continuous monitor for particles 0.4 μm to greater than 3.0 μm . Sizes in five ranges, but also can be used with pulse height analyzer for greater resolution.
Mass monitor	Kanomax (TSI) unit combines a piezobalance and an electrostatic precipitator for rapid determination of mass concentrations.
Electrostatic precipitator	Collects particles for geometric size distribution analysis in conjunction with transmission or scanning electron microscopy
Condensation particle counter (CPC)	TSI units used to continuously monitor number concentration of particles too small to detect with an optical particle counter.
Diffusion battery	Used with CPC to measure size distribution of particles from 0.004 to 0.5 μm

Pulmonary Function Equipment

Equipment	Function	Specific Measures
Small whole body plethysmograph with semi-automated software data collection system (Buxco)	Determine static lung mechanics in sedated, spontaneously breathing infant monkeys	Standard lung volumes/capacities and flows, quasi-static lung compliance, and functional residual capacity
Large whole body plethysmograph with semi-automated software data collection system (Buxco)	Determine static lung mechanics in sedated, spontaneously breathing juvenile and adult monkeys	Standard lung volumes/capacities and flows, quasi-static lung compliance, and functional residual capacity
Small head-out transfer impedance plethysmograph with semi-automated software data collection system (Pulmetrics)	Determine respiratory transfer impedance in sedated, spontaneously breathing infant monkeys	Respiratory transfer impedance: central airway resistance, tissue resistance, and tissue compliance
Large head-out transfer impedance plethysmograph with Pulmetrics	Determine respiratory transfer impedance in sedated, spontaneously breathing juvenile and adult monkeys	Respiratory transfer impedance: central airway resistance, tissue resistance, and tissue compliance
Physiology platform for measurement of cardio-pulmonary parameters (PoNeMah)	Measure and collect cardio-pulmonary data during aerosol challenges or treatments	Breathing frequency, tidal volume, ventilatory rate, pulmonary flow resistance, and dynamic compliance, blood pressure, heart rate, esophageal pressure
Positive-pressure ventilators (2) (Bird)	Positive pressure mechanical ventilators	Ventilator
16-channel bio-telemetry system (Data Sciences Int.)	Collect and process physiological data from implantable sensors in free roaming monkeys. Remote sensing of breathing pattern and mechanics	EKG, EMG, blood pressure, pleural pressure, core body temperature
4 gas infrared analyzer	Analyze inspired and expired breath samples from rebreathing apparatus	Lung diffusing capacity, cardiac output and pulmonary capillary volume
Rapid Thoracolumbar Compression Testing	Mechanics in sedated, monkeys	Forced expiratory flow parameters, lung compliance

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Ex duded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	12,651.00	5,046.00	17,697.00	
2.					Core Scientist			0.0	0.0	9,075.00	3,036.00	12,111.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person		29,808.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		8,876.00	2,969.00	11,845.00
1	Core Manager	Excluded by Requester			34,230.00	18,108.00	52,338.00
2	Core Technical Support	Excluded by			39,588.00	20,942.00	60,530.00
	Excluded by Requester						
4	Total Number Other Personnel				Total Other Personnel		124,713.00
					Total Salary, Wages and Fringe Benefits (A+B)		154,521.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,000.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	17,500.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	18,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	176,021.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	176,021.00	39,957.00
		Total Indirect Costs	39,957.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	215,978.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IEC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	12,777.00	5,392.00	18,169.00	
2.					Core Scientist			0.0	0.0	9,075.00	3,196.00	12,271.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person		30,440.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by	EFFORT		8,964.00	3,157.00	12,121.00
1	Core Manager	Excluded by			35,107.00	19,419.00	54,526.00
2	Core Technical Support	Excluded			39,984.00	22,118.00	62,102.00
	Excluded by Requester						
4	Total Number Other Personnel				Total Other Personnel		128,749.00
					Total Salary, Wages and Fringe Benefits (A+B)		159,189.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,090.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,090.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	18,025.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	19,055.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	181,334.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	181,334.00	41,163.00
		Total Indirect Costs	41,163.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	222,497.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IEC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	13,421.00	5,863.00	19,284.00
2.					Core Scientist			0.0	0.0	9,075.00	3,305.00	12,380.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						31,664.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		9,416.00	3,429.00	12,845.00
1	Core Manager	Excluded by Requester			36,314.00	20,741.00	57,055.00
2	Core Technical Support	Excluded by			41,999.00	23,988.00	65,987.00
	Excluded by Requester						
4	Total Number Other Personnel				Total Other Personnel		135,887.00
					Total Salary, Wages and Fringe Benefits (A+B)		167,551.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,183.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,183.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	18,566.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	19,627.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	190,361.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	190,361.00	43,212.00
Total Indirect Costs			43,212.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	233,573.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IEC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	13,824.00	6,218.00	20,042.00	
2.					Core Scientist			0.0	0.0	9,075.00	3,405.00	12,480.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person		32,522.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		9,699.00	3,639.00	13,338.00
1	Core Manager	Excluded by Requester			37,403.00	21,999.00	59,402.00
2	Core Technical Support	Excluded by Requester			43,259.00	25,443.00	68,702.00
	Excluded by Requester	Requester					
4	Total Number Other Personnel				Total Other Personnel		141,442.00
					Total Salary, Wages and Fringe Benefits (A+B)		173,964.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,278.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,278.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	19,123.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	20,216.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	197,458.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	197,458.00	44,823.00
Total Indirect Costs			44,823.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	242,281.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IEC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	14,239.00	6,602.00	20,841.00
2.					Core Scientist			0.0	0.0	9,075.00	3,504.00	12,579.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						33,420.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Affiliate Scientist	Excluded by Requester	EFFORT		9,990.00	3,858.00	13,848.00	
1	Core Manager	Excluded by Requester			38,526.00	23,347.00	61,873.00	
2	Core Technical Support	Excluded by Requester			44,556.00	27,001.00	71,557.00	
		Excluded by Requester						
4	Total Number Other Personnel					Total Other Personnel		147,278.00
					Total Salary, Wages and Fringe Benefits (A+B)		180,698.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,376.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,376.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	19,697.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	20,823.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	204,897.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	204,897.00	46,512.00
Total Indirect Costs			46,512.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	251,409.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: IEC_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

CORE SERVICES: INHALATION EXPOSURE CORE**BUDGET JUSTIFICATION**

All funds requested in the Core are for developmental and administrative activities only. Services provided to users are fully charged to those activities based upon approved rates.

PERSONNEL

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

		Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Affiliate Scientist				
	Core Scientist				
	Core Manager				
	Technician				
	Technician				
Excluded by Requester	PhD, Core Scientist	EFFORT	months	% Effort	Excluded by Requester has responsibility for overall direction of the Core. He provides oversight for the Core and conducts and supervises the pulmonary function testing. He is responsible for establishing new pulmonary function tests as well as maintaining existing tests and impedance measurements.
Excluded by Requester	MD, Affiliate Scientist	EFFORT	months	% Effort	Excluded by Requester will provide expertise on bronchoscopy and aerosol delivery. He serves as the primary collaborator for investigators in the region interested in using the Inhalation Exposure Core for airway specific analysis of inhaled therapeutic agents.
Excluded by Requester	PhD, Core Scientist	EFFORT	months	% Effort	Excluded by Requester serves as the primary resource for inhalation studies involving particulates. His role in the Core is to provide oversight and expertise concerning biological measurements of the impact of tobacco smoke and particulates on the biology of the respiratory system.
Excluded by Requester	Core Manager	EFFORT	months	% Effort	Excluded by Requester is the manager of the Inhalation Exposure Core and responsible for all technical aspects of exposure and supervision of personnel. She will be responsible for maintenance of equipment, development of new exposure strategies, and coordination of Core use and personnel activities. She will supervise and train personnel as required to enhance and maintain operation of the Inhalation Exposure Core.
Excluded by Requester	Technician	EFFORT	months	% Effort	Excluded by Requester designs and oversees fabrication, installation, and testing of new exposure systems and the modification of existing systems, making certain that engineering is appropriate. He will set up and/or operate a variety of exposure equipment that includes maintenance/repair and calibrations, perform analysis of air samples from chambers, and operate and upgrade computer data acquisition system/data maintenance. In addition, Excluded by Requester will provide day-to-day coordination of pulmonary function testing, direct supervision of each test, analysis of test results and development of new methods.
Excluded by Requester	Technician	EFFORT	months	% Effort	Excluded by Requester will provide technical support. She operates exposure systems to execute various regimens as required, and maintains the facility. She will also ensure all record keeping and reporting is completed.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

Requests for equipment are identified in the **Facilities Improvement** section.

SUPPLIES

\$11,000 is requested for Pulmonary Function Test general supplies and maintenance.

\$6,500 is requested for exposure chamber supplies based on chamber operating costs anticipated for the development of exposure protocols, including: oxidant gas and tobacco smoke generation and monitoring, and generation and characterization of aerosols (such as allergens, respiratory syncytial virus, microspheres, ammonium nitrate). They are based on the previous 20 years of experience with the requirements for the types of exposure studies the Core performs.

TRAVEL

A total of \$3,000 is requested (2 x \$1,500) to attend courses and conferences related to developing new methods to be utilized in the Core.

OTHER EXPENSES

\$1,000 is requested for manuscripts related to new technology development.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		157,854.00
Section B, Other Personnel		678,069.00
Total Number Other Personnel	20	
Total Salary, Wages and Fringe Benefits (A+B)		835,923.00
Section C, Equipment		0.00
Section D, Travel		15,927.00
1. Domestic	15,927.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		98,221.00
1. Materials and Supplies	92,911.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		950,071.00
Section H, Indirect Costs		215,667.00
Section I, Total Direct and Indirect Costs (G + H)		1,165,738.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	60,000.00	Services
2	63,300.00	Services
3	66,782.00	Services
4	70,455.00	Services
5	74,330.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?* ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	IEC_SpecificAims.pdf
3. Research Strategy*	IEC_ReserachStrategy.pdf
4. Progress Report Publication List	IEC_ProgressReportPubs.pdf
Human Subjects Sections	
5. Protection of Human Subjects	
6. Inclusion of Women and Minorities	
7. Inclusion of Children	
Other Research Plan Sections	
8. Vertebrate Animals	IEC_VertebrateAnimals.pdf
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	
11. Consortium/Contractual Arrangements	
12. Letters of Support	
13. Resource Sharing Plan(s)	IEC_ResourceSharingPlan.pdf
Appendix (if applicable)	
14. Appendix	

CORE SERVICES: INHALATION EXPOSURE CORE

SPECIFIC AIMS

The California National Primate Research Center (CNPRC) Inhalation Exposure Core encompasses state-of-the-art facilities for the short- and long-term generation, analysis, and delivery of precisely controlled atmospheres to investigate health impacts of environmental challenges using both *in vitro* and *in vivo* laboratory animal models. The Inhalation Exposure Core also provides expertise for pulmonary function testing and bronchoscopy as outcome measures for health impacts as a result of exposures. The Inhalation Exposure Core provides a resource that is exclusive to the CNPRC; no other National Primate Research Center (NPRC) has a comparable facility. In order to accomplish the overall goal of supporting studies in pulmonary toxicology and animal models of respiratory disease, the Inhalation Exposure Core proposes the following Specific Aims:

Specific Aim 1. Support state-of-the-art research by providing stable, well-characterized exposures to air pollutants, allergens, therapeutic agents, aerosols, and other test atmospheres.

Plan. The Inhalation Exposure Core will continue to develop unique systems for *in vivo* inhalation exposure and *in vitro* atmospheric exposure with an emphasis on nonhuman primates as a translational animal model. This effort includes testing and optimization of new Inhalation Exposure Core facilities housed in the Respiratory Diseases Center.

Specific Aim 2. Provide nonhuman primate services for investigators to evaluate health effects of atmospheric exposures.

Plan. In conjunction with atmospheric exposures, the Inhalation Exposure Core will continue to provide pulmonary function testing services and bronchoscopy expertise. Leveraging the CNPRC resource, the Core will work with the Multimodal Imaging Core and Primate Medicine Services to enhance capabilities in lung function measures.

Specific Aim 3. Provide training in inhalation exposure technology for the next generation of nonhuman primate investigators.

Plan. The Inhalation Exposure Core will train graduate students, postdoctoral fellows, and faculty in the science of atmosphere exposure and analysis technologies. Training in lung function testing parameters and other biological response measures will also be provided.

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

The inhalation of outdoor and indoor air pollutants is a major environmental health risk worldwide. In 2014 the World Health Organization (WHO) reported that one in eight of total global deaths or approximately 7 million people died as a result of chronic air pollution exposure. The 2013 State of the Air report by the American Lung Association estimates that 38% of the people in the U.S. (119 million people) live in areas with unhealthy levels of ozone and that 15% of the people in the U.S. (47.7 million people) live in areas where particle matter air pollution reaches unhealthy levels on multiple days each year. In addition to the outdoor air pollutants such as ozone and particulate matter, the inhalation of second-hand tobacco smoke is a major health concern contributing to significant morbidity in children and adults. While a large body of epidemiological evidence confirms that children and adults with pre-existing cardiorespiratory morbidities are at risk of experiencing disease exacerbation with exposure to indoor and outdoor air pollutants, there is also growing evidence that prenatal or postnatal exposure increases the risk of developing cardiorespiratory morbidities later in life. In the U.S., chronic obstructive pulmonary disease (COPD) is one of the leading causes of death in adults and is strongly linked to tobacco smoke exposure [Hoyer, 2012]. Globally, COPD was reported by the WHO to be the fourth leading cause of death in 2011; biomass smoke exposure significantly contributes to disease in developing countries [reviewed in Excluded by Requester 2012]. Given the prevalence and high mortality of lung diseases in adults, questions regarding the identification of predictive biomarkers of exposure across the lifespan and curative treatments for chronic respiratory disease remain a major research focus for NIH, EPA, and pharmaceutical companies.

During the current funding period, multiple nonhuman primate studies have been conducted using Core facilities to examine the influence of experimental and ambient airborne pollutant exposure on lung

immunological, neurological, structural, and functional development. The Core also contributed to the assessment of biological responses to house dust mite (HDM) allergen, which is the primary allergen associated with allergic asthma in humans. Emphasis has been placed on how early exposure-dependent changes may affect health outcomes in adulthood, and whether there are critical developmental windows where these effects are greatest. The Core was also utilized for measurement of respiration and calorimetry in studies involving diet-induced obesity in nonhuman primates. The sources and services provided for nonhuman primate studies by the Inhalation Exposure Core in the current funding period are shown in Table 3.

Table 3. Nonhuman Primate Projects Conducted in the Inhalation Exposure Core (May 1, 2010 to April 30, 2014)

Investigator	Source	Project Title	Services	Recharge (\$)
Excluded by Requester (UC Davis)	Private Source	Development of a Rhesus Monkey Model of COPD using Diluted Cigarette Smoke	• Cigarette smoke exposure	48,675
Excluded by Requester (University of Washington)	CNPRC P51 Pilot Project	Role of Oxytocin Signaling in the Amelioration of Diet-Induced Obesity	• Measured oxygen consumption and carbon dioxide production • Indirect calorimetry system design and support	448
Excluded by Requester (UC Davis)	Private Source	MicroRNA Treatment on Development of Insulin Resistance and Dyslipidemia in Obese Monkeys	• Measured oxygen consumption and carbon dioxide production • Indirect calorimetry system design and support	1,854
Excluded by Requester (UC San Diego)	CNPRC P51 Pilot Project	Nonhuman Primate Model of How Airborne Immunostimulants Regulate Development of Aeroallergen Hypersensitivity and Tolerance in Children	• Exposed infant rhesus macaques to house dust mite (HDM) and ovomucoid aerosol	10,488
Excluded by Requester (UC Davis)	R01-HL097087	Role of Epithelium in Airway Immunity	• Cyclic exposure of infant rhesus macaques to ozone and HDM	76,370
Excluded by Requester (UC Davis)	California Air Resources Board	Persistent Immune Effects of Wildfire PM Exposure During Childhood Development	• Pulmonary function testing	40,022
Excluded by Requester (UC Davis)	P01-ES00628	Pulmonary Effects of Environmental Oxidant Pollutants: Rhesus Macaque Asthma Model	• Exposed infant rhesus macaques to HDM aerosols • Exposed infant rhesus macaques to episodic ozone • Pulmonary function testing	15,824
Excluded by Requester (University of Alabama)	P01-ES011617	Mechanisms of Species Dependent Environmental Lung Injury	• Exposed young rhesus macaques to ozone • Used ozone and oxygen delivery system to maintain exposure during bronchoscopy	6,974
		<i>Ex Vivo</i> Ozone Exposure	• Exposed rhesus monkey trachea to 8 hours of ozone and/or filtered air	5,709
TOTAL				\$206,364

In addition to providing support for research projects, extensive Core staff effort was expended on the design of the newly constructed Specific Animal Inhalation Core facilities housed in the new Respiratory Diseases Center. Excluded by Requester worked very closely with UC Davis Design and Construction Management. Along with providing support for nonhuman primate research projects, the Inhalation Exposure Core conducts exposure studies and provides technical support for local and regional investigators using rodent models as well as human subjects. The sources and services provided for rodent studies and technical support by the Inhalation Exposure Core in the current funding period are shown in Table 4.

With the completion of the Respiratory Diseases Center, Inhalation Exposure Core capabilities and holding capacity have increased; it is anticipated that continued effort to complete setup and testing of the new facilities will be required in the CNPRC P51 base grant renewal.

Table 4. Additional Projects Conducted in the Inhalation Exposure Core (May 1, 2010 to April 30, 2014)

Investigator	Source	Project Title	Services
Excluded by Requester (UC Davis)	Private Source	Effect of Ozone on Innate Pulmonary Response and Role of Gamma Delta T Cells	• Exposed mice to ozone
Excluded by Requester (UCSF)	K23-HL083099	Osteopontin and Oxidative Injury and Airway Remodeling in Asthma	• Exposed targeted mutant mice to ozone
Excluded by Requester (UC Davis)	Private Source	Exposure of Human Subjects to Ozone	• Calibration Dasibi ozone analyzer
Excluded by Requester (UC Davis)	USEPA	EPA Particle Center Project	• Exposed postnatal and adult rats to ultrafine particulate air pollution
Excluded by Requester (UC Davis)	USEPA	EPA Particle Center Project	• Designed, fabricated and characterized exposure of postnatal rats to ultrafine particulate air pollution exposures

INNOVATION

Unique Services and Research Opportunities for the Nonhuman Primate Research Community

The Inhalation Exposure Core provides a unique resource for the NPRC system that is exclusive to the CNPRC. To the best of our knowledge, there is no other facility in the United States or internationally that provides the broad technical capabilities, capacity, and expertise available within the Inhalation Exposure Core. The Core has generated six gaseous atmospheres and 27 aerosol atmospheres for short and long-term exposure studies (Table 5). These atmospheres are delivered by multiple modalities utilizing exposure equipment housed in the Inhalation Exposure Core (see Facilities and Equipment for details).

Table 5. Inhalation Exposure Core Test Atmospheres

Gases	Generation	Concentration Measurement
Ozone	Electric discharge or UV	UV absorption, absolute ozone photometer, gas phase titration
Carbon monoxide	• Cigarette smoke • Endogenous production by monkeys	• NDIR absorption, span gas • Gas chromatographic with reduction gas detector for very low ppb range concentrations
Carbon dioxide	Endogenous production by monkeys	IR absorption, span gas
Oxygen	Consumption by monkeys	High temperature galvanic cell, span gas
Nitrogen dioxide	Gas cylinders or liquid N ₂ O ₄	Chemiluminescence, span gas, gas phase titration
Sulfur dioxide	Gas or liquid cylinders	Flame photometry, span gas, permeation tube
House Dust Mite	High flow rate nebulizer	Gravimetry, ion chromatography, protein analysis
Endotoxin	Nebulizer, concurrent flow spirometry aerosol inhalation system	Biological effects; estimated and controlled total inhaled endotoxin units
Ethylene combustion products including ultrafine particles, both low and high PAH modes	Controlled burner system	Gravimetry, thermal oxidation, GC/mass spectrometry
Ovalbumin allergen	High flow rate nebulizer	Gravimetry, ion chromatography, protein analysis
Immunostimulatory sequence DNA	Nebulizer, concurrent flow spirometry system	Biological effects, DNA analysis, ion chromatography
Budesonide (inhaled steroid)	Nebulizer	HPLC for aerosol; plasma levels by LCMS
Respiratory syncytial virus	Nebulizer, concurrent flow spirometry system	Biological effects, virus assay
Mouse influenza virus	Nebulizer	Biological effects, virus assay
CF genes in adenoviral vectors or liposomes	Nebulizer, concurrent flow spirometry	Biological effects

Simulated "particulate matter (PM)" as ammonium nitrate and carbon	Nebulizer, recirculation limited	Gravimetry, ion chromatography, thermal oxidation
Diluted cigarette smoke	Cigarette smoking machine	Gravimetry, IR absorption, gas chromatography
Fluorescent microspheres	Nebulizer	Gravimetry, fluorimetry
Ammonium persulfate	Babington-type nebulizer	5% potassium iodide
Ammonium sulfate	Babington-type nebulizer	Ion chromatography
Bacterial aerosols	Babington-type nebulizer	Culture, protein analysis
Concanavalin A	Babington-type nebulizer	Gravimetry, protein analysis
Ferrous sulfate a. Monodisperse (1-2 μm) b. Submicron (0.5 μm)	Vibrating jet Babington-type nebulizer	Atomic absorption, ferrozine
Fly ash	Wright Dust Feed-cyclone	Gravimetry, particle induced emissions
Iron oxide	Babington-type nebulizer from hydrosol	Gravimetry, direct colorimetric analysis
Nitric acid	Babington-type nebulizer or condensation system	Ion chromatography
Penicillamine	Babington-type nebulizer	Gravimetry, specific analysis
Sodium chromate	Babington-type nebulizer	Gravimetry, atomic absorption
Sodium sulfite	Babington-type nebulizer, oxidation limited	Gravimetry, ion chromatography, pararosaniline
Sulfuric Acid a. Nuclei mode (0.004 μm) b. Submicron (0.5 μm)	SO ₃ (g) + H ₂ O(g) Babington-type or Lovelace nebulizer	Ion chromatography
Zinc oxide	Retec nebulizer and tube furnace	Gravimetry, atomic absorption
Zinc sulfate	Wright Dust Feed-cyclone	Gravimetry, atomic absorption, ion chromatography
Zinc sulfite	Wright Dust Feed-cyclone	Gravimetry, atomic absorption, ion chromatography, pararosaniline

During the current a funding period, innovative approaches developed or refined by the Inhalation Exposure Core include:

- Design and construction of a stainless steel room-based system for exposure of 32 monkeys (animal weights ≤ 10 kg) or 24 animals (> 10 kg) to environmental tobacco smoke, located within the new Respiratory Diseases Center. The rationale for this design was to increase efficiencies and capacity for conducting large-scale nonhuman primate and rodent exposures to environmental tobacco smoke. To the best of our knowledge, there is no other national or international facility that has a comparable room-based system for tobacco smoke exposure (Figure 3).
- A combustion particle generation system has been developed in collaboration with engineers from the EPA Particle Center, San Joaquin Valley Aerosol Health Effects Research Center under the direction of Dr. Excluded by Requester (UC Davis College of Engineering). This advance makes it possible to expose animals to environmentally relevant and reproducible levels of particulate matter. An advantage of this approach is the ability to change the composition of particulate matter in order to examine how different known components may influence broad biologic responses in test animals.
- Large *in vitro* exposure system used for the study of the effects of different atmospheres on cells in culture and tissue explants.
- Concurrent Flow Spirometry Aerosol Inhalation System used to deliver a broad range of aerosols to sedated monkeys while assessing the inhaled dose of aerosol. Aerosols delivered using this system include allergens, endotoxin, and pharmaceutical agents.
- Respiratory transfer impedance systems for the evaluation of dynamic lung mechanics in spontaneously breathing infant and adult rhesus macaques.

Proprietary Info

- Multiple gas rebreathing system designed and built in collaboration with [REDACTED] from the Oakcrest Laboratory in Glendale, CA for the measurement of lung diffusing capacity, thoracic gas volume, pulmonary capillary blood volume, and pulmonary blood flow in infant to adult rhesus macaques.
- External thoracic compression device for obtaining forced expiratory flow data in monkeys that is comparable to that obtained with human COPD and asthma patients.

Approximately 30% of the effort of the Core faculty and staff has been dedicated to developing and characterizing new technology for inhalation exposure and pulmonary function testing of monkeys during the current funding period. Recent examples of such new technology include: (1) a new cigarette smoke generator, (2) LabView replaced the old data acquisition system which now provides a modern, user-friendly system for monitoring the various exposures and temperatures as well as provides insight when troubleshooting malfunctions, (3) enhancement of the large *in vitro* exposure chambers, (4) a complex one-of-a-kind exposure room for cigarette smoke designed and completed as part of the new facility, (5) development of new respiratory transfer impedance data acquisition and analysis software, and (6) development of multiple gas rebreathing hardware and software.

APPROACH

Plans for the Next Funding Period

The overall vision of the Inhalation Exposure Core is to become the premiere resource for environmental airborne material studies in the United States. To the best of our knowledge, no other national or international facility provides precision controlled atmospheric exposures at this capacity. Moreover, faculty and staff expertise available within the Inhalation Exposure Core offer unique consultative technical support and evaluation of health outcomes that significantly enhance the resource. The primary areas of service will continue to emphasize our published strengths in pulmonary toxicology and animal models of respiratory disease.

As illustrated by schematic in Figure 4, the Inhalation Exposure Core has an established service pipeline provided by Core and Affiliate Scientists from the CNPRC for completion of studies in pulmonary toxicology and animal models of respiratory disease.

Inhalation Exposure Core faculty and staff assist investigators with study design, conduct airborne material exposures with precision, direct evaluation of biological outcome measures by pulmonary function testing and bronchoscopy, and support data analysis. An important goal for projects executed by the Inhalation Exposure Core is to contribute towards the publication of study outcomes, ultimately leading to funding of new grant proposals to enhance our knowledge base. Along with study design, Inhalation Exposure Core faculty and staff provide budgets and methodology for grant proposals as requested by investigators.

Outreach Efforts

In order to execute our vision of becoming a premiere resource for environmental airborne material studies, multiple outreach strategies will be implemented during the next funding period to increase visibility to external investigators. On a national level, Respiratory Diseases Unit Core Scientists promote use of the Inhalation Exposure Core by providing informational brochures and presentations at scientific conferences such as the annual American Thoracic Society (ATS) International Conference, American Asthma Foundation, and the Society for Toxicology (Figure 5). In particular, [REDACTED] serves on multiple national committees related to air quality policy and will promote the Core as a national resource. One potential strategy to increase visibility of the Inhalation Exposure Core is to request a booth at the Society for Toxicology meeting; nonprofit organizations are charged a nominal fee of \$600 for the five-day conference, which includes two staff registrations. Although the membership of the Society for Toxicology is considerably smaller (approximately 4,000 members), pulmonary toxicology is a

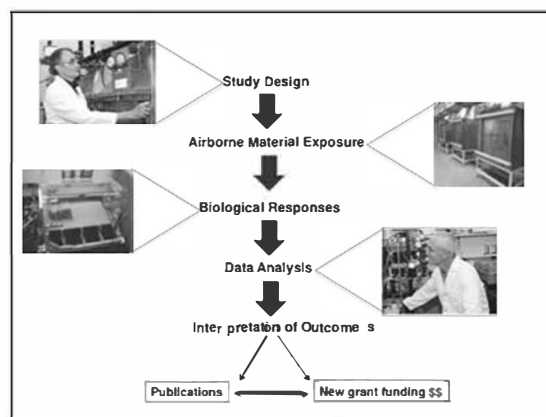


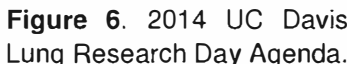
Figure 4. Schematic of service pipeline provided by the Inhalation Exposure Core.



Figure 5. RD Unit brochure used for scientific conference outreach.

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points are critical to answer the specific research question. This process often includes the consideration of statistical power balanced against the budgetary constraints when using nonhuman primates.

One mechanism to optimize study design is to enhance exposure efficiencies. The predominant inhalation chamber types used for studies are large stainless steel and glass units [Proprietary Info] in volume suitable for exposing large or small animals to gases and aerosols [Hinners et al., 1968]. New generation [Proprietary Info] inhalation exposure chambers designed by Inhalation Exposure Core staff and constructed for the Respiratory Diseases Center during the current funding period will be able to house up to four nonhuman primates in individual cages. Comparatively [Proprietary Info] chambers in the previous facility were limited to a maximum of two rhesus macaques per unit for animals with body weights < 1 kg at 4-6 months of age. Increased animal capacity per chamber results in greater exposure efficiencies, translating into significant savings by way of costs and time to investigators.

Doors on opposite sides of the new [Proprietary Info] chamber facilitate veterinary access to animals, ease loading and unloading of chambers, and allow increased light diffusion within the chamber. A central air handling system supplies chemical, bacteriological, and radiological (CBR) filtered air to each [Proprietary Info] chamber at a flow rate of [Proprietary Info] per minute for a complete air change every two minutes. The chamber air supply system consists of pre-filters, high efficiency particulate air (HEPA) filters, and activated charcoal absorbers to remove most air pollutants. The high rate of ventilation causes rapid chamber atmosphere equilibration and lowers the level of airborne contaminants from the housed animals. Temperature control is also precisely maintained. These design features were included to further enhance care and housing conditions for animals.

While undergoing exposure, monkeys are housed in stainless steel, open mesh cages. Prior to exposure, animals are given an appropriate period to become acclimated to the chamber environment. Automatic watering systems are used, and the exposure chambers are equipped with spray rings to facilitate daily cleaning, which reduces the build-up of ammonia and volatile amines. Young monkeys can be housed in small, socialized groups. For long periods in the chambers, adult monkeys are housed in specially designed pair cages with removable panels for enrichment purposes. The panel between two monkeys is first removed under supervision for certain periods until the compatibility of the pair is proven. Then the panel is removed and the two animals are free to interact. Identical chambers in the same room are used for the exposed groups and for the filtered air control groups. Animals remain in the chambers for the duration of study. These methods, combined with rigorous health screening and monitoring, ensure that animal health problems and their resulting impact on studies are kept to a minimum.

The university provides 24-hour emergency response service for the large air handling and electrical equipment. An emergency electrical generator ensures the Core is fully operational at all times. Because high peak excursions of concentration can profoundly affect the biological response, preventing animals from exceeding exposure conditions due to failures of equipment or power loss is an important consideration. Limit controls are employed to turn off exposures and an alarm is activated if pre-set levels are exceeded during power failures or air handling system failure. Exhaust systems composed of CBR filters prevent release of contaminants into the ambient air. All of these safety features ensure optimal health of animals, which ultimately contributes to outcome measures that can be interpreted with confidence.

Goal 2. Develop, Characterize, and Deliver Well-Characterized Test Atmospheres. Whether there is a need to develop new technologies for airborne materials or generate atmospheres that have been used previously by Inhalation Exposure Core investigators, *in vivo* and *in vitro* exposures are precisely monitored. Concentrations and other parameters are continuously evaluated and logged with a personal computer based data acquisition and control system. To ensure that pollutant concentrations and aerosol size distributions are accurate, continuous monitoring is used and careful comparisons are made between alternate methods. Exposures can be run seven days per week, 24 hours per day. Appropriate control strategies are implemented in the event of failures of airflow, power, or other equipment. Reports are provided to investigators at completion of each exposure study. Exposure reports consist of mean, standard deviation, range, percentiles in excess of a given level, calibration statistics, and other parameters. The Facilities and Other Resources section describes equipment used for generation of gases and aerosols. Some aerosol exposure methods have been described in detail in numerous publications [Excluded by Requester] 1977; [Excluded by Requester] 1978; [Excluded by Requester] 1980; [Excluded by Requester] 1993; [Excluded by Requester] 1979]. Well-characterized atmospheres and exposure modalities that are critical for accomplishing this goal include the following:

- Chamber O₃ Generation and Delivery.** O₃ is produced by electric discharge ozonizers from vaporized liquid medical grade oxygen. O₃ is delivered via Teflon™ lines to the mixing inlet of the exposure chamber or *in vitro* exposure vessel. The O₃ concentration is monitored from every 30 seconds to at least once every eight minutes with an ultraviolet O₃ analyzer (Model 400E, Teledyne API Corp., San Diego, CA). A single analyzer can be used to monitor up to four chambers via computer-controlled valves. Analyzer calibration is performed according to the national reference method [US Code of Federal Regulations, 1988] and is traceable to National Institute of Standards and Technology absolute O₃ photometer located at the California Air Resources Board Quality Assurance Laboratory in Sacramento, California. Proportional O₃ control systems are also used to dynamically stabilize exposure concentrations. They are particularly valuable for exposures that must be started at odd hours and for exposures involving multiple groups of animals that must be replicated with very high precision. Certain analyses performed by investigators are now so detailed and labor intensive that only a few or even just one animal can be evaluated in a day. Therefore, individual exposures must be replicated with very high precision. The controllers can also serve as interfaces between the computer and O₃ generation systems. O₃ exposure of anesthetized monkeys can be maintained by using a humidified atmosphere of air and delivered through a tracheal tube or nasal cannula. Adjustable flows of purified compressed air and medical grade oxygen, humidified to about 75% relative humidity at 25°C and then filtered through a Teflon™ membrane (47 mm, Part No. R2PJ047, Pall Corp. East Hills, NY). This mixture is introduced to the zero air inlet of an ultraviolet O₃ analyzer/generator (Model 1008-PC, Dasibi Environmental Corp., Glendale, CA) that generates, monitors and controls a constant concentration of O₃. Air containing O₃, travels to a 0.5 liter gas bag (Catalog No. TE1, BGI Inc., Waltham, MA) and then to a manifold to which the tracheal tube (Catalog No. 86224, Mallinckrodt Inc., St. Louis, MO) or nasal cannula (Item No. 163055, Kendall-LTP, Chicopee, MA) are connected. Excess flow from the manifold is exhausted through tubing at a slight positive pressure (4 cm H₂O). All materials in contact with the O₃ containing stream are Teflon® except for the tracheal tube that is polyvinyl chloride and silicone nasal cannula. O₃ reactivity of both has been found to be negligible or not detectable.
- In Vitro* O₃ Exposure.** A relatively large scale *in vitro* exposure system enables the simultaneous exposure of cells to three O₃ levels with a filtered air control and is ideal for dose response studies [Excluded by Requester 1982] [Excluded by Requester 1994] [Excluded by Requester al., 1994a/b] [Excluded by Requester al., 2002]. Culture plates with wells containing the cells on inserts are exposed to O₃ or filtered air in specially designed 3.66 liter cylindrical glass vessels. Atmospheres contain 95% air and 5% carbon dioxide by volume and are saturated with water vapor at 37.5°C. This mixture flows through each vessel at a total rate of 15 liters per minute. In vessel lids, a diffuser plate with 19 symmetrically located holes, each 1.6 mm in diameter, is incorporated to evenly distribute flow. Exhaust is taken from a central point below a perforated desiccator plate. Vessel geometry and flow patterns ensure a homogeneous pollutant concentration is maintained and each culture receives the same concentration. The biological response data indicates that homogeneous exposure is achieved [Excluded by Requester 1994] [Excluded by Requester 2002]. Three vessels are used for O₃ and one for control.
- Generation and Characterization of House Dust Mite (*Dermatophagoides pteronyssinus*) (HDM) Aerosols.** Lyophilized HDM extract (Greer Laboratories, Inc., Lenoir, NC) diluted in PBS is nebulized with a high flow rate at a flow rate of 20 liters/min (HEART®, Westmed, Inc., Tucson, AZ) using a nebulizer immersed in an ice-water bath to reduce water evaporation. To reduce electrostatic charge polydisperse droplets about 2 µm in diameter are diluted with a 48.3 liters/min stream of dry air and conveyed upward through a 33.6 liter krypton-85 discharging column [Excluded by Requester 1978]. The aerosol is mixed with the inlet air stream of a 4.2 m³ exposure chamber, producing an aerosol of solid particles composed of the allergen with salt residue. HDM aerosol total mass concentrations are measured by weighing samples collected on pre-weighed Teflon® coated glass fiber filters (Pallflex Fiberfilm, Pall Gelman Sciences, Ann Arbor, MI). Total protein concentration is determined by amino acid analysis [Excluded by Requester 1990] at the UC Davis Molecular Structure Core. Aerodynamic size distributions are determined with a Mercer-type 7 stage cascade impactor [Excluded by Requester 1970]. On each impactor stage and after-filter, the content of chloride anion derived from saline residue in the particles is measured by ion chromatography (Model ICS-1000, Dionex Corp., Sunnyvale, CA). The values reported are the mass median aerodynamic diameter (MMAD) and the geometric standard deviation (a_g). Typically, for these HDM particles, the MMAD is 1.4 µm with a a_g of 2.6. An optical photometer is used to continuously monitor the concentration of particles during exposure and to indicate when the chamber can be opened safely [Excluded by Requester 2001].
- Bioaerosols.** The expertise of the Inhalation Exposure Core is available for exposures to bioaerosols, including exposures with immunostimulatory sequence DNA, proteins, endotoxin, cystic fibrosis genes in liposomes or viral vectors, and other viruses including respiratory syncytial virus [Excluded by Requester].

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2002]. High concentration aerosols containing these agents are delivered via mask to sedated monkeys, with a portable concurrent flow spirometry aerosol inhalation exposure system [Excluded by Requester 1976] in which respirable aerosol is generated with a nebulizer (MiniHEART[®], Westmed, Inc., Tucson, AZ). Exhaust is drawn from an outlet port on the mask and across a breathing circuit filter (Model BB50T, Pall Gelman Sciences, Ann Arbor, MI). A heated pneumotachograph (Model 3850A, Hans Rudolph, Inc., Shawnee, KS) is connected to a tee upstream from the exhaust filter. As the monkey inhales and exhales the aerosol, pressure changes in the mask are automatically compensated and held to a minimum by the changes in a bias flow across the pneumotachograph. Pressure changes are analyzed using a computer based pulmonary physiology platform (Ponemah, DSI, Inc., Valley View, OH) that provides measurements of respiratory rates and volumes. With aerosol concentration, aerodynamic size, estimated deposition fraction and volume inhaled, the dose delivered during an inhalation period can be estimated. To ensure that potentially infectious or toxic aerosol does not escape into the exposure room, the system is operated at a slight negative pressure in an appropriate containment area, breathing circuit filters are used on the main exhaust and spirometer leg of the system, and a HEPA cartridge filter is used downstream from the breathing circuit filter on the main exhaust line.

- **Environmental Tobacco Smoke Generation and Exposure.** The new environmental tobacco smoke room is designed to produce homogeneous, stable and repeatable cigarette smoke contaminated atmospheres at a mass concentration of 1 mg/m³ and 6 ppm CO. Low air turnover rates result in smoke aging conditions that are representative of second-hand exposure in buildings occupied by human smokers. The design consists of a clean air anteroom that houses a cigarette smoke generator, gas and particulate monitors and a cigarette smoke exposure room.

Metrics. With increased outreach efforts by Inhalation Core faculty and Respiratory Diseases Unit Core Scientists, we anticipate increased usage of the facility. As new exposure atmospheres are requested, developed, and applied we expect that the number of clients and associated research publications will increase. We further expect that the recruitment of new Core and Affiliate Scientists will have a significant positive impact on Core usage.

Alternative Strategies. When *in vivo* inhalation exposure methods cannot be developed or adapted to meet requests, the Inhalation Exposure Core will explore the possibility of expanding current *in vitro* and cell-based exposure systems that have been proven to provide information regarding the toxicology of test atmospheres.

[Excluded by Requester] (Respiratory Diseases Unit) has significant expertise in this area and will provide consultation for both Core faculty, staff, and external investigators as needed.

With global research interests in the role of biomass smoke in COPD pathogenesis, we will explore the feasibility of developing exposure methods to assess the biologic effects of chronic inhalation of wood smoke in nonhuman primates.

Specific Aim 2. Provide nonhuman primate services for investigators to evaluate health effects of atmospheric exposures.

Pulmonary function testing measures progressive change of static lung mechanics and airway responsiveness to specific and nonspecific stimuli. Central to the assessment of lung function in modern translational respiratory research is to have an optimized approach to understand, measure, and detect the heterogeneous changes that occur in chronic respiratory diseases. Whether the question is focused on airway diseases such as asthma or COPD, or parenchymal diseases such pulmonary fibrosis, the relationship of lung function to lung appearance is critical to understanding disease pathophysiology. Pulmonary function testing capabilities in the Inhalation Exposure Core include the ability to do traditional measurements of airflow (FEV1 and FVC), lung volume and diffusing capacity but also include the capability to perform cutting edge techniques that can provide a more granular assessment of proximal and distal airway function. These techniques open the door to assessment of small airway function and dynamic heterogeneity that can exist in the early stages of chronic lung disease. Moreover, pulmonary function testing can complement the CNPRC new imaging capabilities with high resolution CT in the Multimodal Imaging Core to fully integrate assessment of lung function and lung appearance.

The Inhalation Exposure Core offers pulmonary function testing as a service, along with bronchoscopy that is typically used to evaluate airways inflammation. In addition, the Inhalation Exposure Core pulmonary function testing service develops new and refines existing measures of pulmonary function, including the development

of the lung diffusing capacity in nonhuman primates. The pulmonary function testing laboratory is a unique 918 sq. ft. facility located within the Inhalation Exposure Core. The laboratory is equipped to evaluate multiple lung function endpoints in infant, juvenile, and adult nonhuman primates. Pulmonary function testing modalities that are critical for accomplishing this aim that are in place or being developed for the CNPRC P51 renewal include:

- **Static Lung Mechanics.** Sedated and intubated monkeys are placed into the whole-body plethysmograph (Buxco Electronics) and connected to a 3-way valve assembly. The semi-automated software, Maneuvers XA (Buxco Electronics), controls positive pressure inflation and negative pressure deflation to the lung. Standard static lung volumes/capacities, forced expiratory volumes and flows, quasi-static lung compliance, functional residual capacity, and thoracic gas volume are obtained.
- **Aerosol Challenges.** All challenges are administered as aerosols at a set tidal volume and breathing frequency (size and age appropriate) using a compressed air nebulizer (Vortran, Inc., Miniheart Model) in series with a positive pressure ventilator (Bird Mark 7A respirator). Allergen challenge is performed using a set concentration of house dust mite allergen (0.02 mg protein/ml) delivered for 1 minute followed by 4 minutes of data collection and repeated up to 12 times. Allergen challenge is terminated when airway resistance (Raw) doubles or arterial oxygen saturation falls below 75%. Histamine or methacholine challenges are performed using repeated 30-second challenge periods separated by 4 minute data collection periods. Histamine or methacholine challenges are performed with the initial concentration of 0.0625 mg/ml and ending at 32.0 mg/ml. The final concentration of histamine or methacholine to be delivered is 32.0 mg/ml or decreases O₂ saturation to 75%.
- **Breathing Pattern and Arterial Oxygen Saturation.** Tidal volume (VT) and breathing frequency are recorded on a breath-by-breath basis by integrating the output of the pneumotachograph using a digital data acquisition system (Po-Ne-Mah, Inc). Arterial oxygen saturation (O₂Sat%) is recorded at the beginning and end of each data collection period.
- **Pulmonary Mechanics via Transfer Impedance.** Pulmonary mechanics are measured using a transfer impedance method [Excluded by Requester 1997]. The monkey breathes spontaneously through the pneumotachograph while the thorax of the monkey is vibrated using a pseudo-random noise waveform (4 to 128 Hz) produced by speakers mounted in the walls of the head-out plethysmograph (Pulmetrics Group, Boston, MA). The small changes in flow produced at the mouth, along with the changes in pressure inside the plethysmograph are measured at 4-second intervals. Transfer impedance (Ztr) is calculated as the ratio of the Fourier transform of box pressure versus that of airway flow [Excluded by Requester 1997]. Impedance data is fit to the six-element model [Excluded by Requester 1956] using a gradient optimization technique [Excluded by Requester 1988]. This six-element model includes central airway resistance (Raw), airway inertance (Iaw), alveolar gas compressibility (Cg), tissue resistance (Rti), tissue inertance (Iti), and tissue conductance (Cti) [Excluded by Requester 1976]. These techniques give investigators the opportunity to utilize forced oscillatory techniques (FOT) to assess dynamic changes in airflow in a spontaneously breathing subject. This technique is particularly valuable in subjects that are not able to perform consistent and precise breathing maneuvers. FOT has successfully been used to assess dynamic airway closure, now believed to be a key element in airway hyperresponsiveness [Excluded by Requester 2007].
- **Multiple Gas Rebreathing Diffusing Capacity.** The development of a multiple gas diffusing capacity measurement increases capacity to evaluate the effects that altered lung development and pulmonary pathologies have on gas exchange and at what level these changes occur. When an inert gas is used, researchers can measure the Lung Clearance Index (LCI), which is a reflection of dynamic changes in small airway function. The LCI has been reported to complement high resolution computed tomography (HRCT) in providing functional data on peripheral airway function [Excluded by Requester 2014].
- **Development of an External Thoracic Compression System.** For the measurement of forced expiratory flow parameters in nonhuman primates, this system is used to obtain forced expiratory flow data comparable to that obtained in chronic obstructive pulmonary disease and asthma patients.

Metrics. As lung function evaluation methods are requested, applied, and developed, both the number of clients and associated research publications will increase. Usage of lung function testing will increase as new Core and Affiliate Scientists utilize the Inhalation Exposure Core. Increased outreach to pharmaceutical companies will also enhance usage of the Inhalation Exposure Core, as measures of therapeutic efficacy typically require pulmonary function testing and bronchoscopy.

Alternative Strategies. An additional strategy to enhance biological measures of exposure is to integrate assessment of airways remodeling via high resolution CT (available in the Multimodal Imaging Core) with lung function testing and/or bronchoscopy to provide a more thorough non-invasive evaluation of changes in lung

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structure as a result of exposure. Preliminary studies by [REDACTED] in collaboration with [REDACTED] (University of Iowa) suggest that the use of a high resolution CT approach to track airways remodeling changes longitudinally is feasible in a nonhuman primate model of COPD. VIDA software (VIDA Diagnostics, Inc.) for quantitative image analysis of lung parenchyma and airways is available for purchase or data can be uploaded online and quantified on a recharge basis. Little is known about the chronologic progression of airways disease; relatively non-invasive lung function testing in conjunction with imaging of airways remodeling will be highly informative for investigators and pharmaceutical companies testing the efficacy of curative therapeutics.

When traditional assay methods cannot be development or adapted to meet requests, we will explore the possibility of using *in vitro* isolated airway methods that have been proven to provide valuable information regarding airway function and control.

Specific Aim 3. Provide training in inhalation exposure technology for the next generation of nonhuman primate investigators.

As a CNPRC resource, the Inhalation Exposure Core will provide training to graduate students, postdoctoral fellows, and new investigators as requested. Core faculty are active participants in multiple UC Davis campus graduate programs, where their expertise in inhalation exposure methodologies and pulmonary function testing are used to train PhD students in the classroom as well as in the laboratory. UC Davis has one of the largest concentrations of faculty (over 70) with air pollution expertise at any one university in the U.S, therefore the ability to train in a state-of-the-art facility for inhalation exposure will have significant appeal for recruitment of new trainees. As Director for the Center for Environmental Health and member of the UC Davis Air Quality Research Center [REDACTED] is particularly well-positioned for identifying students and junior investigators who have specific interests in developing careers in inhalation exposure technology. The UC Davis Air Quality Research Center is a unique collaborative research organization supporting multidisciplinary approaches to address questions in air pollution science, with the goal of contributing expertise towards regulation of air quality and climate change. The UC Davis Air Quality Research Center frequently partners with the California Air Resources Board in hosting air pollution conferences on the UC Davis campus; this forum also serves as an opportunity to engage new trainees and junior investigators interested in inhalation exposure technology. As discussed in Outreach Efforts, increased visibility at the national level at the Society for Toxicology meetings may further facilitate interest by prospective trainees and junior investigators. Collectively, these activities will support the development of future nonhuman primate investigators, in addition to ensuring continued innovation in pulmonary toxicology and animal models of respiratory disease.

Metrics. Trainee number and productivity will increase as new Core and Affiliate Scientists utilize the Inhalation Exposure Core. Enhanced visibility of the Inhalation Exposure Core at the local, regional, and national levels will increase recruitment of new trainees in inhalation exposure technology. Increased mentoring and training will generate more publications, produce publications of higher quality, and support the development of new grant proposals for investigators.

Alternative Strategies. Consistent with the overall vision to serve as a premiere resource for airborne materials exposure methods, the Core will provide detailed standard operating procedures (SOPs) and protocols through investigator inquiries.

CORE SERVICES: INHALATION EXPOSURE CORE

PUBLICATIONS (May 1, 2010 to April 30, 2014)

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- Excluded by Requester Secondhand tobacco smoke exposure differentially alters nucleus tractus solitarius neurons at two different ages in developing non-human primates. Toxicol Appl Pharmacol 242:199-208, 2010. PMC Journal-in-progress
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VERTEBRATE ANIMALS

Requester	Excluded by
Requester	Requester

Specific
Animal
Location

Specific Animal Location

3. **Veterinary Care.** The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian). Excluded by Requester Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations.

Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

Centralized Research Support. The various services represented in Primate Services work synergistically to provide high quality, technical research support to all investigators utilizing the CNPRC, as needed, whether located locally or at a distant site. Staff veterinarians also provide extensive clinical support to animals on long-term research protocols (see Primate Medicine Services).

Staff Training. The program emphasizes occupational safety, as well as increasing demands for technical expertise in the care and research support of nonhuman primates. Training is viewed not only as the initial step at hire, but as an ongoing process through in-house classes and support to attend relevant training programs, meetings, and conferences. A spectrum of training opportunities is available specific to the CNPRC and to meet campus-wide training requirements. These include: UC Davis Primate Handling and Husbandry Training, Campus Laboratory Animal Care Classes (AAALAC preparation); Injury / Illness Prevention Plan; Infection Control Plan; Exposure Control for Blood-borne Pathogens; Medical Waste Management; Hazardous Chemical Disposal Management; Campus Back Safety Class; Campus Radiation Safety Class; Pesticide and Antimicrobial Safety; Training in Good Laboratory Practices; Supervisor Training with Job Skills Worksheet; and position specific training for all levels of husbandry, animal care, and technical skills. The training program also includes a series of "*Attention to Detail*" documents that provide very detailed information for each of the training and skill areas the staff is expected to meet including information to enhance understanding and the need to adhere to defined guidelines for critical procedures.

Standard Operating Procedures (SOPs). Primate Services has an extensive collection of 185 SOPs that provide detail on all operational procedures including: husbandry, animal health checks, preventive health, calibration of equipment, and a full array of medical and experimental procedures. SOPs are reviewed annually by all staff and undergo full review and revision every three years. SOPs are available in an electronic format online on the CNPRC internal website. All SOPs are reviewed and approved by the UC Davis IACUC, and SOPs by number can be noted in IACUC protocol submissions.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For some procedures, animals are intubated and maintained under isoflurane (to effect) and monitored by the veterinary staff. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.

5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

CORE SERVICES: INHALATION EXPOSURE CORE

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CORE SERVICES: INHALATION EXPOSURE CORE

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Alyssa Bunn
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 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Multimodal Imaging Core

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename MI_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	MI_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	MI_FacilitiesOtherResources.pdf
11. Equipment	MI_Equipment.pdf

CORE SERVICES: MULTIMODAL IMAGING CORE

ABSTRACT

The **Multimodal Imaging Core** (*formerly the Computational Imaging Core*) provides services to investigators locally, regionally, and nationally, encompassing scales that range from cellular to whole-animal imaging. The change in the Core name reflects the spectrum of services, imaging modalities, and continued growth of the *in vivo* imaging program within the Core. The goal of the Core is to support the research of investigators and trainees in qualitative and quantitative imaging applications and to assist with study design, data interpretation, grant submissions, and to conduct preclinical and IND-enabling studies. The Core has two distinct yet integrated components. The *first* component provides extensive microscopy/pathology-based services including whole slide scans, confocal microscopy, stereology training, methods development, and analysis. The Core also assists with the production of publication quality images, and provides consultation on experimental approaches for all imaging modalities. The Core is engaged in digitizing archived film images from various sources, including those created by the Anatomic and Clinical Pathology Services in Primate Services at the California National Primate Research Center (CNPRC). Microscopy instruments housed in the Core are available to trained users. The *second* component consists of *in vivo* imaging services provided by Core faculty and trained professionals and includes ultrasound imaging, optical imaging, positron emission tomography/computed tomography (PET/CT), and microPET, in addition to radiochemistry and pharmacokinetic analyses of new radiopharmaceuticals. Core faculty work in an integrated manner to implement the imaging goals of the program, and to ensure investigators have the depth and breadth of innovative imaging opportunities to conduct their research and to submit NIH grant applications. Dedicated faculty and staff are responsible for imaging services, radiotracer synthesis, administrative support, day-to-day operational management, computer support, preventive and routine maintenance, and quality assurance. CNPRC Information Technology staff provides networking for the imaging systems, install firewalls, integrate imaging systems with database systems, and perform daily backup operations.

CORE SERVICES: MULTIMODAL IMAGING CORE

FACILITIES AND OTHER RESOURCES

Laboratories: The Core includes 6 laboratories for microscopy and histology in the laboratory building (829 sq. ft.), imaging suites in the animal quarters for ultrasound and optical imaging, a microPET scanning room, a dedicated facility for PET/CT imaging, and a laboratory for HPLC and related activities for pharmacokinetic analysis of radiopharmaceuticals. The CMGI, a campus facility for small animal *in vivo* and biospecimen imaging directed by [redacted] has a biomedical cyclotron and a radiochemistry laboratory, led by [redacted] and managed by [redacted]. This laboratory contains an RDS 111 (Siemens Molecular Imaging, Knoxville, TN) 11 MeV negative ion biomedical cyclotron, primarily for the production of ^{18}F and ^{11}C to support PET imaging studies. Routine radiotracers available include ^{18}F -FDG, ^{18}F -FHBG, ^{18}F -FLT, ^{18}F -PBR111, ^{18}F -FMISO, ^{11}C -PK11195, ^{18}F -FMT, ^{11}C -raclopride, ^{11}C -SCH23390, ^{64}Cu -PTSM, and ^{64}Cu , ^{89}Zr , or ^{124}I -labeled biomolecules. This facility supplies all necessary radionuclides and radiotracers for *in vivo* PET studies and staff are certified for packaging and transporting radioactive materials to the Primate Center. In addition, the CMGI supports a MicroXCT-200 scanner (Xradia, Santa Rosa, CA) for high resolution specimen CT with a resolution of 1-20 μm , a fluorescence cryomicrotome (Barlow Scientific, Olympia, WA) that supports high resolution imaging of fluorescence in large tissue samples/whole organs, and a phosphor storage autoradiography system (Amersham Storm 860). All three instruments are available for use through the Core. UC Davis Radiation Use Authorizations are in place for all activities.

Clinical: Clinical care and related procedures in the Primate Center are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see Primate Services).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and an IT unit provides desktop support and other related services. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are available. There are several computers attached to a variety of microscopes that are used for hardware control, preprocessing and image acquisition, and image post-processing are available in the Core. A Linux based image workstation for processing DeltaVision images, a PC graphics workstation for stereological analysis, and a PC workstation for handling general graphics are available. Data storage servers (expandable multi-terabyte volumes) are available for archiving client, pathology, and Core data. Computer systems are also linked with the imaging systems and include advanced image visualization (Amira) and tracer kinetic modeling (PMod) software, along with commercial vendor software for image analysis, image registration, and image fusion.

Office: [redacted] each occupy an office at the Primate Center. [redacted] has an office at the Genome and Biomedical Sciences Facility, approximately 1 mile from the Primate Center. Core staff share offices at the Primate Center and the Genome and Biomedical Sciences Facility.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities, support services available, and extensive expertise as described in this application. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

CORE SERVICES: MULTIMODAL IMAGING CORE

EQUIPMENT

Microscopy and Stereology:

- Cryostat for frozen sections (1) and microtomes for paraffin and plastic sectioning (2)
- Olympus BX61 research microscope with 1 color and 2 B/W cameras, Olympus DSU spinning disk confocal system, computer controlled stage and focusing system, Molecular Devices MetaMorph image capture, analysis software, Intelligent Imaging Innovations SlideBook software for stereology and image data collection, and Visiopharm VIS software for advanced stereological analysis using microscope hardware
- Olympus BX61 microscope with Intelligent Imaging Innovations SlideBook software for stereology technique development by the Core staff
- Graphics workstation, flatbed scanner, and a high-quality color corrected printer which are used for publication quality prints, converting film to digital images, image correction, and image archiving
- Document scanners for rapid digitization and OCR conversion of paper records
- Delta Vision Microscopy System and computer workstation for very high resolution multi-dimensional fluorescence imaging with deconvolution
- Two computer workstations for offline analysis of stereology data and large multidimensional image analysis
- Annually updated Visiopharm VIS/CAST Grid Stereology System for quantitative data collection and automated image analysis
- Fluorescence stereomicroscope outfitted with a high sensitivity color camera coupled to a computer system
- Dual-head brightfield stereomicroscope
- Olympus VS110 virtual microscopy/whole slide scanning system for brightfield, DIC, and fluorescence imaging
- Cell Biosciences FluorChem-E scanner for gels and blots
- Transmission and Scanning Electron Microscopy (located in the Diagnostic and Research Electron Microscopy Laboratory on the UC Davis campus)

In Vivo and Biospecimen Imaging:

- Phillips HDI@5000 SonoCT Ultrasound Imaging System
- Xenogen IVIS@200 imaging system (*in vivo* bioluminescence/fluorescence)
- Siemens microPET P4 imaging system
- GE Discovery@ 610 PET/CT, 64 slice CT, whole-body BGO PET scanner
- Siemens RDS 111 biomedical cyclotron and radiochemistry facilities
- Xradia, MicroXCT-200 for high resolution CT (1-20 μm) (located in the CMGI)
- Barlow Scientific Fluorescence Cryo-microtome (located in the CMGI)
- Amersham Biosciences, Storm 860 for autoradiography (50-100 μm) (located in the CMGI)

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	18,150.00	3,957.00	22,107.00
2.					Core Scientist			0.0	0.0	9,075.00	3,619.00	12,694.00
3.					Core Scientist			0.0	0.0	9,075.00	281.00	9,356.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

44,157.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Imaging Manager Excluded by Requester	EFFORT			4,085.00	2,161.00	6,246.00
1	Microscopy Manager Excluded by Requester				37,201.00	19,679.00	56,880.00
1	Project Support Excluded by Requester				4,692.00	1,569.00	6,261.00
1	Imaging Technical Support Excluded by Requester				16,689.00	8,828.00	25,517.00
1	Radiochemistry Technical Support: Excluded by Requester				23,692.00	12,533.00	36,225.00
1	Microscopy Technical Support: Excluded by Requester				18,793.00	9,941.00	28,734.00
6	Total Number Other Personnel				Total Other Personnel		159,863.00
Total Salary, Wages and Fringe Benefits (A+B)							204,020.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	3,000.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	13,000.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Gigabyte Network Rental Fee	2,500.00
Total Other Direct Costs	16,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	223,520.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	223,520.00	50,739.00
Total Indirect Costs			50,739.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	274,259.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: MI_Budget_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	18,150.00	4,144.00	22,294.00
2.					Core Scientist			0.0	0.0	9,075.00	3,830.00	12,905.00
3.					Core Scientist			0.0	0.0	9,075.00	281.00	9,356.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

44,555.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Imaging Manager	Excluded by	EFFORT		4,126.00	2,283.00	6,409.00
1	Microscopy Manager	Excluded by			37,573.00	20,784.00	58,357.00
1	Project Support	Excluded by Requester			4,738.00	1,669.00	6,407.00
1	Imaging Technical Support	Excluded by			16,856.00	9,324.00	26,180.00
1	Radiochemistry Technical Support	Excluded by			23,928.00	13,236.00	37,164.00
1	Excluded by Requester						
1	Microscopy Technical Support	Excluded by			18,982.00	10,500.00	29,482.00
1	Excluded by Requester						
6	Total Number Other Personnel					Total Other Personnel	163,999.00
						Total Salary, Wages and Fringe Benefits (A+B)	208,554.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,090.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,090.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	13,390.00
2. Publication Costs	1,030.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Gigabyte Network Rental Fee	2,575.00
Total Other Direct Costs	16,995.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	228,639.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	228,639.00	51,901.00
Total Indirect Costs			51,901.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	280,540.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: MI_Budget_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	18,150.00	4,280.00	22,430.00
2.					Core Scientist			0.0	0.0	9,075.00	3,964.00	13,039.00
3.					Core Scientist			0.0	0.0	9,075.00	289.00	9,364.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

44,833.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Imaging Manager: Excluded by	EFFORT			4,176.00	2,385.00	6,561.00
1	Microscopy Manager: Excluded by				37,623.00	21,489.00	59,112.00
1	Project Support: Excluded by Requester				4,789.00	1,744.00	6,533.00
1	Imaging Technical Support: Excluded by				16,906.00	9,656.00	26,562.00
1	Radiochemistry Technical Support: Excluded by Requester				23,979.00	13,695.00	37,674.00
1	Microscopy Technical Support: Excluded by Requester				19,031.00	10,870.00	29,901.00
6	Total Number Other Personnel				Total Other Personnel		166,343.00
					Total Salary, Wages and Fringe Benefits (A+B)		211,176.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,183.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,183.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	13,792.00
2. Publication Costs	1,061.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Gigabyte Network Rental Fee	2,652.00
Total Other Direct Costs	17,505.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	231,864.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	231,864.00	52,633.00
Total Indirect Costs			52,633.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	284,497.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: MI_Budget_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Core Leader/ Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	18,150.00	4,407.00	22,557.00
2.					Core Scientist			0.0	0.0	9,075.00	4,082.00	13,157.00
3.					Core Scientist			0.0	0.0	9,075.00	298.00	9,373.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

45,087.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Imaging Manager	Excluded by Requester	EFFORT		4,209.00	2,476.00	6,685.00
1	Microscopy Manager	Excluded by Requester			38,329.00	22,544.00	60,873.00
1	Project Support	Excluded by Requester			4,834.00	1,814.00	6,648.00
1	Imaging Technical Support	Excluded by Requester			17,195.00	10,114.00	27,309.00
1	Radiochemistry Technical Support	Excluded by Requester			24,409.00	14,357.00	38,766.00
1	Microscopy Technical Support	Excluded by Requester			19,362.00	11,388.00	30,750.00
6	Total Number Other Personnel				Total Other Personnel		171,031.00
						Total Salary, Wages and Fringe Benefits (A+B)	216,118.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,278.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,278.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	14,205.00
2. Publication Costs	1,093.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Gigabyte Network Rental Fee	2,732.00
Total Other Direct Costs	18,030.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	237,426.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	237,426.00	53,896.00
		Total Indirect Costs	53,896.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	291,322.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: MI_Budget_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
Excluded by Requester													
1.					Core Leader/	Institutional	EFFORT	0.0	0.0	18,150.00	4,534.00	22,684.00	
					Core Scientist	Base Salary							
2.					Core Scientist			0.0	0.0	9,075.00	4,208.00	13,283.00	
3.					Core Scientist			0.0	0.0	9,075.00	307.00	9,382.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons: File Name:												Total Senior/Key Person	45,349.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Imaging Manager: Excluded by Requester	EFFORT			4,251.00	2,576.00	6,827.00
1	Microscopy Manager: Excluded by Requester				38,711.00	23,459.00	62,170.00
1	Project Support: Excluded by Requester				4,883.00	1,886.00	6,769.00
1	Imaging Technical Support: Excluded by Requester				17,367.00	10,524.00	27,891.00
1	Radiochemistry Technical Support: Excluded by Requester				24,654.00	14,940.00	39,594.00
1	Microscopy Technical Support: Excluded by Requester				19,555.00	11,851.00	31,406.00
6	Total Number Other Personnel					Total Other Personnel	174,657.00
Total Salary, Wages and Fringe Benefits (A+B)							220,006.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,376.00
2. Foreign Travel Costs	0.00
Total Travel Cost	3,376.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	14,631.00
2. Publication Costs	1,126.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Gigabyte Network Rental Fee	2,814.00
Total Other Direct Costs	18,571.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	241,953.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	241,953.00	54,923.00
		Total Indirect Costs	54,923.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	296,876.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: MI_Budget_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

CORE SERVICES: MULTIMODAL IMAGING CORE**BUDGET JUSTIFICATION**

All funds requested in the Core are for developmental and administrative activities only. Services provided to users are fully charged to those activities based upon approved rates. The Core leverages opportunities and services provided through the UC Davis Center for Molecular and Genomic Imaging (CMGI) directed by Core Scientist [REDACTED]. This service primarily entails the provision of radioisotopes and additional expert personnel to assist as the workload demands; these individuals do not receive support from the P51 base grant as noted below (shown in *italics*).

PERSONNEL

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist	% Effort			
	Core Scientist				
	Core Scientist				
	Imaging Technician				
	Radiochemistry Manager				
	Project Support				
	Imaging Manager				
	Microscopy Technician				
	Microscopy Manager				
	<i>Imaging Technician</i>				
	<i>Project Support</i>				
	<i>Imaging Technician</i>				

Individuals shown in italics are not supported by the P51 base grant; their salary support is provided by Program Income

Excluded by Requester **PhD, Core Scientist** [REDACTED] months - [REDACTED] % Effort Excluded by Requester is Professor in the Departments of Pediatrics and Cell Biology and Human Anatomy, School of Medicine. She is the Lead of the Multimodal Imaging Core and provides ultrasound, optical, and PET/CT imaging services. [REDACTED] has a long-standing commitment to, and productive track record in, providing research opportunities to investigators and fostering partnerships and collaborations. [REDACTED] is an internationally-renowned expert in the use of nonhuman primates for translational research, and has provided investigators new ways to incorporate state-of-the-art *in vivo* imaging techniques and procedures in their research programs. She is a leader in ultrasound imaging in nonhuman primates, and developed the growth charts and imaging paradigms specific to rhesus and long-tailed macaques used nationally/internationally. She has also initiated unique interventional procedures for model development and experimental procedures. [REDACTED] initially developed the imaging program with a focus on ultrasound imaging. Due to the success of this approach, the program expanded to optical imaging, which is also unique to the CNPRC, and more recently microPET and PET/CT with the addition of [REDACTED] to the program.

Excluded by Requester **PhD, Core Scientist** [REDACTED] months - [REDACTED] % Effort Excluded by Requester is Professor in the Department of Biomedical Engineering, College of Engineering, with a joint appointment in the Department of Radiology, School of Medicine. [REDACTED] the Director of the CMGI, a state-of-the-art center dedicated to small animal imaging in the Genome and Biomedical Sciences Facility, within 5 minutes of the Primate Center. The CMGI houses a biomedical cyclotron and chemistry facilities (hot and cold) for contrast agent development (directed by [REDACTED] see letter) and functions as a resource for all of UC Davis. [REDACTED] has over 25 years of experience in biomedical imaging science, with expertise that spans instrumentation, image reconstruction, quantitative imaging, and molecular imaging applications in animals and humans. He developed the microPET scanner that became a commercial product for small animal and nonhuman primate imaging through Concorde Microsystems and, subsequently, Siemens. His laboratory has developed microCT scanners, a combined PET/MRI instrument, and a hyperspectral fluorescence tomography system. He has

expertise in a broad range of imaging modalities and has published widely in the areas of image reconstruction, image quantification, and image registration. [Excluded by Requester] have a long-standing and productive collaboration as evident by several collaborative grants and joint publications. [Excluded by Requester] is a Core Scientist in the Reproductive Sciences and Regenerative Medicine Unit, complementing the long-standing commitment of [Excluded by Requester] to *in vivo* imaging.

[Excluded by Requester] **PhD, Core Scientist** [EFFORT] months [Excluded by Requester] is Professor in the Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine. He provides the training and direction for quantitative assays and computational approaches focused on microscopy and morphology performed in the Core. He also teaches seminars and courses in sampling and stereology. He provides the training and direction for fluorescence microscopy, whole mount tissue microscopy, immunohistochemistry, and *in situ* hybridization. He has extensive and unique expertise in stereology and novel applications of this methodology for a spectrum of research applications.

[Excluded by Requester] **BA, Imaging Technician** [EFFORT] months [Excluded by Requester] is a technical staff member in *in vivo* imaging services and is responsible for routine maintenance and operation of the microPET and PET/CT imaging systems and quantitative data analysis. She is also a staff member of the CMGI.

[Excluded by Requester] **MS, Radiochemistry Manager** [EFFORT] months [Excluded by Requester] provides radiochemistry support for the *in vivo* imaging component of the Core. He is responsible for radionuclide production, new tracer radiosynthesis, and their applications for PET imaging, as well as the HPLC system.

[Excluded by Requester] **PhD, Senior Scientist** [EFFORT] months [Excluded by Requester] is an Assistant Adjunct Professor in the Department of Cell Biology and Human Anatomy, School of Medicine. He has extensive expertise in morphology and *in vivo* imaging, and has worked closely and published extensively with [Excluded by Requester]. He will primarily provide PET/CT and optical imaging support, routine quality assurance testing, and HPLC analysis.

[Excluded by Requester] **Imaging Manager** [EFFORT] months [Excluded by Requester] provides organizational and managerial support for the Core, including scheduling, assisting investigators in coordination of projects, oversight of the facilities, and with HPLC analysis and other assays and procedures as needed.

[Excluded by Requester] **Microscopy Technician** [EFFORT] months [Excluded by Requester] is responsible for support of research, development, and administration of computational imaging and stereologic applications. She is also responsible for immunohistochemistry, *in situ* hybridization, and support for the Primate Pathology Image Database for research and development.

[Excluded by Requester] **Microscopy Manager** [EFFORT] months [Excluded by Requester] provides the oversight and managerial support for microscopy, stereology, digital imaging, histology, and microscopy consultation services. He assists faculty, staff, and students with their research needs for qualitative and quantitative applications.

Additional in vivo imaging support is provided for microPET and PET/CT. HPLC analysis, new protocol development, and tracer kinetic modeling through staff in the CMGI. [Excluded by Requester]
This provides additional personnel support to the Core through recharge activity.

EQUIPMENT

Requests for equipment are shown in the **Facilities Improvement** section.

SUPPLIES

\$10,000 is requested for general supplies, reagents, and miscellaneous supplies to support the technical development of new methodologies in the Core.

\$3,000 is requested for upgrades for data storage and network hardware for all imaging applications.

TRAVEL

\$3,000 is requested to attend two professional meetings annually to advertise Core services and update on new developments and research applications that are available at the CNPRC.

OTHER EXPENSES

\$1,000 is requested for manuscripts related to new technology development.

\$2,500 is requested for the gigabyte network rental fee.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		223,981.00
Section B, Other Personnel		835,893.00
Total Number Other Personnel	30	
Total Salary, Wages and Fringe Benefits (A+B)		1,059,874.00
Section C, Equipment		0.00
Section D, Travel		15,927.00
1. Domestic	15,927.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		87,601.00
1. Materials and Supplies	69,018.00	
2. Publication Costs	5,310.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	13,273.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,163,402.00
Section H, Indirect Costs		264,092.00
Section I, Total Direct and Indirect Costs (G + H)		1,427,494.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☒ Yes ☐ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
1	25,000.00	Services
2	26,375.00	Services
3	27,826.00	Services
4	29,356.00	Services
5	30,971.00	Services

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☐ No ☒ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

0043

0062

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

MI_SpecificAims.pdf

3. Research Strategy*

MI_ResearchStrategy.pdf

4. Progress Report Publication List

MI_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

MI_VertabrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

MI_LettersofSupport.pdf

13. Resource Sharing Plan(s)

MI_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

CORE SERVICES: MULTIMODAL IMAGING CORE

SPECIFIC AIMS

The Multimodal Imaging Core (*formerly the Computational Imaging Core*) provides expertise; state-of-the art instrumentation; and assistance in the design, execution, and analysis of imaging studies at the California National Primate Research Center (CNPRC) that spans cellular imaging, tissue imaging, and whole-body imaging. The goal of the Multimodal Imaging Core is to support the research activities of investigators and trainees in qualitative and quantitative imaging applications across multiple spatial scales, and to facilitate the use of the latest imaging techniques and methods in nonhuman primates. The change in the Core name reflects the expanded spectrum of services and imaging modalities provided, and the continued growth of the *in vivo* imaging services. Animal models, particularly nonhuman primates, are essential to understand biological functions, study complex human diseases, and address safety of new diagnostics and therapies proposed for human use. The Core provides researchers with the infrastructure and expertise to conduct imaging studies in the monkey model with significant translational impact. The Core also supports the colony through implementation of the Primate Pathology Image Database and diagnostic imaging services, both at the microscopic level and through *in vivo* imaging. Dedicated Core Scientists and staff are responsible for imaging services (including radiotracer production), administrative support, day-to-day operational management, computer support, preventive and routine maintenance, and quality assurance/quality control (QA/QC). The Core provides access to essential expertise and eliminates the need for investigators to purchase costly equipment providing efficiency and economy of scale. The Core provides a broad range of primary service activities including image adjustment, restoration, rendering, qualitative analysis, and presentation; image and text database development, data archiving, and retrieval; microscopic image acquisition; quantitative imaging of cells, sectioned tissue, and whole mounts (stereology); immunohistochemistry and *in situ* hybridization; biospecimen imaging (microCT, autoradiography, fluorescence cryo-microtome); and *in vivo* whole-organ and whole-body imaging (ultrasound, optical/bioluminescence, microPET, PET/CT). The Specific Aims for the Core are as follows:

Specific Aim 1. Provide expertise, state-of-the-art equipment, and a range of imaging services across different spatial scales to ensure cutting-edge imaging technologies are available to the research community for studies with nonhuman primate models of human health and disease.

Plan. The Core will continue to maintain high quality imaging services and expand the range of imaging assays performed in nonhuman primates by introducing new protocols, new contrast agents, and new data analysis methods. The Core will also continue to ensure data integrity/security, archival/retrieval, and QA/QC.

Specific Aim 2. Acquire new technologies/instruments and replace instrumentation as needed through NIH and related equipment grant applications.

Plan. Core faculty members have shown a strong record of achievement in obtaining NIH S10 instrumentation grants for imaging and related equipment. They will continue to identify sources of support to ensure the Core is equipped with state-of-the-art equipment and methods for investigators, and expand the imaging tools dedicated for use with nonhuman primates located on-site at the CNPRC.

Specific Aim 3. Provide integrated assays, techniques, and tools to enhance the nonhuman primate resource for research, training, and colony management needs, and align with the broader translational imaging program at UC Davis.

Plan. Experienced Core faculty and staff will continue to provide a variety of tools and technologies to enhance the nonhuman primate resource and through key colony diagnostic services (e.g., assistance with the pathology database; ultrasound imaging, CT). New opportunities will be provided to trainees at all career stages through novel imaging programs and ongoing research. The Core will promote faculty and staff expertise for advanced imaging techniques through attendance at workshops and interactions with collaborators and consultants at national institutions. Expansion of services and opportunities for preclinical testing and commercialization of novel radiopharmaceuticals will be accomplished in collaboration with UC Davis infrastructure focused on translational imaging. An overriding objective is to ensure the CNPRC *in vivo* imaging program is closely aligned and integrated with the translational imaging program at UC Davis to effectively translate new imaging agents and radiopharmaceuticals from nonhuman primates to human applications.

CORE SERVICES: MULTIMODAL IMAGING CORE

RESEARCH STRATEGY

INTRODUCTION

The Core provides the infrastructure, support, and expertise for assessment of cells and tissues by microscopy following biopsy or tissue harvests, and whole-organ or whole-body imaging for real-time investigations and diagnostics in nonhuman primates (Figure 1). A spectrum of NIH-funded studies benefit substantially from the availability of the unique expertise and technologies on-site. Services in the Core are readily available to investigators locally, regionally, and nationally, and outreach is provided through multiple websites, presentations, advertisements, and through presentations at national meetings and the NIH. This established and highly innovative Core works very efficiently to meet the nonhuman primate imaging needs of investigators. Members of the Core are shown in Table 1 and the sources of support for the Multimodal Imaging Core in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Figure 1. Organizational Chart: Multimodal Imaging Core

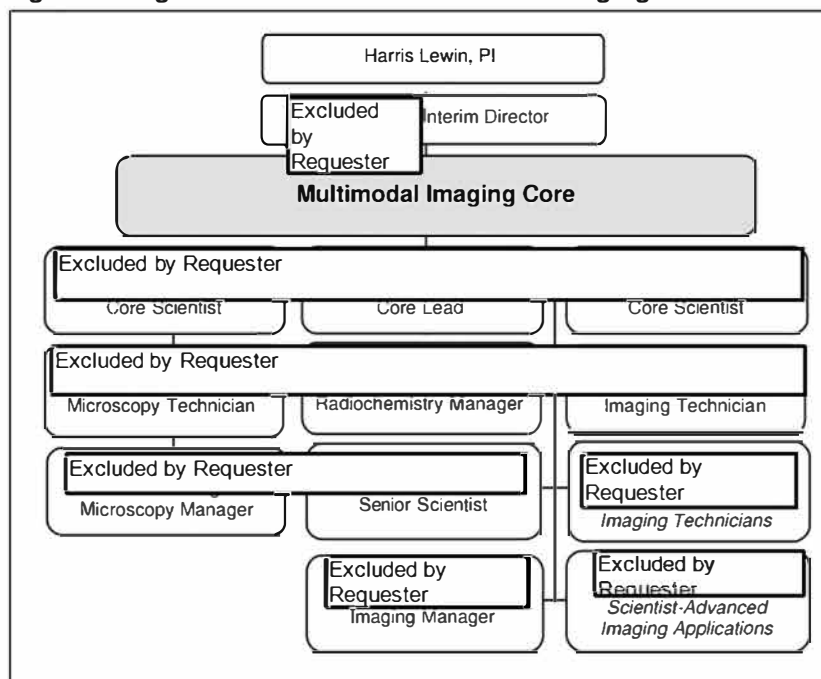


Table 1. Multimodal Imaging Core Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Pediatrics and Cell Biology and Human Anatomy, School of Medicine	Core Scientist
	Department of Biomedical Engineering, College of Engineering	Core Scientist
	Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine	Core Scientist
	CNPRC/ Center for Molecular and Genomic Imaging	Core Manager
	CNPRC/ Center for Molecular and Genomic Imaging	Radiochemistry Manager
	Department of Cell Biology and Human Anatomy, School of Medicine	Senior Scientist
	CNPRC	Imaging Manager
	CNPRC	Microscopy Technician
	CNPRC	Microscopy Manager
	Center for Molecular and Genomic Imaging	Imaging Technician
	Center for Molecular and Genomic Imaging	Project Support
	Center for Molecular and Genomic Imaging	Imaging Technician

Table 2. Support for the Multimodal Imaging Core

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$217,307	\$223,520
Program Income from P51	\$20,000 (microscopy only)*	\$25,000 (microscopy only)*
Other Sources	\$405,009 (\$10 equipment grant)	\$0**
TOTAL	\$642,316	\$248,520

*Recharge rates for new PET/CT scanner expected to be approved Fall 2014. **microPET and radiochemistry services have been recharged through the Center for Molecular and Genomic Imaging. The CNPRC is currently transitioning all recharge activity directly through the Core thus additional sources of support for the Core are based on the last 24 months of actual data as follows:

\$10,000 (PET/CT)*	\$20,000 (PET/CT)*
Other Recharge Activity** \$65,000	Other Recharge Activity** \$70,000

Response to Summary Statement

reviewers' comments

reviewers' comments

SIGNIFICANCE**Progress and Major Accomplishments: Contributions to the CNPRC Mission**

The Core provides services, expertise, training, and access to microscopy-based equipment that supports routine imaging modalities such as digital image capture with brightfield, Nomarski/differential interference contrast (DIC), and fluorescence microscopy; and advanced imaging applications such as unbiased stereology and high resolution multidimensional microscopy, with corrections for optical aberrations. The *in vivo* imaging program provides a unique depth and breadth of services offered for whole-animal imaging to meet a broad spectrum of investigator and colony needs. The Core functions within an organized structure with the high level of expertise for imaging and interpretation. Scheduling is driven by investigator needs, coordinated by staff, and with on-line calendars or direct request to the Core member responsible for the service activity (Table 3).

Table 3. Multimodal Imaging Core Use (May 1, 2010 to April 30, 2014)

Grant Year	Services	Users	User Affiliation (N)	Recharge (\$)
2010 - 2011	Slide Scans	4	UC Davis (3), National (1)	1,087
	Microscopes	17	Core Scientists (5), UC Davis (9), National (3)	2,481
	Microtomes	8	Core Scientists (4), UC Davis (3), National (1)	510
	Labor / Supplies	7	Core Scientists (4), UC Davis (1), National (2)	6,863
	Ultrasound*	18	Core Scientists (8), P51 Pilot (1), UC Davis (6), National (3)	11,390
	Optical*	6	Core Scientists (3), National (3)	19,345
	microPET	4	Core Scientists (3), UC Davis (1)	71,428
2011 - 2012	Slide Scans	4	Core Scientists (2), National (2)	1,746
	Microscopes	17	Core Scientists (5), UC Davis (10), National (2)	3,600
	Microtomes	7	Core Scientists (4), UC Davis (2), National (1)	464
	Labor / Supplies	3	Core Scientist (1), UC Davis (1), National (1)	933
	Ultrasound*	20	Core Scientist (7), UC Davis (2), National (11)	12,160
	Optical*	6	Core Scientists (3), National (3)	24,585
	microPET	3	Core Scientists (2), UC Davis (1)	37,180
2012 - 2013	Slide Scans	10	Core Scientists (4), UC Davis (5), National (1)	7,122
	Microscopes	13	Core Scientists (5), UC Davis (5), National (3)	2,229
	Microtomes	7	Core Scientists (4), UC Davis (2), National (1)	438
	Labor / Supplies	2	Core Scientist (1), UC Davis (1)	118
	Ultrasound*	14	Core Scientist (5), UC Davis (3), National (6)	10,135
	Optical*	7	Core Scientists (3), National (4)	18,425
	microPET	4	Core Scientists (1), UC Davis (1), National (2)	69,550
2013 - 2014	Slide Scans	3	Core Scientist (1), UC Davis (1), National (1)	7,668
	Microscopes	12	Core Scientists (5), UC Davis (5), National (2)	2,487
	Microtomes	7	Core Scientists (4), UC Davis (2), National (1)	352
	Labor / Supplies	2	Core Scientist (1), UC Davis (1)	8,583
	Ultrasound*	12	Core Scientist (3), UC Davis (3), National (6)	6,940
	Optical*	7	Core Scientists (3), National (4)	22,352
	microPET	4	Core Scientist (1), UC Davis (1), National (2)	62,959
	PET/CT	6	Core Scientists (3), P51 Pilot (1), UC Davis (2)	16,554
TOTAL				\$430,201

*Supplies only charged directly to grants, no labor costs

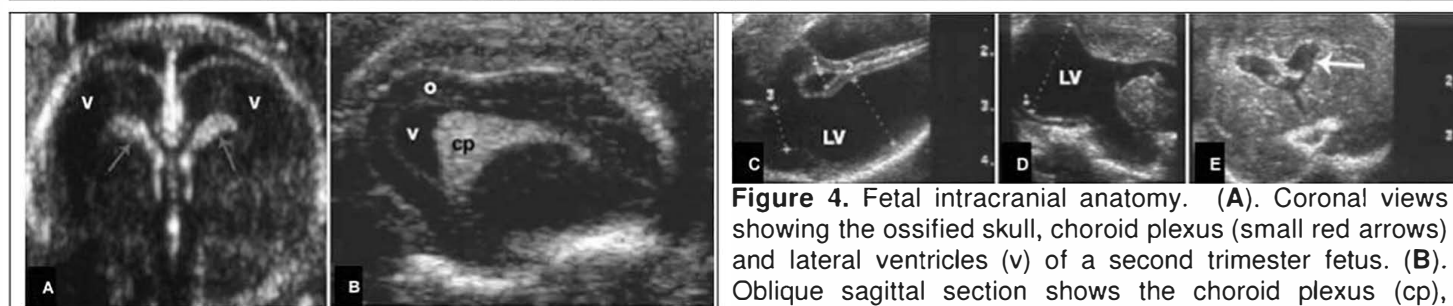
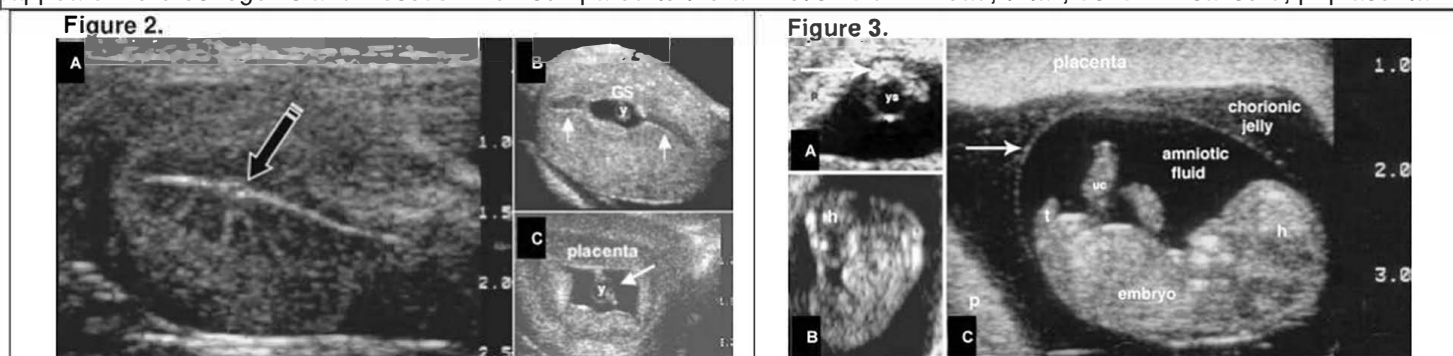
All users must have approved Institutional Animal Care and Use Committee (IACUC) protocols and use authorization approvals (e.g., biological, radiation) depending on the research. Priority is given to NIH-funded investigators. The IT staff host the web-based calendars for scheduling. Maintenance of all equipment is routinely performed and the need to replace older equipment is monitored annually with new funding opportunities sought. Imaging services are also advertised through a variety of websites including the UC Davis Clinical and Translational Science Center (CTSC) searchable Facilities, Cores, and Resources website and the CNPRC website. All Core faculty members present to research and education groups, at functions in UC Davis schools and colleges and through the Office of Research, through seminar series and CTSC sponsored workshops, in established courses, at national meetings, and at the NIH level. The Core also hosts special training sessions throughout the calendar year.

New Instrumentation [Excluded by Requester] received a base grant supplement to purchase a **whole slide scanner** and computer hardware for storage of the image files generated; and to identify and prioritize sets of histology slides from a wide range of studies for scanning based on clinical, pathology, research, and teaching value. The identified slides were scanned and archived for future analysis using rigorous sampling and stereological methods (Figure 2). The database allows for the collection of gross, histological, and other useful clinical images together with the pertinent case histories of nonhuman primates.

[Excluded by Requester] secured funding through the NIH S10 program for a new **EPIQ 7G Ultrasound Imaging System**. The system to be replaced (Phillips HDI®5000) was previously obtained by [Excluded by Requester] through a supplement to the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases and is over 10 years old (see **Reproductive Sciences and Regenerative Medicine Research Unit**). The Ultrasound Imaging Program developed by [Excluded by Requester] continues to provide state-of-the-art services and expertise in all aspects of ultrasound imaging to investigators and for colony management purposes (Figures 2-4).

Figure 2. Normal developmental features observed at 12 days gestation (arrow) (A); by 18 days gestation (B) the yolk sac (y) is evident within the gestational sac (GS). Note implantation bleeding (arrows). By 25 days gestation (C), the yolk sac (y) and embryo (arrow) with a beating heart is observed. Term=165±10 days; cm marks on right of images

Figure 3. Embryonic development. (A). At 27 days gestation, the embryo (arrow) is closely associated with the yolk sac (ys). (B). By 32 days gestation, the C-shape of the embryo is evident. h=head. (C). By 50 days gestation (late first trimester), the embryo has grown significantly. The amnion (arrow) and chorion have not yet fused, and the chorionic jelly appears more echogenic and viscous when compared to the amniotic fluid. h=head, t=tail, uc=umbilical cord, p=placenta



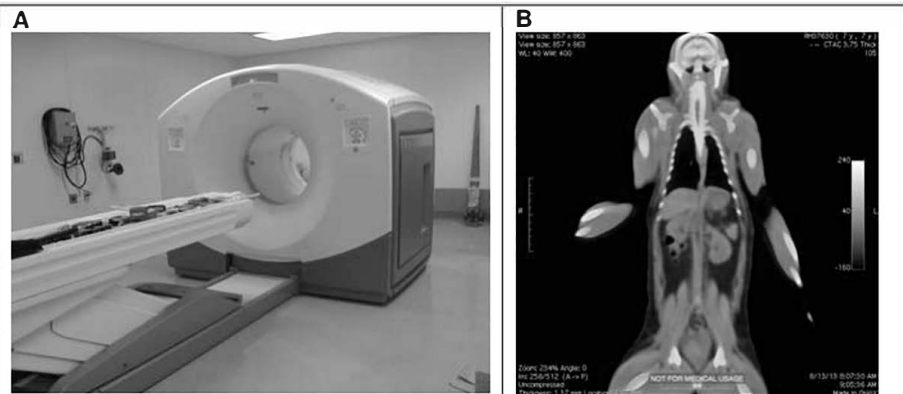
Second trimester fetus with hydrocephalus resulting from rhesus cytomegalovirus (RhCMV) infection [Tarantal et al., 1998] in transverse (C), sagittal (D), and coronal (E) views. Note lateral ventricles (LV) (arrow in C). Cursors in (A) indicate the 3rd ventricle width (0.3 cm) and lateral ventricles (0.8-1.4 cm)

This program has allowed investigators to incorporate non-invasive ultrasound-related techniques and procedures in their research programs, and to use non-surgical ultrasound-guided methods to develop new monkey models of human disease. Ultrasound imaging includes a spectrum of applications during pregnancy

and an array of ultrasound-guided procedures that provide an efficient means for sample collection and delivery into a variety of anatomical locations in all age groups (fetal to aged). From a colony management perspective, established fetal growth charts are routinely used to confirm gestational age in time-mated animals, and to predict gestational age in outdoor-housed animals where the time of conception is not known [2005]. Time-mated animals are screened annually, and for assignment to research projects.

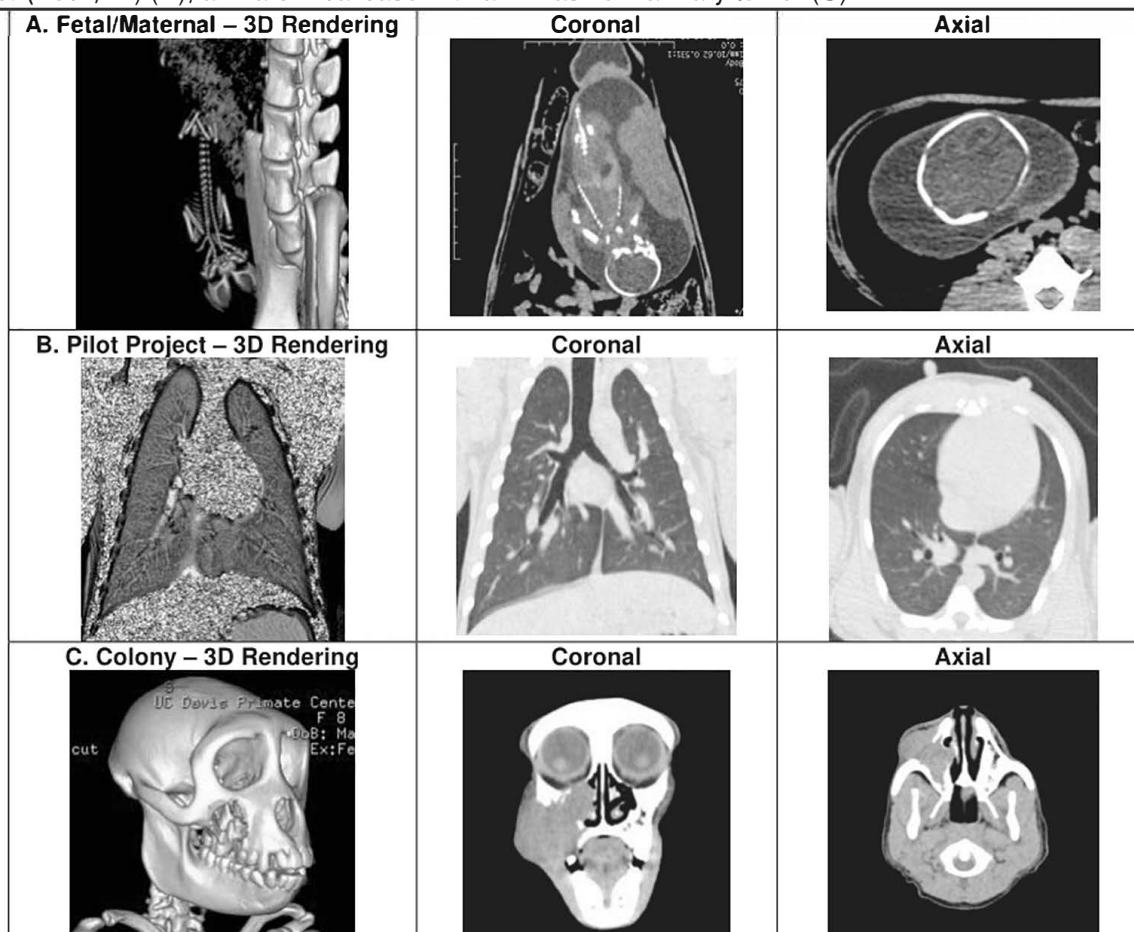
A new state-of-the-art human **GE Discovery® 610 PET/CT Imaging System** was acquired by [Excluded by Requester] with funding from an NIH S10 High-End Instrumentation grant (Figure 5). Dedicated space in a fully remodeled building was accomplished through a **P51 base grant supplement**. New imaging services are coordinated by dedicated Core faculty and staff that maintain the new PET/CT imaging facility and ensure all operational details, supplies, and reagents for imaging and related needs are met. The PET/CT imaging system provides a spectrum of new opportunities for research and expands existing capabilities in translational *in vivo* imaging for investigators locally, regionally, and nationally. This new system also provides important translational imaging opportunities to assess, for example, new radiopharmaceuticals developed at UC Davis for human imaging.

Figure 5. A. GE PET/CT installed at the CNPRC. **B.** Coronal fused PET/CT image showing multi-bed whole-body ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET image (color scale) of a rhesus monkey superimposed on the CT scan (gray scale). Image was acquired approximately 1 h after radiotracer injection.



An advantage of PET/CT technology is the ability to integrate two imaging modalities simultaneously, with PET providing functional information and CT the anatomical detail (Figure 6).

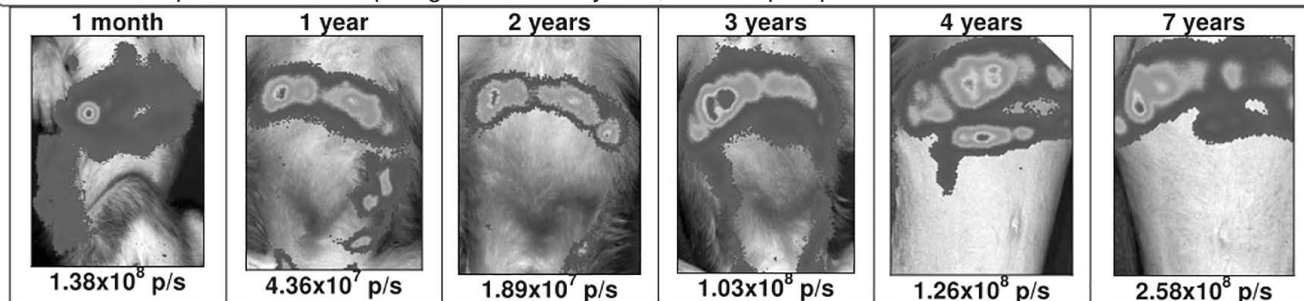
Figure 6. CT images shown include newly developed fetal/maternal imaging protocols (**A**), lung imaging for a P51 pilot project (Rock, PI) (**B**), and a clinical case with an invasive maxillary tumor (**C**).



Excluded by
Requester

was also recently funded through the NIH S10 program to replace the current IVIS@200 optical imaging system with a new **IVIS Spectrum Optical Imaging System** (Figure 7).

Figure 7. Postnatal bioluminescence imaging (BLI) in a monkey administered a dual fusion lentiviral vector using an intraperitoneal approach in the late first trimester. High levels of firefly luciferase expression were shown to persist in the muscular component of the diaphragm for over 7 years, to date. p/s=photons/sec/cm²/sr

Excluded by
Requester

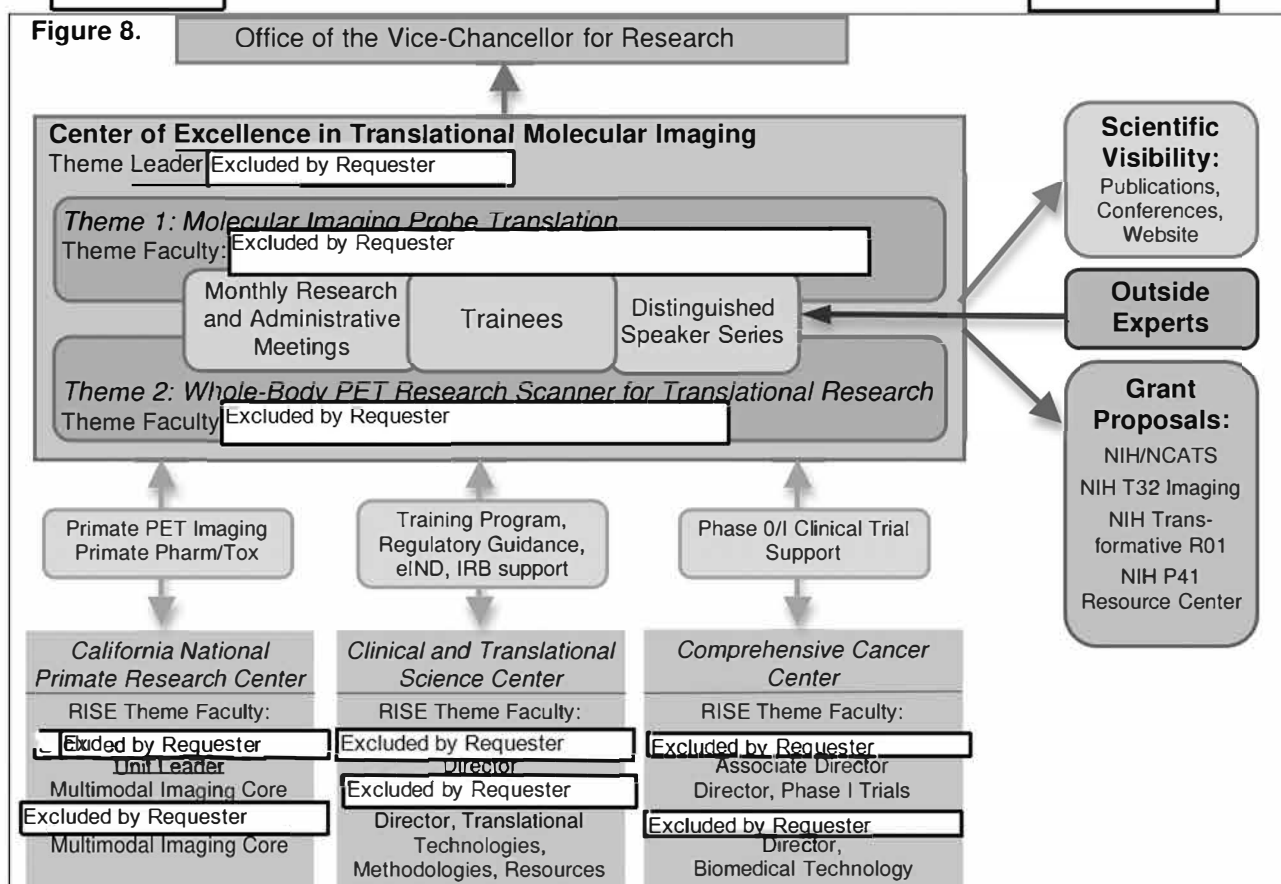
received funding through the NIH S10 program for an **Xradia microCT Biospecimen Scanner** that provides high resolution (1-20 μ m) x-ray images of tissues up to 3 cm, which is now available in the Core. He was also funded through the NIH S10 program for an **Imaging Cryo-Microtome** (Barlow Instruments) that permits fluorescence imaging of frozen tissue to produce 3D registered volumetric datasets showing fluorescence distribution at 20-40 μ m spatial resolution. Six combinations of excitation and emission filters cover a wide range of fluorescent proteins and fluorophores used to label molecular imaging agents.

Campus Investment in Translational *In vivo* Imaging

Excluded by
Requester

and team were selected by the UC Davis Office of Research to receive a RISE (Research Investments in Science and Engineering) Theme Proposal entitled: "**UC Davis Center of Excellence in Translational Molecular Imaging**" (Figure 8). The goal of the RISE proposal is to take a novel molecular imaging agent into humans for the first time after testing in nonhuman primates. Excluded by Requester is a team member leading the nonhuman primate studies with Excluded by Requester.

Figure 8.



These studies are enhanced by the **UC Davis Radiochemistry Research and Training Facility**. The new facility (12,000 sq. ft.) is directed by Excluded by Requester and will vastly improve logistics for bench-to-bedside

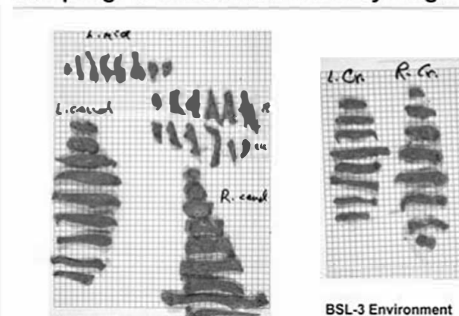
radiopharmaceutical conveyance. The facility is located within the building that houses the UC Davis CTSC and the Institute for Regenerative Cures. This new facility was developed cooperatively by the UC Davis Health System, PETNET Solutions Inc., and the Northern California PET Imaging Center. The unique partnership with PETNET functions as a pipeline for commercialization of the concepts and compounds that researchers develop. These new compounds and imaging agents will be produced in the UC Davis Good Manufacturing Practices (GMP) facility, tested preclinically in nonhuman primates, then the CTSC will expedite translation of successful diagnostic and therapeutic agents. The research component is aimed at developing specialized molecular agents for use in disciplines such as oncology, neurology, cardiology, and regenerative medicine, and will be expanded to other areas as well. *These activities form the basis for a range of new tools, techniques, and assays that will be developed and made available in the Core for investigators nationally.*

New Sampling Techniques

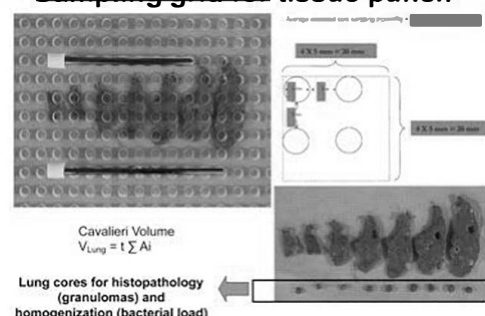
Excluded by Requester in collaboration with the Aeris Foundation, hosted a group of international pathologists to learn sampling of tuberculosis (TB) infected lungs for subsequent quantitative analysis. Excluded by Requester developed a fast tissue sampling method that uses a clear plastic overlay with 5 mm sampling holes at a specific density (Figure 9). A circular knife (similar to a skin biopsy punch) was used to accurately sample TB infected lungs in a BSL-3 necropsy environment. Participants also received a half-day of lectures on stereology for estimation of the volume and number of granulomatous lesions in the lungs of TB infected monkeys. Excluded by Requester also provided his graduate course lectures and exercises to participating pathologists through a website.

Figure 9. Stereology sampling technique for TB-related study developed in the Core.

Sampling: 5 mm slices of monkey lung lobes



Sampling grid for tissue punch



Training

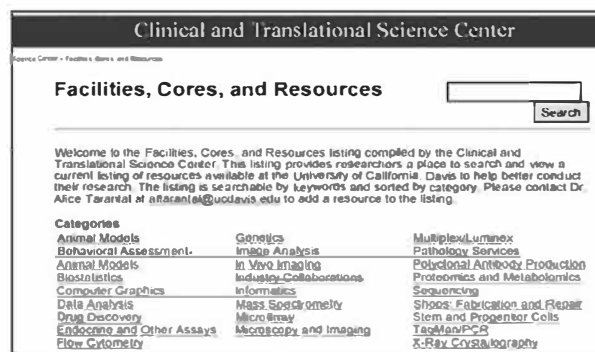
Excluded by Requester presented a half-day of lectures and exercises in stereology for the NPRC Pathologists Meeting at the Oregon NPRC (April 4-5, 2012). Additionally, individual investigators (~4-5 per year) have visited the Core for short stereology training sessions lasting 1-3 days that address the specific needs of ongoing research. The UC Davis CMGI, directed by Excluded by Requester, hosted three workshops on preclinical imaging during the current funding period. The first two workshops were targeted to new users of imaging and attracted participants from across the world. The third was for UC Davis researchers. Each workshop included lectures on the basics of each imaging modality (how it works, key applications), as well as tours, hands-on demonstrations, and live image analysis training.

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also utilizes student assistants for basic maintenance of morphology instruments, and to assist with digital imaging. One area of service provided by the students is digitizing and adjusting archived film images for Pathology services. The expertise of the Core has been optimized to convert many unusable film images to very high quality digital versions. To date, approximately 10,000 film slides have been digitized and individually adjusted for a variety of photographic problems.

Outreach. Imaging services are advertised through a variety of sources including websites such as the CTSC Facilities, Cores, and Resources searchable website which has "In vivo Imaging" as one of the resources available at UC Davis (see right). Core Scientists present to various research and education groups, at functions in the schools and colleges and through the Office of Research, through seminar series and CTSC sponsored workshops, at faculty meetings, and at the NIH level. Presentations at national meetings include advertisements describing the imaging services.

In addition, there is very broad dissemination of information and communication about new imaging techniques, methodologies, and resources through the NHLBI Center for Fetal Monkey Gene Transfer for



Heart, Lung, and Blood Diseases [Excluded by Requester] PI; see **Reproductive Sciences and Regenerative Medicine Unit**), which has an annual full page ad in the journal *Molecular Therapy* and similar posting on the NHLBI website under *Resources*.

INNOVATION

Unique Services and Research Opportunities for the Nonhuman Primate Research Community

The Core develops innovative methods and techniques using state-of-the-art technologies. Examples include:

[Excluded by Requester] and colleagues published guidelines for sampling and microscopic quantitation methods in the lung that were sponsored by the American Thoracic and European Respiratory Societies [Excluded by Requester] 2010].

- A simple sampling approach to *Mycobacterium tuberculosis*-infected lungs was developed as a method to evaluate deposition and granuloma volume essential for evaluating efficacy of vaccine studies [Excluded by Requester] 2011] (Figure 9). Similarly [Excluded by Requester] developed an isotropic uniform random sampling method to evaluate macroscopic and microscopic changes and applied it on proximal ascending colon in monkeys to evaluate idiopathic chronic diarrhea [Excluded by Requester] 2013]. Stereologic data showed significant increases in lamina propria (1.9-fold) and epithelium (1.4-fold) that were highly correlated with cytokine, chemokine, and growth factor levels in peripheral blood in monkeys with microscopic colitis.

- A new model of pulmonary fibrosis was developed using a prenatal intrapulmonary ultrasound-guided approach to address the role of overexpression of transforming growth factor- β 1 (Figure 10), and to provide insight into human lung development particularly when compared to mouse models [Excluded by Requester] 2010]. This study is an example of a pilot project supported through the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases, where all costs for the study were supported by the NHLBI [Excluded by Requester] PI; R24-HL085794).

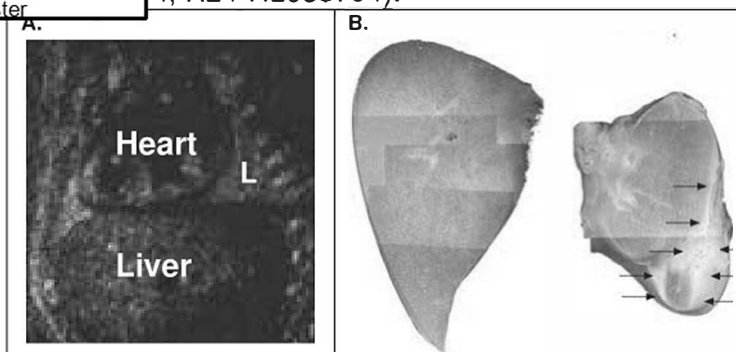
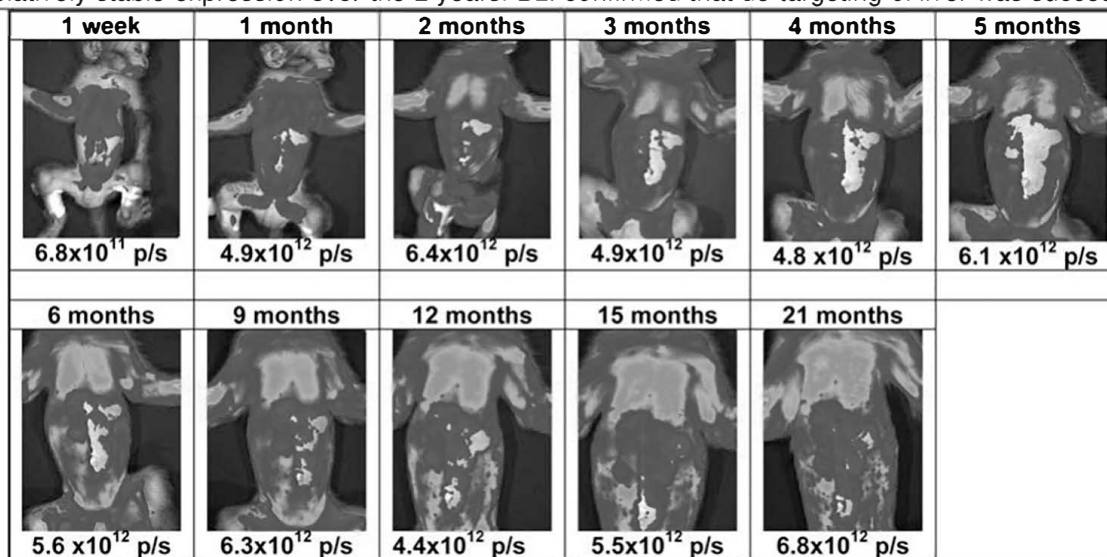


Figure 10. Overexpression of human TGF- β 1 resulted in prenatal pulmonary fibrosis and lobular fusion. **A.** A direct intrapulmonary ultrasound-guided injection into the left lung lobes was performed (see sonogram; L=lung lobe). **B.** At tissue harvest a comparison of right and left lung lobes showed normal right lung lobes and fibrotic surface and sublobular fusion of the left lung lobes (arrows). Direct ultrasound-guided injection into the left lung lobes did not result in abnormalities in the right lung lobes, as noted.

- Highly innovative methods for bioluminescence imaging (BLI) in monkeys have been developed and applied for a spectrum of gene therapy and stem cell transplantation studies [Excluded by Requester] 2010 [Excluded by Requester] 2012 [Excluded by Requester] 2012]. These include studies performed for investigators in the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases (see **Reproductive Sciences and Regenerative Medicine Unit**) (Figure 11).

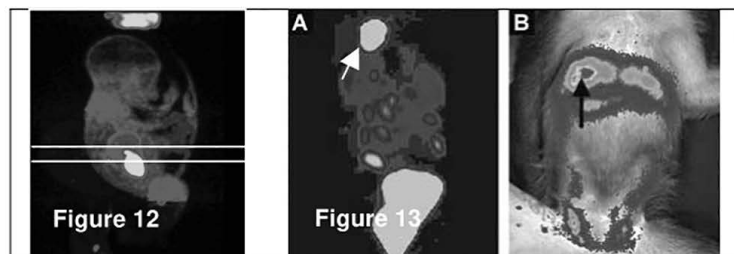
Figure 11. BLI of monkey administered a chimeric adeno-associated virus (AAV) vector at birth and monitored for 2 years. Using photons/sec (p/s) as a semi-quantitative method the comparison of a chimeric vector to AAV9 (not shown) indicated relatively stable expression over the 2 years. BLI confirmed that de-targeting of liver was successful.



A correlative BLI/PET imaging protocol has also been developed providing imaging capabilities unique to the CNPRO [Excluded by Requester] 2006] (Figures 12 and 13).

Figure 12. Fetal PET scans in the second trimester. No adverse findings, isotope uptake in abdominal region greater than controls [Excluded by Requester] 2006].

Figure 13. PET scan (A) and BLI (B) at 2 months postnatal age. Note focal density (arrow).



- Improved contrast-to-noise imaging performance for cell trafficking studies has been accomplished with the development of new copper (^{64}Cu) and zirconium (^{89}Zr) radioimmunoconjugates for successfully radiolabeling and tracking stem and progenitor cells post-transplantation [Excluded by Requester] 2012; 2013] (Figures 14 and 15).

Figure 14. Synthesis of newly designed ^{64}Cu -CD45 and ^{89}Zr -CD45 immunoconjugates was performed and the evaluation of the potential toxicity of radiolabeling human peripheral blood stem cells (hPBSC) was assessed *in vitro* (e.g., viability, population doubling times, colony forming units) using previously established techniques [Excluded by Requester] 2008]. Young monkeys that had been transplanted prenatally with 25×10^6 hPBSC expressing firefly luciferase were assessed with BLI, then 0.3 mCi of ^{89}Zr -Df-CD45 was injected intravenously and animals scanned, providing evidence of radiolabeling and imaging efficiency [Excluded by Requester] 2013].

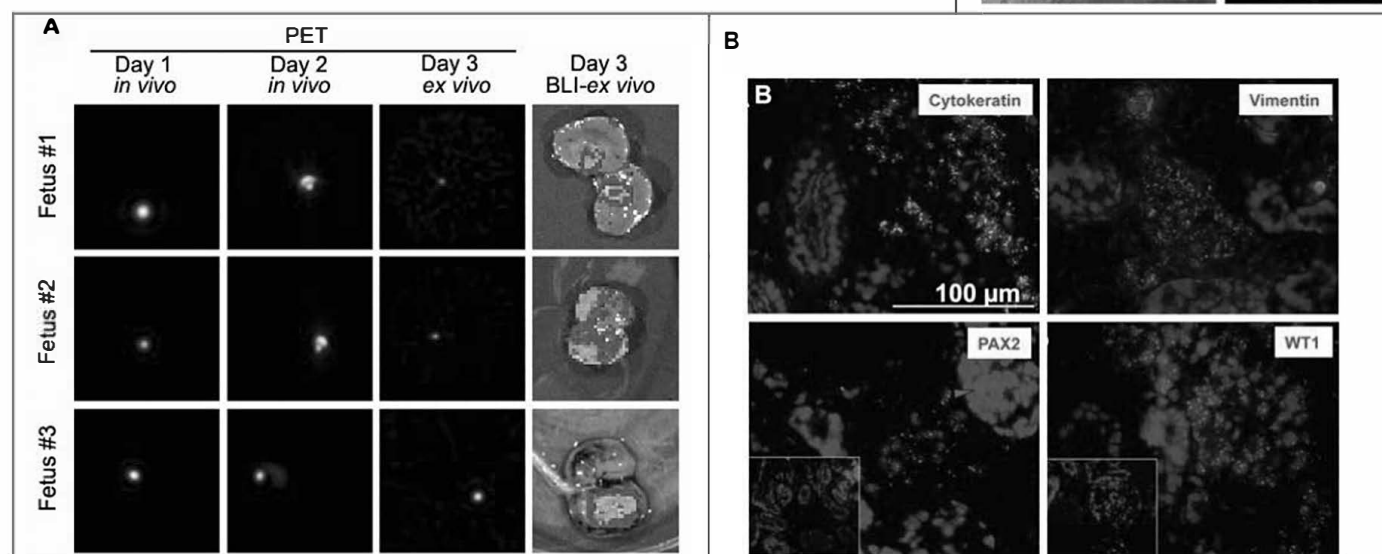
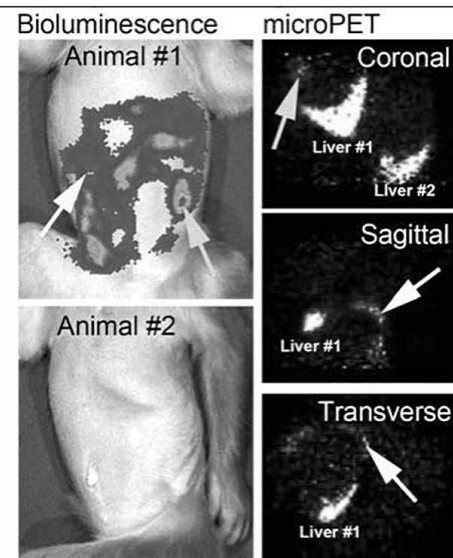


Figure 15. A. Imaging of transplanted renal precursors radiolabeled with ^{64}Cu -PTSM and expressing firefly luciferase. PET shows transplanted cells in fetal kidneys *in utero* (Days 1-3) and BLI was used *ex vivo*. Cells were transplanted into Fetus #1 in the renal hilum, Fetus #2 in the renal cortex, and Fetus #3 in the renal medulla. **B.** Immunohistochemistry for Cytokeratin, Vimentin, PAX2, and WT1. DAPI (blue) for cell nuclei, Green for the human centromere probe used for human cell localization, Red=antibodies. qPCR indicated 76.7 copies of the human specific MRGPRX4 gene/50,000 copies ϵ -globin (equivalent to 1 human cell per 650 monkey kidney cells) [Excluded by Requester] 2012].

- Development and use of new technologies includes advanced imaging tools. For example, emerging applications for PET, particularly for stem and progenitor cell trafficking and engraftment, requires the ability to image very low activity source distributions. Studies have focused on comparing the performance of PET scanners and showed that for PET studies in a very low activity range (e.g., the case for stem cell tracking), bismuth germanate (BGO)-based scanners have better performance because of the lack of significant background counting rates due to the inherent radioactive ^{176}Lu within the lutetium oxyorthosilicate (LSO)

detector material [Excluded by Requester] 2012]. These studies, which were conducted by a graduate student co-mentored by [Excluded by Requester] informed the choice of the GE PET/CT scanner purchased.

- New PET radiotracers have been developed which are now available in the Core and include ^{11}C -PK11195 and ^{18}F -PBR111 that bind to the translocator protein (TSPO) for neuroinflammation, ^{18}F -FMT for studying dopamine synthesis, and ^{11}C -PIB for amyloid imaging.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Provide expertise, state-of-the-art equipment, and a range of imaging services across different spatial scales to ensure cutting-edge imaging technologies are available to the research community for studies with nonhuman primate models of human health and disease.

In addition to continued efforts in the areas identified above, several developmental activities are in progress based on investigator needs and new grants funded, submitted, and planned with the goal of expanding capabilities in strategic areas with high impact, and where novel imaging tools are needed.

Primate Pathology Image Database. There are currently ~2,400 pathology cases in the CNPRC Primate Pathology Image Database; expansion to store and display whole slide scan images has just begun. The Visiopharm software (for stereology/image analysis) will read whole slide scan images and whole organ sampling methods and was developed for collecting blocks that represent the entire organ on one to a few slides. It is anticipated that the database will store "stereology ready" scans in order to allow sampling repeatedly by the Visiopharm software for estimation of organ subcompartments and cells. With the implementation of the ARMS database, pathology cases will be imported from the pathology database as a new pathology module is integrated into the ARMS electronic health record. To maximize the utility of the database, a goal is to integrate the locally (CNPRC) curated database with ARMS to create a robust centralized system that affords access to all nonhuman primate related information for users. The Primate Pathology Image Database will be used more efficiently if image loading is a simple and quick process that does not require multiple segregated steps. The intent is to create a system whereby pathologists and investigators can quickly and easily communicate important findings with others on the Primate Pathology Image Database network. The integration of this system will be accomplished during the next funding period.

Lung Stereology. [Excluded by Requester] collaborates with numerous colleagues providing expertise in lung stereology. The work is brought into the Core as recharge activity. A recent example is recharge for the stereological evaluation of human airway biopsies for inflammatory and immune cells through the Atlantis Group (Assessment of Small Airways Involvement in Asthma) comprised of investigators from Duke University, National Jewish Health, and the University of Modena, Italy that is funded through [Private Source]. In addition, combining quantitative stereology with quantitative CT measurements will be explored.

Inflammation Biomarkers. An inflammation biomarker, TSPO, which is found in the cell membrane; has been shown to be associated with apoptosis regulation, protein import, and cell cycle regulation; and used in PET imaging studies primarily to explore neuroinflammation. TSPO is currently under study for use in other organ systems. For example, a study has been initiated to assess its expression using immunohistochemical techniques in monkey kidneys across the lifespan for new applications that focus on the role of inflammation as a common disease mechanism; there is also recognition that chronic inflammation increases with advancing age. Thus, the Core is developing the TSPO radioligand, ^{18}F -PBR111, for new PET imaging applications that could be applied to other organ systems and used under a variety of experimental conditions. These new applications form the basis of several NIH grant submissions that address inflammation.

Lifespan Health Initiatives and Models of Human Disease. One of the Core objectives is to develop and validate the rhesus monkey model for lifespan health research initiatives. There are many studies in progress and planned through NIH grants funded and submitted such as those that address the role of maternal weight, diet, and inflammation on childhood health and future chronic disease. For example, one goal is focused on linking imaging findings in key tissues with endocrine/metabolic and inflammatory signatures at the blood and tissue level; new paradigms for imaging brown and white fat are also being explored. Several investigators have expressed a keen interest in the study of the developmental onset of adult disease and prenatal mechanisms such as those associated with neurodevelopmental disorders including autism and the role of circulating maternal antibodies [Excluded by Requester] 2013 [Excluded by Requester] 2013]. New imaging paradigms under development focus on concurrent maternal/fetal imaging (see Figure 6A), and utilize extensive expertise in the

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Core on the trafficking of cells and DNA during pregnancy [2014; [2003], and the multimodal application of ultrasound imaging with BLI and PET/CT. Spontaneous diseases that occur with aging also present opportunities for new imaging applications that can have significant research and colony impact. For example, ileocolic adenocarcinomas are known to be the most common malignant neoplasm in aging monkeys. [] are members of the UC Davis Comprehensive Cancer Center and have recognized that improvements are needed in early cancer diagnostics and have initiated studies to address this need (see Figure 17, below).

Metrics. Primary objectives are to increase the number of users on the new PET/CT scanner through dissemination of information, pilot project funding opportunities (e.g., CNPRC, CTSC, CMGI), continuing to work directly with investigators on novel imaging approaches that include PET/CT in grant submissions, and to introduce new advanced imaging including contrast-enhanced CT scanning, quantitative CT measures, and ECG and respiratory-gated CT methods. Several grants have been submitted from Core and Affiliate Scientists in all Scientific Research Units.

Alternative Strategies. CTSC workshops will be held and efforts to secure more pilot funds through partnering with other potential pilot programs (e.g., Cancer Center, Metabolomics Center) will focus on aiding investigators to acquire preliminary imaging data.

Specific Aim 2. Acquire new technologies/instruments and replace instrumentation as needed through NIH and related equipment grant applications.

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[] have demonstrated significant success in acquiring funds for new and replacement equipment during the current funding period (see above). The Core will continue to explore extramural sources for additional capabilities on-site. Nonhuman primates can accelerate the development of promising new therapies for humans and are necessary as translational models and for preclinical, IND-enabling studies. However, the biohazards and occupational health concerns when working with nonhuman primates, specifically macaques, are not trivial, as monkeys carry many zoonotic diseases. Of greatest concern is Herpes B virus, and monkeys may also be infected with other agents either naturally (e.g., *Shigella sp.*, *Salmonella*, *Yersinia*) or experimentally (e.g., SIV, TB) thus presenting additional human health risks. Monkeys are also highly prone to human infectious diseases. Thus, imaging modalities located on-site with experienced faculty and staff provides substantial benefits and opportunities for the continued growth of the program. The first goal is to secure funding for a GE Healthcare Discovery™ MR750, 3.0T dedicated for on-site magnetic resonance imaging (MRI) for nonhuman primates for a range of research projects. Many funded studies currently in progress and planned will benefit substantially from this technology on-site (Figure 16).

Figure 16. A novel cell-based strategy for stem cell therapy is under development to treat Huntington's disease. The use of nonhuman primates is crucial for these investigations and to provide essential safety data for cells proposed for transplant into the human striata. A pre-IND discussion with the FDA supported the need for these safety studies in monkeys. MRI-based stereotactic injection of human mesenchymal stem/stromal cells into the brain is required, and two preliminary juvenile monkeys have been imaged using MRI located off-site to obtain the coordinates for the injections through pilot funds provided by the CTSC. This is a very labor and cost-intensive process that would be most efficient and safe with the MRI instrumentation located on-site.



The selected scanner is compatible with the recently installed PET/CT that provides software compatibility and allows for easy integration of PET and MRI data. It is anticipated that many animals scheduled for PET will also be scheduled for MRI, therefore the compatibility and ease of registration is crucial to the efficiency of the program, and to provide complementary and highly efficient imaging paradigms while ensuring cost effectiveness. Of available systems today, the GE MR750 has the highest gradient specifications for slew rate and amplitude, and the best functional MRI (fMRI) stability, which was the subject of a UC San Diego publication [2012] on recommendations for multi-center fMRI studies. In all cases (studies at multiple sites and with all vendors), the GE MR750 was shown to have the best performance. Thus, a combination of pricing, compatibility for multimodal scans involving PET/CT and MRI, in addition to outstanding fMRI performance, formed the basis for this choice. To further enhance expertise the Core has enlisted the aid of UCSF colleague, [] has extensive expertise with GE instrumentation in both human and nonhuman primates, and a wealth of relevant experiences that will aid in implementation; Dr. [] will also assist with development and optimization of MRI protocols. In addition to participating as a

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member of our team, she will serve on an internal working group along with our colleague who serves as a member of the CNPRC National Scientific Advisory Board (see Overview).

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Another goal is to find a suitable replacement for the microPET P4 scanner (Siemens) that is utilized for neuroimaging studies at the CNPRC. This scanner represents 15-year-old technology no longer supported by the manufacturer. Currently, there are no vendors of high-resolution brain PET scanners for nonhuman primates. However, several companies are developing brain scanners for the human market, and the Core will continue to explore opportunities for a partnership with one of these companies to provide a viable replacement for the microPET P4, likely through the NIH S10 program when instrumentation is available.

In order to further expand the Cores imaging capabilities for regenerative medicine, the Core is collaborating with translational and clinical faculty in the UC Davis Center for Vision Science to develop capabilities for translational vision research in nonhuman primates. In 2012, Center for Vision Science faculty received \$23 million in research grants, making the UC Davis program one of the largest and most successful programs in the nation. UC Davis was also awarded NEI facilities and training grants, and team leader Ed Pugh received a RISE grant to establish the "EyePod", a facility for imaging the retina, cornea, and other components of living eyes of small animals. However, to translate the gene- and cell-based regenerative therapies that need to be developed for blinding eye diseases (e.g., glaucoma, diabetic retinopathy) nonhuman primates and dedicated state-of-the-art imaging is needed (e.g., optical coherence tomography, scanning laser ophthalmoscopy, adaptive optics technologies). This instrumentation is currently a roadblock to conducting translational studies in nonhuman primates that can capitalize on the extensive expertise at the CNPRC in regenerative medicine. Current plans include a grant submission in response to an RFA entitled: "*NEI Audacious Goal Initiative: Addressing Technical Needs and Opportunities for Imaging the Visual System (U01)*" as a collaborative effort which will include an aim focused on nonhuman primates and with matching funds from the campus for the necessary imaging equipment. Thus, plans are underway to obtain the funds to establish these technologies with the necessary technical expertise within the Core.

Metrics. Primary deliverables include new instrumentation that is directly translational. All modalities will be readily accessible to NIH-funded investigators nationally through established outreach efforts and widely publicized through a number of venues including accessible websites comparable to other imaging modalities and with campus approved recharge rates. These technologies will provide unprecedented opportunities and expand existing capabilities with a focus on translation to human imaging applications.

Alternative Strategies. regularly pursue opportunities for the purchase of instrumentation through the NIH S10 Shared Instrumentation Grant Program. Other funding opportunities will be explored through the private sector and philanthropy. The Center for Vision Science includes faculty (clinical, basic science) that have been highly successful in obtaining funds from generous donors.

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Specific Aim 3. Provide integrated assays, techniques, and tools to enhance the nonhuman primate resource for research, training, and colony management needs, and align with the broader translational imaging programs at UC Davis.

In the current funding period, the Core has developed a complement of new techniques including those used to explore the pharmacokinetics of novel radiopharmaceuticals with the addition of expertise in analysis of blood and other fluids by high performance liquid chromatography (HPLC). A laboratory has been established and is dedicated for this purpose, and *in vivo* imaging staff provides the expertise for these services. These new capabilities benefited from ongoing collaborations with the private sector where support was received to develop protocols for HPLC analysis of plasma samples, and are directly related to the campus RISE imaging program noted. The RISE initiative was designed to promote large-scale interdisciplinary research at UC Davis and to facilitate the formation and enhancement of interdisciplinary teams to carry out joint research activities in areas of strategic importance globally. Successful proposals were considered those with the greatest potential for future high impact discoveries and innovation, judged by their scientific merit, potential impact on society, and sustainability. For the imaging proposal led by dynamic PET/CT imaging using the new CNPRC imaging system is of primary importance and has as a major goal to translate findings in nonhuman primates to human imaging protocols using new fluorine-18 compounds developed by (Figure 17). These studies represent a strong example of campus investment but also the unique capabilities for translational *in vivo* imaging at the CNPRC and UC Davis that will be further developed during the next funding period. *The new Radiochemistry Research and Training Facility is directly related to these efforts, and together with the available imaging modalities, collaborations with academic*

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institutions and industry are expanding and anticipated to continue to increase during the next funding period.

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Additionally, the RISE focus in the vision sciences provides a strong impetus to expand these capabilities to the nonhuman primate model. [REDACTED] has been working closely with [REDACTED] Chair, Department of Cell Biology and Human Anatomy, in the recruitment of junior faculty with interests in regenerative medicine and the monkey model. Recent hires and new funding initiatives are being pursued.

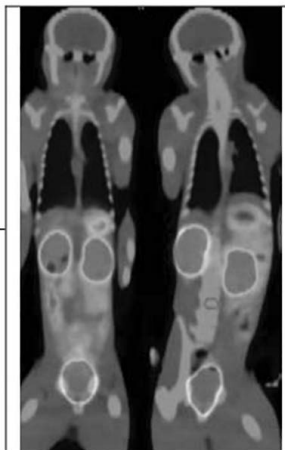
Trainees also have a primary involvement in all of the RISE proposals and present outstanding training opportunities provided through the Core during the next funding period. For example, undergraduate/graduate students and postdoctoral/clinical fellows will be educated and integrated in collaboration with the established and highly successful framework of the CTSC Research Education, Training, and Career Development Program. This program has a comprehensive approach to translational research training that provides scholars with a rich array of career development opportunities through program curricula, mentored research training, and partnerships with other programs, departments, and institutions. Through collaborations and infrastructure, excellence in scholarship across the continuum of training is fostered. Core curriculum includes an intensive "Introduction to Clinical Medicine" summer course, didactic courses on clinical and translational research, responsible conduct of research, and grant writing, as well as group experiences that include journal clubs, seminars, research presentations, and CTSC workshops. Trainees also receive training specific to nonhuman primates. Other related training opportunities include the NIH T32 training grant entitled "*Engineering Approaches to Molecular Imaging*" which supports 4 predoctoral students per year. Many other UC Davis training grants (e.g., CTSC T32 and K12, Stem Cell, Autism Research, Comparative Lung Biology and Medicine), and a new Broadening Experiences in Scientific Training (BEST) Award linked with the CTSC all provide examples of the rich training environment available.

The Core also has developed relationships with the private sector. Genentech has been a long-term collaborator and accesses the Core for PET studies of drug distribution and brain kinetics. They also were instrumental in supporting the new HPLC and blood metabolite services. Negotiations with others are currently in progress. The Core sees such relationships as crucial in maintaining a viable financial model as grant funding for imaging studies can fluctuate from year to year. These studies also support new methodologies and techniques that are then made available to all Core users, thus expanding the range of services available.

Metrics. One metric is to perform PET imaging and pharmacology/toxicology studies with novel molecular imaging agents in nonhuman primates to generate information for Radioactive Drug Research Committee (RDRC)/e-IND filing. Another is to complete GMP protocols and obtain approval for first-in-human studies, thus developing a standardized format for other imaging agents and related protocols.

Alternative Strategies. In regard to the concepts addressed in the RISE proposal, if compounds under study show suboptimal biodistribution/clearance properties, modifications to the labeling and preparation of the radiotracer will be pursued to determine if the kinetics can be improved. Preliminary results currently suggest excellent biodistribution and clearance for the radiotracer under development that is directly associated with the RISE proposal (Figure 17).

Figure 17. Three novel ^{18}F -labeled peptides have been studied in 6 juvenile rhesus monkeys. Each peptide was tested in an N of 2; as shown in this figure they were injected intravenously and imaged simultaneously side-by-side which significantly reduced the time and costs associated with such protocols. This is a unique imaging paradigm developed in the Core. PET/CT scans were performed at 2 and 4 hours post-injection with blood and urine samples (under ultrasound-guidance) collected for pharmacokinetic analysis and correlation with PET imaging outcomes.



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Long-term luciferase expression monitored by bioluminescence imaging after adeno-associated virus-mediated fetal gene delivery in rhesus monkeys (*Macaca mulatta*). Human Gene Ther 21:143-148, 2010. PMID: PMC2829449

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Radiolabeling and *in vivo* imaging of transplanted renal lineages differentiated from human embryonic stem cells in fetal monkeys. Mol Imaging Biol 14:197-204, 2012. PMC Journal-in-Progress

Excluded by Requester

Radiolabeling human peripheral blood stem cells for positron emission tomography (PET) imaging in young rhesus monkeys. PLoS One 8:e77148, 2013. PMID: PMC3789702

Excluded by Requester

Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases: An NHLBI Resource for the Gene Therapy Community. Hum Gene Ther 23:1130-1135, 2012. PMID: PMC3498881

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CORE SERVICES: ENDOCRINE CORE

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian

Excluded by
Requester

Excluded by
Requester

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of Specific Animal of indoor animal space. The outdoor animal housing area includes Specific Animal Location field corrals Specific Animal Location corn cribs Specific Animal Location. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) Excluded by Requester. Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem.

and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

- 4. Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For some imaging procedures, animals may be intubated and maintained under isoflurane (to effect). The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
- 5. Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

CORE SERVICES: MULTIMODAL IMAGING CORE

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- Excluded by Requester [redacted] Radiolabeling human peripheral blood stem cells for positron emission tomography (PET) imaging in young rhesus monkeys. *PLoS One* 8:e77148, 2013. PMCID: PMC3789702
- Excluded by Requester [redacted] Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases: An NHLBI Resource for the Gene Therapy Community. *Hum Gene Ther* 23:1130-1135, 2012. PMCID: PMC3498881

CORE SERVICES: MULTIMODAL IMAGING CORE

LETTERS OF SUPPORT

Letters of support from the individuals named below are provided on the pages that follow.

- 1

Excluded by
Requester

 PhD, Associate Professor, Department of Internal Medicine and Department of
Biomedical Engineering; Director, Cyclotron and Radiochemistry Facility, University of California, Davis

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO



SANTA BARBARA • SANTA CRUZ

Excluded by Requester

UC DAVIS HEALTH SYSTEM (UCDHS)
DEPARTMENT OF INTERNAL MEDICINE
DIVISION OF HEMATOLOGY/ONCOLOGY
SACRAMENTO, CALIFORNIA 95817

July 13th 2014

Excluded by Requester

Unit Leader, Reproductive Sciences and Regenerative Medicine, California National Primate Research Center
University of California, Davis
Davis, CA 95616-8542

Excluded by Requester

Dear

I am writing to express my strong support for your renewal of your base grant for the California National Primate Research Center, my support for Multimodal Imaging Core and more specifically my keen interest in the *in vivo* imaging services this core offers such as the positron emission tomography/computed tomography (PET/CT), and microPET.

As you know my expertise is in targeted molecular probe development. After spending 10 years in clinical PET in the UK I came to UC Davis to establish the preclinical imaging center, the Center for Molecular and Genomic Imaging (CMGI) with colleague Excluded by Requester CMGI is a state-of-the-art small animal imaging facility housing all imaging modalities including its own biomedical cyclotron. More recently I spearheaded the public private partnership with PETNET, a wholly owned subsidiary of Siemens, and recently opened our radiochemistry facility on the Sacramento campus. This facility houses two biomedical cyclotrons as well as a fully equipped radiotracer development laboratory. This facility will be a resource for radiotracer development for both academia and industry for first-in-human studies, will vastly improve logistics for bench-to-bedside radiopharmaceutical conveyance and will serve as a training site for radiotracer development. As you are well aware to expedite translation into the clinical setting it is critical that we test our probes in nonhuman primates rather than stopping at mouse models that have been shown to not be predictive. Our recent studies performed in the imaging core (data you present in the proposal) enabled us to rapidly screen several of our new radiotracers and facilitated the selection of the best radiotracer for further investigations for toxicity and efficacy. It is expected that an eIND will be obtained for this radiotracer for first-in-human studies by the end of 2014.

I believe that the California National Primate Research Center and the Multimodal Imaging Core will not only benefit my own research interests in radiotracer development and translational imaging but also numerous other colleagues with an interest in molecular imaging who are already users of CMGI (at least 40 principal investigators including collaborators in industry as well as those from other academic institutions).

I wish you the best of luck with your renewal and look forward to continuing our studies at the Primate Center.

Yours sincerely

Excluded by Requester

CORE SERVICES: MULTIMODAL IMAGING CORE

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

NPRC Consortium Activities

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename Consort_Absttract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	Consort_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	Consort_FacilitiesOtherResources.pdf
11. Equipment	Consort_Equipment.pdf

NPRC CONSORTIUM

ABSTRACT

The mission of the National Primate Research Center (NPRC) Consortium is to strengthen communications, leverage system-wide resources, and facilitate sharing of information and best practices. Established in part to address NIH directives for increased collaboration, the **NPRC Consortium** Working Groups, comprised of experts from major disciplines within each NPRC, collaborate to apply their combined expertise to priority issues, and to challenges identified within their respective domains. The Specific Aims for the NPRC Consortium are to: (1) Provide increased support for nonhuman primate research through the NPRC Director leadership and prioritization of Working Group goals and tasks, (2) Creation of ad hoc Working Groups to drive specific improvements in nonhuman primate expertise and services, and (3) Continued support for sharing of information and best practices to mentor and train NPRC members throughout the Consortium and inform external stakeholders as appropriate.

NPRC CONSORTIUM

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: All participants have computers available in their respective offices.

Office: Excluded by Requester have offices on-site for use for Consortium-based activities.

Other: Not applicable

NPRC CONSORTIUM

EQUIPMENT

Not applicable

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.					Core Scientist					3,904.00	1,557.00	5,461.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						5,461.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Affiliate Scientist	Excluded by Requester	EFFORT		2,325.00	927.00	3,252.00	
1	Total Number Other Personnel					Total Other Personnel		3,252.00
					Total Salary, Wages and Fringe Benefits (A+B)		8,713.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	13,500.00
2. Foreign Travel Costs	0.00
Total Travel Cost	13,500.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	25,826.00
2. Publication Costs	0.00
3. Consultant Services	454,430.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	480,256.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	502,469.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	502,469.00	114,060.00
Total Indirect Costs			114,060.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	616,529.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Consort_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional	EFFORT			0.00	0.00	0.00
2.					Core Scientist	Base Salary				3,943.00	1,664.00	5,607.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	5,607.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		2,348.00	991.00	3,339.00
1	Total Number Other Personnel				Total Other Personnel		3,339.00
					Total Salary, Wages and Fringe Benefits (A+B)		8,946.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	13,905.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	13,905.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	26,601.00
2. Publication Costs	0.00
3. Consultant Services	468,063.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	494,664.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	517,515.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	517,515.00	117,476.00
Total Indirect Costs			117,476.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	634,991.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Consort_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional	EFFORT			0.00	0.00	0.00
2.					Core Scientist	Base Salary				4,142.00	1,809.00	5,951.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:		File Name:								Total Senior/Key Person	5,951.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester	EFFORT		2,467.00	1,078.00	3,545.00
1	Total Number Other Personnel				Total Other Personnel		3,545.00
					Total Salary, Wages and Fringe Benefits (A+B)		9,496.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	14,320.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	14,320.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	27,398.00
2. Publication Costs	0.00
3. Consultant Services	482,106.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	509,504.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	533,320.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	533,320.00	121,064.00
Total Indirect Costs			121,064.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	654,384.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Consort_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester				Interim Director	Institutional	EFFORT			0.00	0.00	0.00	
2.					Core Scientist	Base Salary				4,266.00	1,919.00	6,185.00	
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:								Total Senior/Key Person		6,185.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Affiliate Scientist	Excluded by Requester			2,541.00	1,143.00	3,684.00
1	Total Number Other Personnel					Total Other Personnel	3,684.00
Total Salary, Wages and Fringe Benefits (A+B)							9,869.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	14,751.00
2. Foreign Travel Costs	0.00
Total Travel Cost	14,751.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	28,221.00
2. Publication Costs	0.00
3. Consultant Services	496,570.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	524,791.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	549,411.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	549,411.00	124,716.00
Total Indirect Costs			124,716.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	674,127.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Consort_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Interim Director	Institutional	EFFORT			0.00	0.00	0.00
2.					Core Scientist	Base Salary				4,394.00	2,037.00	6,431.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:		File Name:								Total Senior/Key Person		6,431.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
	Secretarial/Clerical							
1	Affiliate Scientist	Excluded by Requester	EFFORT		2,617.00	1,213.00	3,830.00	
1	Total Number Other Personnel					Total Other Personnel		3,830.00
					Total Salary, Wages and Fringe Benefits (A+B)		10,261.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	15,193.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	15,193.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	29,068.00
2. Publication Costs	0.00
3. Consultant Services	511,467.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	540,535.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	565,989.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	565,989.00	128,480.00
Total Indirect Costs			128,480.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	694,469.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Consort_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

NPRC CONSORTIUM

BUDGET JUSTIFICATION

PERSONNEL

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC. All effort for the Director in the NPRC Consortium is budgeted in the Director's Office.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Interim Director	% Effort			
	Core Scientist				
	Affiliate Scientist				

Excluded by Requester **Interim Director, Lead** (EFFORT months). As a part of the leadership role in the National Primate Research Centers (NPRCs), the Director works cooperatively with the other NPRC Director's in helping set the priorities of the Consortium Working Groups. The role of the Director in the Consortium is primarily supported through the Director's Office budget.

Excluded by Requester **PhD, Affiliate Scientist** (EFFORT months) (% Effort Excluded by Requester) has extensive experience in population genetics and primate genetic management, is directly responsible for analysis of pedigree and population genetic data used in the management of both conventional and specific pathogen-free (SPF) breeding colonies, and technical development and testing of Single-Nucleotide Polymorphisms (SNP) panels for Consortium use. Support is requested to continue to process samples and to generate reports for the Consortium.

Excluded by Requester **PhD, Core Scientist** (EFFORT months) (% Effort Excluded by Requester) has overall responsibility for oversight of colony population genetics management. This role has been key in leading the development of the SNP assays in use across the NPRCs allowing standardized genetic data across sites. Support will continue to facilitate the adoption of the SNP panels.

TRAVEL

Travel for six meetings is provided by the Consortium-Related Travel Supplement (3 x \$354 = \$1,062 and 3 x \$1,146 = \$3,438). Additional funding to support travel is provided by the CNPRC (6 x \$1,500 = \$9,000) for the Behavior Management, Pathology, and Occupational Health and Safety face-to-face Working Group meetings and for outreach activities by participation in NPRC booths at national meetings.

CONSULTANT COSTS

Funding of \$454,430 is requested for the consultants that comprise the NPRC Consortium Project Management and Informatics Group. While this represents a consortium-wide effort, the administrative and financial aspects are managed on behalf of the Consortium through the CNPRC. This group consists of **NyTech Consultants (\$226,430)** including **Excluded by Requester** who is responsible for the coordination of the Working Groups to enable the accomplishment of the objectives. This is facilitated through conference hosting, website support, services, security administration, and platform capabilities that NyTech Consultants provides by leveraging the technical Information Technology expertise of **Excluded by Requester (\$133,000)** and **Excluded by Requester (\$95,000)**. These individuals provide network support, data security and access support, back up of data, integration troubleshooting, production release support, web analysis, curation support, data standardization, demonstration and tool functionality support, upload support, web hosting support, testing services for supported platforms and browsers, and support for other technical issues as needed.

SUPPLIES

Funds are requested for the following:

- Outreach NPRC Booth for the USA Science and Engineering Festival. This is a major outreach activity for the NPRCs that has proven useful in the past, and the funds requested corresponds to the portion contributed by the CNPRC. The request includes booth rental and materials for set up, presentation, and

distribution based on prior conference experiences (\$2,504). The goal is to provide promotion of the NPRCs.

- Hosting of the face-to-face Breeding and Colony Management Meeting (\$2,538). This is a key meeting in the NPRC Consortium that focuses on best practices regarding colony management, and experiences and best practices shared at the meeting continues to improve colony quality and strengthen the ability of NPRCs to advance human health.
- Atlassian Confluence Wiki (\$2,000) and Crowd Security (\$2,000) software license and maintenance to facilitate virtual meeting/information exchange capabilities in a secure environment for Working Group and NPRC meetings. Additional funds (\$900) are requested for miscellaneous software and hardware that may be required for Consortium activities.
- Reagents for genotyping of rhesus macaques for the ancestry informative and parentage SNP panels. The cost per animal for each panel is estimated at \$38 and the total number of animals is estimated to be 418 ($418 \times \$38 = \$15,884$). The work is provided through the California and Oregon NPRCs; this budget request represents 50% of the work that will be conducted at the CNPRC. The overall goal is to continue to facilitate and support the adoption of the SNP panels for parentage and/or ancestry testing by NPRC colony managers and veterinarians.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		29,635.00
Section B, Other Personnel		17,650.00
Total Number Other Personnel	5	
Total Salary, Wages and Fringe Benefits (A+B)		47,285.00
Section C, Equipment		0.00
Section D, Travel		71,669.00
1. Domestic	71,669.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		2,549,750.00
1. Materials and Supplies	137,114.00	
2. Publication Costs	0.00	
3. Consultant Services	2,412,636.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		2,668,704.00
Section H, Indirect Costs		605,796.00
Section I, Total Direct and Indirect Costs (G + H)		3,274,500.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

Consort_SpecificAims.pdf

3. Research Strategy*

Consort_ResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

Consort_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

NPRC CONSORTIUM

SPECIFIC AIMS

The Specific Aims will be accomplished through the approaches described and in close partnership with the Consortium Project Management and Informatics Group. The mission of the National Primate Research Center (NPRC) Consortium is to strengthen communications, leverage system-wide resources, and facilitate sharing of information and best practices to achieve an efficient economy of scale based on input from all NPRCs. Established in part to address NIH directives for increased collaborations, the Consortium Working Groups, comprised of experts from major disciplines within each NPRC, collaborate to apply their combined expertise to priority issues and challenges identified within their respective domains.

Specific Aim 1. Provide increased support for nonhuman primate research through the NPRC Director leadership and prioritization of Working Group goals and tasks.

Plan. The NPRC Directors have committed through a carefully developed strategic planning process to provide direction and priorities for the NPRC Consortium Working Groups. The priorities identified as being of the highest level of importance include: (1) ensuring communication of information about NPRC resources that are available, (2) optimizing access for a larger constituency of investigators to the NPRCs, (3) providing strategic areas of NPRC cooperation and promotion to improve the collective scientific value of the national nonhuman primate resources, and (4) developing strategic information focusing specifically on the value of nonhuman primate research to advance human health. As these priorities develop, the NPRC Consortium Working Groups will be charged with providing contributions from their areas of expertise.

Specific Aim 2. Creation of ad hoc Working Groups to drive specific improvements in nonhuman primate expertise and services.

Plan. The NPRC Directors have affirmed the value of the current Working Groups but will also pursue establishment of temporary ad hoc groups to take on priority issues and provide direction for resolution. These groups may cross the current Working Groups functional boundaries depending on the nature of the specific issue.

Specific Aim 3. Continued support for sharing of information and best practices to mentor and train NPRC members throughout the Consortium and inform external stakeholders as appropriate.

Plan. The Consortium Working Groups will prioritize activities to enable the NPRCs to share challenges, design solutions to those challenges, and develop approaches for resolution at both the individual NPRC and Consortium levels. The three existing Working Group education forums, i.e., Virtual Slide Conferences, Virtual Grand Rounds, and Clinical and Surgical Techniques conferences, will continue as important channels to disseminate NPRC expertise and share best practices across NPRCs and with the external nonhuman primate research community. One of the greatest strengths of these groups has been the identification and sharing of best practices from individual NPRCs to be adopted at other NPRCs and institutions.

NPRC CONSORTIUM

RESEARCH STRATEGY

INTRODUCTION

The mission of the National Primate Research Center (NPRC) Consortium is to strengthen communications, leverage system-wide resources, and facilitate sharing of information and best practices. Established in part to address NIH directives for increased collaboration, the Consortium Working Groups, comprised of experts from major disciplines within each NPRC, collaborate to apply their combined expertise to priority issues, and to challenges identified within their respective domains. Leading the Consortium Project Management and Informatics Group is [Excluded by Requester] of NyTech Strategic Planning LLC, a program/project management professional who, in partnership with the NPRC Directors [Excluded by Requester] the Office of Research Infrastructure Programs (ORIP)/Division of Comparative Medicine (DCM), and the Working Group chairs, has been the primary catalyst of Consortium Working Group activities. While the Consortium Project Management and Informatics Group supports all members of the Consortium, the CNPRC administers the budget and contracts for this group as it is critical to the ongoing advancement and support of the Consortium activities.

Since inception of the first Working Group, the CNPRC Emeritus Director [Excluded by Requester] has been an outspoken champion and active participant in many of the formative aspects of the Consortium. Contributions of the CNPRC Core Scientists and staff have been significant throughout the current funding period, driving major accomplishments in a number of Consortium focus areas including Breeding and Colony Management, Behavioral Management, Consortium Project Management and Informatics Group, Genetics and Genomics, Outreach, and Pathology (Table 1). As is evident from Table 1, the CNPRC has had a strong and enthusiastic commitment to the different NPRC Working Groups.

Table 1. NPRC Consortium Working Groups

Working Group	CNPRC Representative
Behavioral Management	[Excluded by Requester]
Breeding and Colony Management	
Clinical and Surgical Techniques	
Consortium Project Management and Informatics Group	
Data Access Guidelines	
Genetics and Genomics	
Integrity and Compliance	
Occupational Health and Safety	
Outreach	
Pathology	
Training	

Sources of support for the NPRC Consortium during the last year of the current funding period and the first year of the proposed funding period per the FOA are shown in Table 2.

Table 2. Sources of Funding for the NPRC Consortium

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$496,926	\$502,469
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$496,926	\$502,469

Response to Summary Statement. There are no comments to respond to from the prior CNPRC review.

SIGNIFICANCE

Formation of the NPRC Consortium and pursuance of Working Group activities have changed many aspects of NPRC operations and communications. The Working Group concept has facilitated and institutionalized collaborations between colleagues across many NPRC domains to the benefit of the entire NPRC program. Importance of the Working Groups include:

- Regularly scheduled Working Group meetings have provided a forum to significantly improve the quality and frequency of communications between the NPRCs. Most groups meet on a monthly basis via web conference. A subset of the Working Groups conducts periodic face-to-face meetings.
- As a direct result of the Consortium activities, members of the Working Groups have increased their understanding of methods and procedures applicable within their domain.
- "Lessons learned" among Working Group participants has resulted in adoption of improved processes and best practices, resulting in a nationwide increase in capabilities across the NPRC system.
- Standardization of terminology enables extension of studies across multiple NPRCs on a consistent basis.
- Consortium Working Group activities have provided the impetus to share data and information across NPRCs and with the extended nonhuman primate research community. The Available Animal Locator, National Nonhuman Primate DNA Bank, and Primate Pathology Image Database are examples of cross-center data sharing initiated by the Consortium Working Groups.
- Adoption of common methods and best practices has increased capabilities across the NPRC system.
- Adoption of advances, capabilities, and materials from one NPRC reduces time spent on development of similar items at other NPRCs. For example, sharing of immunohistochemical protocols has proven highly advantageous.
- Training-related forums such as the Virtual Slide Conferences, Virtual Grand Rounds, and Clinical and Surgical Techniques conferences include participation of over 25 external organizations involved in nonhuman primate research. Sharing NPRC knowledge and experience with external organizations at the national level demonstrates the added value of NPRC leadership. These forums also provide opportunity for the NPRCs to leverage relevant expertise at external institutions.
- Access to standard panels of single-nucleotide polymorphism (SNP) markers for parentage and ancestry testing enables NPRCs to produce the same genetic information for colony management, thus facilitating accumulation of sharable genetic data across NPRCs.
- Consortium Working Group initiatives have resulted in increased efficiency and cost savings through collaborative development of shared methodologies and materials such as NPRC Outreach materials.

Progress and Major Accomplishments: Contributions to the NPRC Mission

Behavioral Management Working Group. [Excluded by Requester] represents the CNPRC on this Working Group and has been an active participant in the monthly calls and in all Working Group activities since formation of the group in April 2007. Her major contributions to the group include:

- Development of a common categorization system for factors underlying single housing of research primates.
- Development of standardized terminology and behavioral assessment tools. NPRCs are now employing the Working Group scoring system for recording the incidence and severity of potentially self-injurious behavior. The group has also finalized cross-facility definitions of all other abnormal behaviors.
- Analysis and communication of the impact of the 2011 *Guide for the Care and Use of Laboratory Animals*.
- Completion of an alopecia scoring system and development of inter-observer reliability at all NPRCs.

Of note, [Excluded by] led a webinar and an American Society of Primatology workshop to discuss social group management, specifically social instability in large groups. She reached out to engage members of the Behavioral Management and Breeding and Colony Management Working Groups as speakers.

Breeding and Colony Management Working Group. [Excluded by Requester] represent the CNPRC on the Breeding and Colony Management Working Group and have been regular participants in all working group activities. Accomplishments of the group include:

- Enhancements to the Office of AIDS Research (OAR)/ ORIP Specific Pathogen Free (SPF) Program.
- Establishment of colony management best practices: Colony Health Benchmarks.
- Establishment of colony genetics management best practices: Genetic Health Benchmarks.
- Implementation of the Available Animal Locator system and animal needs posting function.
- Survey of expanded SPF colonies.
- Colony demographics survey.
- Cross Working Group interactions with Genetics and Genomics and Behavioral Management.

Of particular significance is the leadership role played by CNPRC staff in coordinating two high priority initiatives; the Virology Testing Quality Improvement Initiative and Measles Vaccine Safety and Efficacy Study.

- **Virology Testing Quality Improvement Initiative:** A third round of proficiency testing was completed for laboratories that provide viral diagnostic services to the NPRC breeding colonies to monitor viral status of

colony animals. The evaluation was performed by the CNPRC Immunology and Pathogen Detection Resources Core and was shared with the Breeding and Colony Management Working Group at the Spring 2013 Face-to-Face meeting. As in previous rounds of proficiency testing, the results demonstrated that resource laboratories are within acceptable limits for agreement. Future plans for proficiency testing include exploration of improved processes for analyzing non-negative "problem" samples. Results from this Initiative led by the CNPRC Immunology and Pathogen Detection Resources Core are now being incorporated in a white paper on virus testing standards commissioned by the DCM and the SPF Directors.

Excluded by Requester is representing the CNPRC as one of the primary authors and similarly as an invited member of the "Expert Panel on Infectious Disease Surveillance" convened by the Southwest NPRC.

- **Multi-Center Measles Vaccination Safety and Efficacy Study:** NPRC breeding colonies are at risk for a measles epizootic since vaccination programs for measles have lapsed with the discontinuation of domestic monovalent measles vaccine. This project has been ongoing since 2011, and Excluded by Requester (Primate Medicine Services) and Affiliate Scientist Excluded by Requester (Infectious Diseases Research Unit) of the CNPRC provided the scientific leadership and expertise in designing this study.
- The CNPRC Breeding and Colony Management Working Group staff hosted the face-to-face meeting on March 27-28, 2013, with a series of presentations and discussion on challenges and priority activities.

Clinical and Surgical Techniques Working Group. This Working Group consists of individuals representing each of the NPRCs who meet via a monthly web conference to discuss commonly performed procedures. These practical discussions serve to improve networking, identify expertise, and accelerate the transmission of information among the NPRC veterinarians with the goal of improving procedural competency and repertoire as well as improve workflow efficiencies associated with the procedures. CNPRC and UC Davis members of this working group include Excluded by Requester

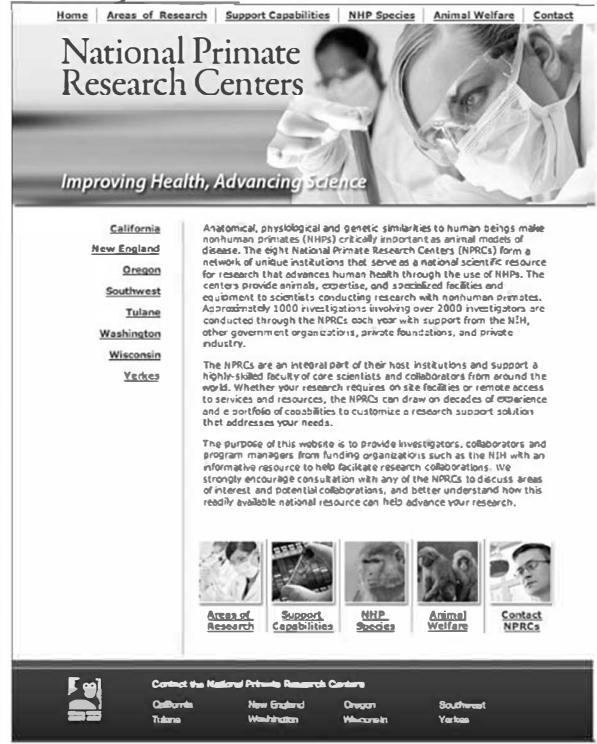
Excluded by Requester The Working Group's reference library continues to grow, consisting of past presentations, which aids in education and training.

Consortium Project Management and Informatics Working Group.

The goal is to provide responsive and effective Program/Project Management and Informatics support to Consortium Working Groups. The scope of the Consortium Project Management and Informatics Working Group's responsibilities includes four primary areas: (1) Working Group coordination and support, (2) support of NPRC program-level objectives identified by the NPRC Directors and ORIP/DCM, (3) development and support of systems to facilitate sharing of data and information, and (4) support of the underlying data sharing infrastructure. The Consortium Project Management and Informatics Working Group assists other Working Groups with meeting coordination, agenda planning, web conference hosting, web-based surveys, website support, and security administration. For Working Groups and program-level initiatives with informatics requirements, the Consortium Project Management and Informatics Working Group provides project management, application development, system integration, testing, training, and documentation support. Those Working Groups benefitting from the support of the Project Management and Informatics Working Group include the Breeding and Colony Management Working Group, the Genetics and Genomics Working Group, and the Pathology Working Group. Examples of Program-level projects include the SPF Testing survey, development of the NPRC Research and Capabilities Inventory website (Figure 1), and coordination and development of the "Extreme Phenotype" survey.

Using systems and infrastructure implemented by the Consortium Project Management and Informatics Working Group, the Consortium Working Groups continue to securely share data and information across the NPRCs and in some cases with the extended nonhuman primate research community. These systems facilitate the sharing of National DNA Bank inventories, available animal information, pathology images and related case information, nonhuman primate SNPs data, genetic panels, and tools for parentage analysis.

Figure 1. NPRC Research and Capabilities Inventory website



Materials include items such as the library of 250 shared immunohistochemistry protocols, common definitions of abnormal behavior, Outreach materials, colony health benchmarks statistics, and links to publications.

The Consortium Project Management and Informatics Working Group also advance utilization of shared reporting and analysis tools across NPRCs. Activities include the implementation and support of the SPF reporting system, Colony Health Benchmarks analysis tools, and post-approval monitoring applications. The role of the Working Group includes consultation and coordination with Working Group participants, website, and application hosting support, extract specifications, security administration, documentation, and training.

The Consortium systems have been implemented in a manner that minimizes local development and support requirements. A secure central leased hosting environment provides development, testing, and production platforms supported on a 24/7 basis by the service provider. Commonly configured servers and Veterinary Managers at each NPRC provide a stable environment that enables federated implementations such as the Available Animal Locator and the Primate Pathology Image Database. The recently developed NPRC Research and Capability Inventory website is the first publicly accessible site implemented. Access to all other Consortium resources requires security credentials.

Data Access Guidelines Working Group. This Working Group is composed of the NPRCs Associate Directors for Administration who develop overall content guidelines and approval processes for data sharing between NPRCs, safeguarding the website, and preventing unauthorized access/unnecessary exposure.

Genetics and Genomics Working Group. [Excluded by Requester] represent the CNPRC on the Genetics and Genomics Working Group and have been regular participants and major contributors to the monthly Working Group calls and all activities. Accomplishments include:

- Completion of a survey regarding current genetic management practices.
- Implementation of the Genetics and Genomics Resource Portal.
- Expanded communications with the Breeding and Colony Management Working Group.
- Development and distribution of a document to the Breeding and Colony Management Working Group outlining recommendations and best practices for the genetic management of primate breeding colonies.
- Presentations as a part of an Invited Symposium on recent advances and available tools in primate genetics at the 2012 Annual Meeting of the Association of Primate Veterinarians.
- Continued Development of the SNP Analysis Pipeline, public Genetics Resource Portal, and the Working Group website.
- Publication of two peer-reviewed papers on new tools and resources developed by the Genetics and Genomics Working Group (see **Genetics Management Services**).
- Conducted additional SNP genotyping using the parentage and/or ancestry panels.
- Development, testing, and validation of a molecular genetic assay that uses 96 SNPs for parentage testing.
- Validation of a second genetic assay that uses 96 SNPs to determine the ancestry (Indian- vs. Chinese-origin) of individual rhesus macaques.
- Conducted SNP genotyping using the parentage panel on 3,890 rhesus macaques from six NPRCs and the Caribbean Primate Center, resulting in the adoption of one or both of the SNP panels at six NPRCs. Access to standard panels of SNP markers for parentage and ancestry testing allows all NPRCs to produce standardized genetic information for colony management, thus facilitating the accumulation of comparable genetic data across NPRCs.
- As a result of these developments, the Genetics and Genomics Working Group has begun communicating regularly with the Breeding and Colony Management Working Group with the goal of establishing practical, ready-to-implement recommendations and best practices for monitoring and managing the genetic composition of NPRC breeding colonies.
- Consultation and testing of the Parentage analysis tool developed by the Consortium Project Management and Informatics Working Group, currently in use at five NPRCs.

Integrity and Compliance Working Group. This Working Group is composed of the NPRC Associate Directors for Administration. The group conducts quarterly web conferences to address topics such as electronic IACUC systems, response to USDA citations, and Harm/Benefit analysis in IACUC protocol review.

Occupational Health and Safety Working Group. This Working Group provides a forum to share ideas, materials, expertise, and experience to improve and support more efficient occupational health and safety programs. Activities of this group include meeting with [Excluded by Requester] at the National Herpes B Virus Laboratory

resulting in a better understanding of Herpes B virus testing practices as well as specifics related to human cases of Herpes B, and meeting and information exchange with the CDC regarding occupational exposures.

Outreach Working Group. The NPRC Consortium Outreach Working Group was founded in February 2010 by [Excluded by Requester] (CNPRC) to provide all of the NPRC Outreach Specialists a means of sharing expertise and experiences. This Working Group has been extremely successful in increasing and improving communications and collaborations between the NPRCs and to the scientific community and public. Briefly, the Outreach Working Group:

- Represents the NPRCs at public and scientific meetings and events. In the past 4 years, the Outreach Working Group has highlighted the NPRC science achievements and opportunities for research at many scientific and public events, and [Excluded by Requester] has led the participation, materials development, and staffing at the USA Science and Engineering Festival, and Advancing Medicine and Health in Washington DC, both in 2012 and 2014 (over 200,000 attendees each year). Collaborates on developing and sharing materials, best practices, and outreach activities. [Excluded by Requester] has shared all of the CNPRC outreach materials with the Outreach Working Group when it was newly formed, and, at the request of many NPRCs, made the CNPRC's coloring book (written and illustrated by Ms. [Excluded by Requester]) available for customized use by each NPRC. The Outreach Working Group members hold monthly conference calls, led by [Excluded by Requester] meet annually at one of the NPRCs to share best practices and discuss outreach plans for the coming year. [Excluded by Requester]
- As the chair of the Working Group, [Excluded by Requester] serves as a liaison between the group and [Excluded by Requester]. She is responsible for the annual budget and the annual report on the Outreach Working Group's activities.
- In 2013, [Excluded by Requester] led an Outreach Working Group project to design a common logo and word mark to brand the NPRCs. This logo is now being used on official NPRC websites and correspondence, and has contributed to increase the visibility and a cohesive image of the NPRCs. [Excluded by Requester]

Pathology Working Group [Excluded by Requester] represents the CNPRC on the Pathology Working Group and has been an active participant in the monthly Virtual Slide Conferences and all Working Group activities. Accomplishments include:

- Development and implementation the Primate Pathology Image Database.
- Expansion of access to the Database to all NPRCs and a number of external organizations.
- Incorporation of Primate Pathology Image Database content contributions from all NPRCs.
- Continuation of the monthly Virtual Slide Conferences.
- Sharing of over 250 immunohistochemistry protocols.

Of particular importance is the CNPRC's significant contribution to development of the Primate Pathology Image Database and leadership in providing services to members of the Consortium by the CNPRC Multimodal Imaging Core (see Core description). The Core provides microscopy expertise, equipment, and services, including technical support and training to a broad range of clients, including to Consortium members through conference calls, Web meetings, and a face-to-face meetings and training sessions. For example, a stereology training session was led by [Excluded by Requester] at the Oregon NPRC meeting held on April 4-5, 2012.

From the time of inception and growth of the Primate Pathology Image Database, the Multimodal Imaging Core has been very active in contributing expert knowledge and services to refine the selection of slide scanning technologies and to guide the development of methods to simplify the application of stereology in pathology. In particular, effort was placed on development and organization of the database used for quantitative analysis. As an example, a punch biopsy approach was developed for tissue sampling in a BSL3 environment for quantitative assessment of tuberculosis-infected lungs (see **Multimodal Imaging Core**).

The Multimodal Imaging Core continues to broadly assist pathologists at all NPRCs. Currently, the Core is creating an image archive of the 500 most valuable histology samples from the New England NPRC. The expertise and equipment in the Core helped preserve a valuable resource of diseased tissue that will be used for reference and teaching. The slides are scanned using high-resolution optics to create digital files. This archive will allow easy access by a broad range of investigators to very high-resolution digital versions of the original microscope slides.

Training Working Group. Three Consortium Working Groups conduct monthly training and education forums via web conference. These include: (1) Pathology Working Group Virtual Slide Conferences, (2) Training Working Group Virtual Grand Rounds, and (3) Clinical and Surgical Techniques Working Group Conferences. Using a rotating schedule, each NPRC presents interesting cases and procedures and leads a discussion regarding practices and observations across the NPRCs. These forums provide an education and mentoring

opportunity for trainees as well as seasoned staff, and frequently result in follow-up discussions regarding the presentation topic and related issues. The CNPRC staff regularly presents interesting cases and procedures in accordance with the published schedule and further leverages opportunities provided through these forums by involving several local staff members in each of the conference sessions.

INNOVATION

- The Consortium Project Management and Informatics Group, administered by the CNPRC, will continue its critical role in providing overall coordination and support of the Working Groups. The group will also select program-level activities, including development and expansion of systems to facilitate sharing of information across the nonhuman primate community and key stakeholders. Increased cross-Working Group collaborations will help address issues that span multiple domains and improve communications.
- The roll out of the NPRC Research and Capabilities Inventory website was accomplished. The website was developed to better align communications with external funding entities and provides investigators, collaborators, and program managers from funding organizations such as the NIH Institutes and Centers with an informative resource to help facilitate research collaborations. The website will be used as a platform to communicate and deliver additional information regarding the NPRCs and research initiatives.
- Creation of small targeted multi-center groups to address specific issues in an expedited manner.
- Leverage advances in NPRC capabilities resulting from the Animal Research Management System (ARMS) and LabKey implementations to more efficiently provide common extracts for sharing data across NPRCs (see **Information Technology Services**). ARMS will be implemented at the CNPRC, Washington NPRC, and Yerkes NPRC, while the LabKey system is being implemented at the Oregon NPRC, Wisconsin NPRC, and Tulane NPRC.
- Integration of the Primate Pathology Image Database with the ARMS and LabKey environments to provide an ongoing mechanism for acquiring pathology cases and images from day-to-day pathology workflows.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Provide increased support for nonhuman primate research through NPRC Director leadership and prioritization of Working Group goals and tasks.

The NPRC Directors have committed through a carefully developed strategic planning process to provide direction and priorities to the Consortium Working Groups. The priorities identified as being of the highest importance include: (1) ensuring information about NPRC resources is readily available and communicated broadly, (2) improving access for a larger constituency of investigators to the NPRCs, (3) providing strategic areas of NPRC cooperation and promotion to improve the collective scientific value of the NPRC resource, and (4) developing strategic information focusing specifically on the value and importance of nonhuman primate research to advance human health. As these priorities develop, the Consortium Working Groups will be charged with providing contributions from their areas of expertise. For example, [REDACTED] from the Southwest NPRC has been working with the NPRC Directors to develop a white paper on Nonhuman Primate Genomics for distribution to NIH institutes. Excluded by Requester

Specific Aim 2. Creation of ad hoc Working Groups to drive specific improvements in nonhuman primate expertise and services.

The NPRC Directors have affirmed the value of the current Working Groups but will also pursue establishment of temporary ad hoc groups to take on priority issues and provide direction for resolution, ensuring maximal flexibility as well as the capability to address emerging issues. The Data Access Guidelines, Integrity and Compliance, Occupational Health and Safety, and Training Working Groups were established on such an ad hoc basis. These groups may cross the current Working Group functional boundaries depending on the nature of the specific issue.

Specific Aim 3. Continued support for sharing of information and best practices to mentor and train NPRC members throughout the Consortium and inform external stakeholders as appropriate.

The Consortium Working Groups will prioritize activities to enable the NPRC's to share challenges, design solutions to those challenges, and develop approaches for resolution at both the individual NPRC and Consortium levels. The three existing Working Group education forums, i.e., Virtual Slide Conferences, Virtual Grand Rounds, and Clinical and Surgical Techniques conferences will continue as important channels to disseminate NPRC expertise and share best practices across NPRCs and with the greater research community. One of the greatest strengths of these groups has been the identification and sharing of best practices from individual NPRCs to be adopted at other NPRCs and institutions.

NPRC CONSORTIUM

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

NPRC CONSORTIUM

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Outreach Program

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: — 1 — 2 — 3 — 4 — 5 — 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename Outreach_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	Outreach_BibliographyReferences.pdf
10. Facilities & Other Resources	Outreach_Facilities.pdf
11. Equipment	Outreach_Equipment.pdf

OUTREACH

ABSTRACT

The California National Primate Research Center (CNPRC) is focused on advancing community awareness on the scientific achievements that the monkey model has contributed to the understanding of human health and disease using three primary **Outreach** sources: a broad portfolio of communications, the Education Outreach Program, and the National Primate Research Center (NPRC) Consortium. The goals of these efforts are to build on the well established communication programs currently in place, enhance the accessibility of information, raise awareness about the value of CNPRC scientific achievements, and to educate trainees, investigators, and the public about the importance of nonhuman primate research through the following Specific Aims: (1) Advance awareness of CNPRC scientific contributions through effective communications to the media and lay community, (2) Ensure that investigators at the local, regional, and national levels have ready access to CNPRC nonhuman primate expertise and resources, and (3) Efficiently communicate information to the next generation of translational nonhuman primate investigators on the spectrum of research and training opportunities at the CNPRC.

OUTREACH

FACILITIES AND OTHER RESOURCES

Laboratories: Not applicable

Clinical: Not applicable

Animal: Not applicable

Computer: All members of the Outreach program have individual computers for their use. Laser printers and fax machines are also available.

Excluded by Requester

Office: [redacted] each have an office at the CNPRC. The Administrative Assistant has a shared office space in close proximity.

Other: The Strategic Communications office, housed in the UC Davis Chancellor's Office, provides oversight and assistance with media relations and news releases.

OUTREACH

EQUIPMENT

Not applicable

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFOR T	0.0	0.0	16,069.00	6,409.00	22,478.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						22,478.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	3.0			8,870.00	4,692.00	13,562.00
1	Information Officer	Excluded by Requester	EFFORT		32,814.00	17,359.00	50,173.00
2	Total Number Other Personnel					Total Other Personnel	63,735.00
Total Salary, Wages and Fringe Benefits (A+B)							86,213.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,500.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,500.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	2,500.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Educational Outreach Program Copying and Printing	3,000.00
9. Newsletter Expenses	4,000.00
10. Brochures and Promotional Materials	2,000.00
Total Other Direct Costs	11,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	99,213.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	99,213.00	22,521.00
Total Indirect Costs			22,521.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	121,734.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Outreach_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	16,230.00	6,849.00	23,079.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	23,079.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	3.0			8,958.00	4,956.00	13,914.00
1	Information Officer	Excluded by	EFFORT		33,142.00	18,333.00	51,475.00
2	Total Number Other Personnel					Total Other Personnel	65,389.00
Total Salary, Wages and Fringe Benefits (A+B)							88,468.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,545.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,545.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	2,575.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Educational Outreach Program Copying and Printing	3,090.00
9. Newsletter Expenses	4,120.00
10. Brochures and Promotional Materials	2,060.00
Total Other Direct Costs	11,845.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	101,858.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	101,858.00	23,122.00
Total Indirect Costs			23,122.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	124,980.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Outreach_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	17,047.00	7,447.00	24,494.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	24,494.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	3.0			9,410.00	5,375.00	14,785.00
1	Information Office	Excluded by Requester	EFFORT		34,812.00	19,883.00	54,695.00
2	Total Number Other Personnel					Total Other Personnel	69,480.00
Total Salary, Wages and Fringe Benefits (A+B)							93,974.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,591.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,591.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	2,652.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Educational Outreach Program Copying and Printing	3,183.00
9. Newsletter Expenses	4,244.00
10. Brochures and Promotional Materials	2,122.00
Total Other Direct Costs	12,201.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	107,766.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	107,766.00	24,463.00
Total Indirect Costs			24,463.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	132,229.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Outreach_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	17,559.00	7,899.00	25,458.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						25,458.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	3.0			9,693.00	5,701.00	15,394.00
1	Information Office	Excluded by Requester	EFFORT		35,857.00	21,090.00	56,947.00
2	Total Number Other Personnel					Total Other Personnel	72,341.00
Total Salary, Wages and Fringe Benefits (A+B)							97,799.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,639.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,639.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	2,732.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Educational Outreach Program Copying and Printing	3,278.00
9. Newsletter Expenses	4,371.00
10. Brochures and Promotional Materials	2,186.00
Total Other Direct Costs	12,567.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	112,005.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	112,005.00	25,425.00
Total Indirect Costs			25,425.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	137,430.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Outreach_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Assoc Director for Admin and Operations	Institutional Base Salary	EFFORT	0.0	0.0	18,085.00	8,385.00	26,470.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						26,470.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	3.0			9,984.00	6,050.00	16,034.00
1	Information Officer	Excluded by Requester	EFFORT		36,932.00	22,381.00	59,313.00
2	Total Number Other Personnel					Total Other Personnel	75,347.00
Total Salary, Wages and Fringe Benefits (A+B)							101,817.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	1,688.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	1,688.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	2,814.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Educational Outreach Program Copying and Printing	3,376.00
9. Newsletter Expenses	4,502.00
10. Brochures and Promotional Materials	2,252.00
Total Other Direct Costs	12,944.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	116,449.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	116,449.00	26,434.00
Total Indirect Costs			26,434.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	142,883.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: Outreach_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OUTREACH**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Interim Associate Director for Administration and Operations	% Effort			
	Public Information Officer				
TBN	Administrative Assistant	25	75	0	100

TBN=to-be-named

Excluded by Requester **Associate Director for Administration and Operations** EFFORT months – % Effort Mr. served as Vice Chancellor for Administration for UC Davis from 2003-2010 and in other leadership positions in the Office of Administration since 1992. Notably, he served as information practices coordinator and director of event management and administrative services, both of which provide him with the background to effectively supervise the CNPRC Public Information Officer.

Excluded by Requester **Public Information Officer** EFFORT months – % Effort Excluded by Requester is responsible for outreach activities at the CNPRC. She coordinates public relations activities under the guidance of the Associate Director of Administration and Operations and through the CNPRC website, newsletter, brochures, media kits, news releases, and fact sheets. She also manages the Education Outreach Program and coordinates outreach activities with campus outreach entities and the NPRC Consortium.

TBN, Administrative Assistant (3.0 calendar months – 25%). The to be named Administrative Assistant provides necessary support with all Outreach activities under the guidance of the Associate Director for Administration and Operations.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None

TRAVEL

\$1,500 is requested for Excluded by Requester to attend an annual meeting related to her Outreach functions.

SUPPLIES

\$2,500 is requested for general supplies to support the program.

OTHER EXPENSES

\$3,000 is requested for Educational Outreach Program document copies and printing.

\$4,000 is requested for preparation and printing of the CNPRC newsletter.

\$2,000 is requested for brochures and promotional materials.

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		121,979.00
Section B, Other Personnel		346,292.00
Total Number Other Personnel	10	
Total Salary, Wages and Fringe Benefits (A+B)		468,271.00
Section C, Equipment		0.00
Section D, Travel		7,963.00
1. Domestic	7,963.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		61,057.00
1. Materials and Supplies	13,273.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	15,927.00	
9. Other 2	21,237.00	
10. Other 3	10,620.00	
Section G, Direct Costs (A thru F)		537,291.00
Section H, Indirect Costs		121,965.00
Section I, Total Direct and Indirect Costs (G + H)		659,256.00
Section J, Fee		0.00

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OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement

5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

Outreach_SpecificAims.pdf

3. Research Strategy*

Outreach_ResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals****9. Select Agent Research****10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support****13. Resource Sharing Plan(s)**

Outreach_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

OUTREACH

SPECIFIC AIMS

The California National Primate Research Center (CNPRC) is focused on advancing community awareness on the scientific achievements and the role nonhuman primate models contribute to the understanding of human health and disease from conception through maturation and aging.

Specific Aim 1. Advance awareness of CNPRC scientific contributions through effective communications to the media and lay community.

Plan. A key goal is to ensure information is readily available to raise awareness about the CNPRC mission and scientific achievements. An ongoing objective is to build upon CNPRC public relations success during the current funding period using established outreach and communications programs such as the National Primate Research Center's Consortium Outreach Working Group. The goal for the next funding period is to broaden outreach goals through interactive websites, educational programs in Northern California schools, at national science events, and through tours, local media, the CNPRC newsletter, and promotional materials. An expanded presence in emerging media will be used to promote the CNPRC and to inform new groups regarding the importance of translational research and the crucial role of nonhuman primates in the advancement of human health.

Specific Aim 2. Ensure that investigators at the local, regional, and national levels have ready access to CNPRC nonhuman primate expertise and resources.

Plan. The primary objective is to ensure ready access to and awareness of expertise, resources, and services for NIH supported studies through: (1) refinement of the CNPRC website functionality and a direct investigator portal to CNPRC Core Scientists and Core Services, (2) enhanced marketing strategies, and (3) printed and electronic marketing materials for scientific meetings and other networking opportunities. Communications between the NPRCs will be expanded through the NPRC Consortium Working Groups to encourage new partnerships and outreach efforts.

Specific Aim 3. Efficiently communicate information to the next generation of translational nonhuman primate investigators on the spectrum of research and training opportunities at the CNPRC.

Plan. The CNPRC website will be enhanced to ensure research highlights, resources, and career opportunities are in a format appealing to trainees at all career stages.

OUTREACH

RESEARCH STRATEGY

INTRODUCTION

During the current funding period significant progress has been made in expanding and enhancing outreach and communications about the California National Primate Research Center (CNPRC) through three primary sources: (1) a broad communication portfolio, (2) the Education Outreach Program, and (3) the National Primate Research Center (NPRC) Consortium. The goals are to build on this well established communication program in place to enhance the accessibility of information, to raise awareness about the value of CNPRC scientific achievements, and to educate trainees, investigators, and the public on the contributions of nonhuman primate research to improvements in human health. The Outreach program integrates with UC Davis Strategic Communications at the local level and with the NPRC Consortium nationally in these efforts. Members of the CNPRC Outreach team are shown in Figure 1 and Table 1.

Figure 1. Organizational Chart: Outreach

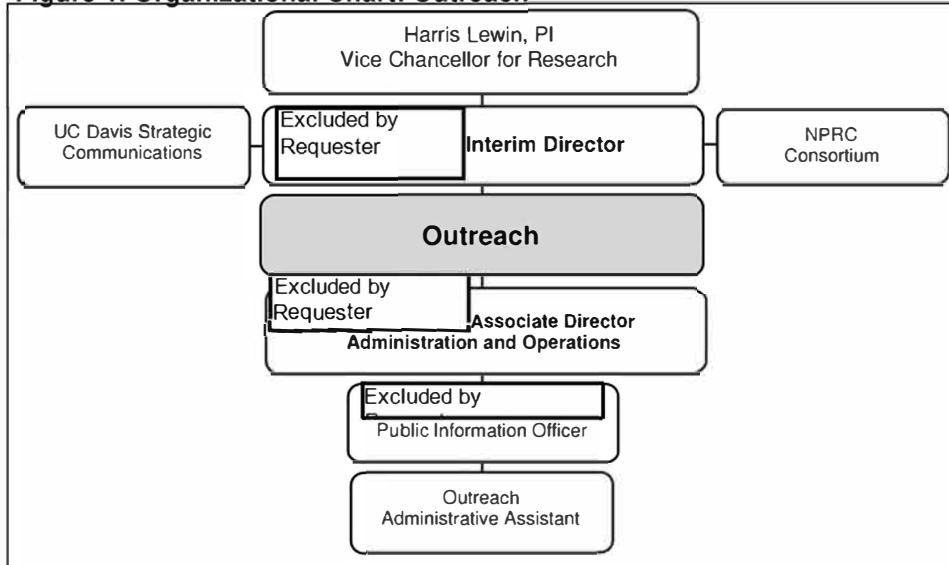


Table 1. Outreach Personnel, UC Davis Affiliation, and CNPRC Role

Personnel	UC Davis Affiliation	CNPRC Role
Excluded by Requester	CNPRC	Associate Director for Administration and Operations
	CNPRC	Public Information Officer
TBN	CNPRC	Outreach Administrative Assistant

TBN=to-be-named

Sources of support in the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 2.

Table 2. Support for the Outreach Program

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$96,153	\$99,213
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$96,153	\$99,213

Response to Summary Statement. There were no comments in the prior review.

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

Communications. The CNPRC Public Information Officer, Excluded by Requester, in collaboration with the UC Davis Strategic Communications Office, produces outreach materials, answers questions and requests, and provides targeted outreach to the greater scientific community, educational institutions, media, and the general public in order to manage communications and promote the mission, interests, values, and research activities on behalf of the CNPRC.

CNPRC Website. The CNPRC website has been significantly revised during the current funding period (Figure 2). The site informs the public and scientific community about the achievements and research opportunities at the CNPRC. The site promotes a positive message in support of nonhuman primate research and provides information on expertise, services, resources, capabilities, and information on the latest research news, events, and seminars. Press releases are posted online as research news is announced. The site is also a source of

information for K-12 teachers to educate their students or make arrangements for interactions with the CNPRC Education Outreach Program. A redesign of the website functionality and architecture has been accomplished to improve aesthetics and use. This has resulted in improved search capability with a more direct pathway to information, and includes social media applications. The site was also designed to increase lay community education with expanded resources for journalists such as fact sheets with current science and related programs.

The CNPRC has unique capabilities for scientific discovery highlighted throughout the website as well as through other outreach materials. One example is the new Respiratory Disease Center, which includes the Inhalation Exposure Core and the Respiratory Diseases Research Unit (see **Inhalation Exposure Core** and **Respiratory Diseases Research Unit**). Core Scientists and staff in all Core Services have direct contact with individuals and network at scientific meetings, through electronic mail, postal mail, and telephone calls, and utilize connections within the **NPRC Consortium** and national website to broadcast services and research opportunities. In addition, the CNPRC Pilot Research Program is an excellent mechanism to familiarize new investigators with the CNPRC program and Core Scientists (see **Pilot Research Program**).

Figure 2. CNPRC Website snapshot



CNPRC Marketing and Newsletter. Marketing materials have been developed (Figure 3). Published twice annually, the CNPRC newsletter informs readers about translational news highlights and current research (Figure 4). The newsletter is distributed electronically to the research community and to the NIH/Office of the Director, industry, research affiliates, and collaborating scientists.

Figure 3. Marketing example



Figure 4. CNPRC newsletter



Media Outreach. News groups are informed of breaking news and research highlights as they are announced. Recent collaborations through **UC Davis Strategic Communications** with the media included a public event that engaged television, radio, and print media for positive coverage of activities at the CNPRC. Over the past 3 years, breaking news and research highlights from the CNPRC have been sent to the Foundation for Biomedical Research Total e-Clips, the California Biomedical Research Association News Blasts, and Newswise SciWire. These organizations have highlighted CNPRC press releases in their daily news announcements, which are circulated to a worldwide audience of scientists, journalists, and the public (Figure 5). Journalists that visit the CNPRC are provided with fact sheets, brochures, educational materials, and a DVD of figures representing key CNPRC activities. In addition, the program assists in connecting to scientists for targeted interviews. The UC Davis Strategic Communications office offers an all-day interactive workshop customized for scientists, faculty, staff, and students who interact with the news media. The workshop covers

the benefits and risks when working with the news media, including strategies for accommodating the differing methods of print and broadcast journalists. A series of exercises teach participants how to prepare for a successful interview and to develop strategic media messages and talking points for public presentations. All media arrangements are coordinated with the UC Davis campus and the CNPRC Director.

Other Activities. Efforts to enhance internal and external communications and news bulletins have increased in frequency. The deans of the Schools and Colleges and Center directors receive news about the CNPRC through the e-mail listserv. Informational brochures, bookmarks, and flyers are distributed to the CNPRC community, students, and visitors. On-site lectures and tours are frequently provided to colleges, university groups, visiting scientists, and the community upon request. Speakers are invited to lecture on relevant topics and visiting groups are able to tour the CNPRC facility via a 44-seat open-air tram. On the tour, CNPRC Core Scientists and staff provide commentary on animal care and management, behavior, research, and other information pertinent to the visiting group's interests. Undergraduate classes are held at the outdoor-housed field cages where students learn behavioral observation techniques (see **Brain, Mind, and**

Behavior Research Unit). Prior to obtaining access to these areas participants are required to complete all screening and health clearance documents that are required to enter the CNPRC (see **Director's Office**).

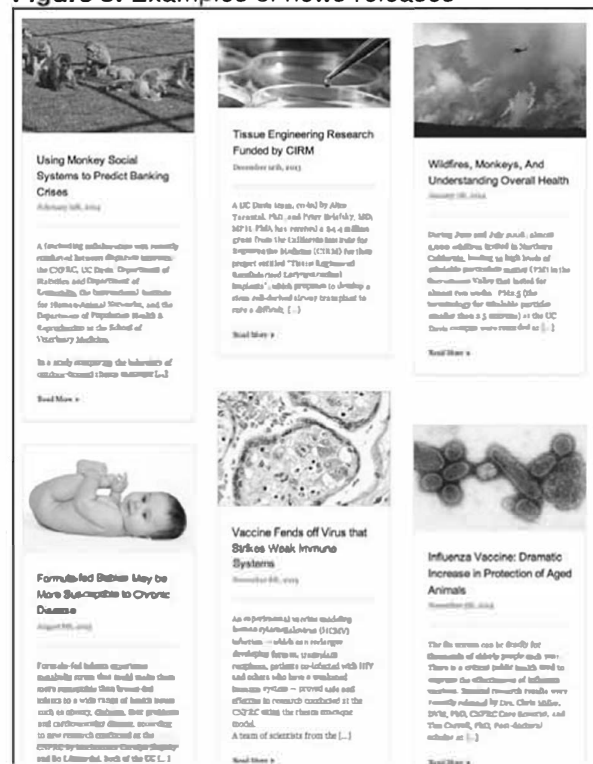
One of the forums for enhanced internal communications is provided in the "Investigator Seminar Series". This is a quarterly informational series provided to the CNPRC staff to enhance their understanding of the research and the importance of their role in this research. These communications between the animal care staff and Core Scientists promote positive interactions and team building, and highlight the importance of husbandry and other related colony management activities in the success of research projects.

Education Outreach Program. The CNPRC Education Outreach Program was founded in 2003 by

and is focused on educating K-12 students in the biology, behavior, and conservation of nonhuman primates, health sciences concepts, the care and use of nonhuman primates in research, CNPRC research programs, and careers in science. The program directly connects higher education and research communities with students, educators, and parents. This approach provides students with the knowledge to balance inaccurate information received from the media and animal extremists groups. Students also develop increased scientific literacy to enhance understanding and knowledge of current science and health-related topics that might directly impact their health and the health of family members. Since its inception, the program has presented in both English and Spanish to over 10,000 K-12 students, teachers, and parents at more than 90 public and private schools all over Northern California, home school groups, nonprofit organizations, Spanish Immersion classes, and developmentally and physically challenged children as well as high-risk schools (Table 3). The K-6 school component of the program is designed with engaging activity stations, and students are presented with a two-hour customized curriculum at their school site (Figure 6). This program allows young children to explore complex concepts and complements the California State Science Standards and the National Science Content Standards. CNPRC faculty and staff assist with the Education Outreach Program and show by example a broad variety of careers in the sciences. They also represent a culturally, racially, educationally, and gender diverse group that are employed in positions ranging from administrative assistants to technicians and trainees to veterinarians and Core Scientists – demonstrating that higher education and science careers are not limited to any particular identity group.

In addition to the K-6 Education Outreach Program, the CNPRC provides speakers upon request to grade 7-12 students at their school site, as well as lectures and tours on-site for older students (≥16-years-old). Core and Affiliate Scientists Excluded by Requester animal care and enrichment staff Excluded by Requester Core Services staff Excluded by Requester veterinarians (Drs. Excluded by Requester and the outreach program

Figure 5. Examples of news releases



Excluded by
Requester

Excluded by
Requester

leader, provide information such as how the CNPRC has contributed to the development of HIV drugs and other topics such as animal care, enrichment, and careers in veterinary medicine.

Table 3. Education Outreach Program (May 1, 2010 to April 30, 2014)

Year	School or Group (California Location)	Grade or Trainee Level
2010	Andros Karperos School twice (Yuba City)	5th
	Home school group held at UC Davis (Davis)	K to 12
	Home school groups held at the CNPRC twice (Davis)	2nd to High School
	Martin Luther King Junior Elementary School (Sacramento)	6th
	National Youth Leadership Forum held at the CNPRC twice (Davis)	High School
	North Davis Elementary (Davis)	3rd
	Sacramento High School (Sacramento)	High School
	UC Davis Early Academic Outreach Program (Davis)	High School
	UC Davis Summer Enrichment Program (Davis)	Undergraduates
2011	Dillard Elementary School twice (Wilton)	5th
	Elitha Donner Elementary School (Elk Grove)	5th
	JFK High School Honors Biology (Sacramento)	High School
	John Bidwell Elementary School (Sacramento)	2nd to 5th
	North Davis Elementary School (Davis)	3rd
	Robbins Elementary School twice (Sutter County)	K to 8th
	Theodore Judah Elementary School (Sacramento)	5th
	Winters Parent Nursery School (Winters)	Pre-K
	Woodland High School (Woodland)	High School
2012	Elitha Donner Elementary School (Elk Grove)	5th
	JFK High School (Sacramento)	High School
	North Davis Elementary School (Davis)	3rd
	Pioneer Child Development Center (Davis)	K to 6th
	Robert Louis Stevenson Middle School (St. Helena)	Junior High School
	Sheldon High School (Elk Grove) held at the CNPRC	High School
	UC Davis Science and Society: Career Discoveries Group (Davis)	Undergraduates
	UC Davis STAR Program for Veterinary Students (Davis)	Veterinary Students
	West Sacramento Preparatory Charter School (Sacramento)	2nd to 8th
	Witter Ranch Elementary School (Sacramento)	4th
	Woodland High School (Woodland)	High School
	Woodland High School Veterinary Science class (Woodland)	High School
2013	Pierce College (Woodland Hills)	Undergraduates
	Cooper Elementary School (Vacaville)	3rd
	Elitha Donner Elementary School twice (Elk Grove)	5th
	4-H Ambassador students, State Leadership Conference held at the CNPRC	High School
	Home school school group held at the CNPRC (Davis)	K to 8th
	Home study Group (Woodland)	1st to 7th
	Jennings Community Learning Center, St Paul MN at the CNPRC	High School
	Los Rios Community College (Sacramento) held at the CNPRC	Undergraduates
	Moorpark College (Moorpark) held at the CNPRC	Undergraduates
	National Youth Leadership Program held at the CNPRC (Davis)	High School
	North Davis Elementary School (Davis)	3rd
	Sheldon High School STEM group (Sacramento)	High School
	UC Davis Aggie Ambassadors (Davis)	Undergraduates
	UC Davis Biotechnology Club (Davis)	Undergraduates
	UC Davis Summer Enrichment Program (Davis)	Undergraduates
	UC Davis Young Scholars held at the CNPRC (Davis)	High School
	Waggoner Elementary School (Winters)	K
	Witter Ranch Elementary School twice (Sacramento)	2nd to 4th
2014	Dixon Girl Scouts (Dixon) held at the CNPRC	6th
	Home school group - Davis Yolo Library (Davis)	4th to 6th
	Los Rios Community College (Sacramento)	Undergraduates
	Martin Luther King Elementary School (Davis)	6th
	UC Davis Anthropology Course (Davis)	Undergraduates
	UC Davis 1st and 2nd year veterinary students: Animal Behavior	Veterinary Students

Figure 6. A. Hands-on activities are used to engage young students in the K to 6 grades. Presentations are given throughout the calendar year at the school site. Teachers are engaged in the training process along with parents. **B.** Members of the CNPRC also represented the NPRC Program in Washington, DC at the USA Science and Engineering Festival in 2012 and 2014. Individual discussions with students and their parents provide opportunities to communicate the importance of nonhuman primate research and future careers in science.

A. Classroom setting



B. Science and Engineering Festival 2012



Presentations are also given in cooperation with several UC Davis outreach programs including GEAR UP (mentors high-risk and minority students from the Sacramento community); the Early Academic Outreach Program (created to help more students meet the requirements to attend college, especially students who are the first in their family to go to college or who are considered socioeconomically disadvantaged); and the School of Veterinary Medicine Summer Enrichment Program (helps disadvantaged applicants improve their chances of getting into veterinary school).

NPRC Consortium Outreach Working Group [Excluded by Requester] founded and has served as Chair for the NPRC Consortium Outreach Working Group since 2010 (see **NPRC Consortium**). The Working Group was formed to provide NPRC Outreach Specialists a format for sharing expertise and experiences. This Working Group has been extremely successful in increasing and improving communications and collaborations between the NPRCs, the scientific community, and the public, enhancing effectiveness, leveraging system-wide resources, sharing data across NPRCs, contributing to the marketing and promotion of the NPRCs, and facilitating sharing of information and best practices. On a day-to-day basis, NPRC Outreach Specialists share research highlights, items of outreach interest, and responses to animal rights activities. The Working Group members hold monthly conference calls and meet annually at one of the NPRCs to discuss outreach plans for the coming year and to exchange best practices; a guest speaker is generally included. The annual meeting has also provided a forum for [Excluded by Requester] to present a formal report on the Working Group's progress to [Excluded by Requester] Division of Comparative [Excluded by Requester] NIH Office of the Director. As Chair [Excluded by Requester] has been responsible for developing and achieving consensus on the proposed annual budget, managing the budget throughout the year, and developing the annual report on Working Group activities. During the current funding period the Working Group has represented the NPRCs at many public and scientific meetings nationally including the Society for Neuroscience, the International Society for Biological and Environmental Repositories, the Annual Symposium for Nonhuman Primate Models for AIDS, the World Stem Cell Summit, and the Science Olympiad.

[Excluded by Requester] has led the participation, materials development, and staffing at the USA Science and Engineering Festival, Advancing Medicine and Health in Washington DC, both in 2012 and 2014 (over 500,000 attendees combined; see Figure 6B). Throughout the year [Excluded by Requester] serves as a liaison between the Working Group and

[Excluded by Requester] Recently [Excluded by Requester] led the development of a common logo and word mark to brand the NPRCs, which is increasing the visibility and cohesive image of the NPRCs. In 2013 [Excluded by Requester] designed and produced an educational brochure for general public distribution (92,000 copies distributed). The NPRC Outreach Specialists worked in collaboration to develop the brochure text, and the new **NPRC Research and Capabilities Inventory website** used this text as a basis for its content. The Outreach Working Group has recently been asked by [Excluded by Requester] to assist in marketing and promoting the new website.

INNOVATION

A number of innovations increase and enhance communications and engagement, both within the scientific community and reaching the lay public. The Education Outreach Program is highly innovative and there are plans to expand impact with middle school students and educators. [Excluded by Requester] is collaborating with a CNPRC junior investigator, [Excluded by Requester] to develop a new program to target junior high-aged girls, who often begin to lose interest in science.

APPROACH

Plans for the Next Funding Period

Specific Aim 1. Advance awareness of CNPRC scientific contributions through effective communications to the media and lay community.

Current plans are to broaden **communications** to the media and lay community, and develop new ways to reach audiences with news of discoveries, to generate curiosity, and to increase the positive perception of the CNPRC. The CNPRC website will be expanded and remain up-to-date with contemporary social media and mobile media applications. New opportunities and additional materials are under development to address animal care and well-being. The CNPRC leads this field in behavior and colony management including positive reinforcement training, and these capabilities and accomplishments will be promoted in brochures, online materials, and incorporated into the Education Outreach Program. The goal is to improve understanding of the CNPRC's commitment to, and progress in, animal care.

The **Education Outreach Program** materials, curriculum, and activities are currently being brought up-to-date to ensure the long-term sustainability of this vital program. Important to this coming year is to bring the curriculum in alignment with the new Federal "Next Generation Science Standards", while working to continue to reflect the science and significance of the research conducted, and the commitment to excellence in the responsible conduct of research. Exciting new breakthroughs in health and science will guide the development of new materials and classroom activities, and will enhance the connection with the public through the use of educational materials with expanded website information and new media platforms. The Education Outreach Program will also work to increase the number of presentations to low-income and high-risk students, reaching families that do not have exposure to and experience in biomedical research, higher education, and broader career opportunities. Existing relationships with UC Davis teaching programs (K-12 Partnership, GEAR UP, University Outreach and International Programs) will be further developed, and new connections will be fostered with local schools and community groups, increasing the number of student and educator interactions with the CNPRC. The program works in alignment with the NIH emphasis on the importance of educating the public through outreach programs on the need for animal research.

The **NPRC Outreach Working Group** will continue to improve on plans to educate the lay community on the value of the NPRCs. Additional outreach materials are under development and preliminary discussions have been held to identify best methods to accomplish outreach efficiencies and effectiveness. Monthly conference calls will continue to define materials and monitor outcomes. The Working Group members will represent the NPRCs at public events to educate and inform the public and investigators at all career stages on the NPRC programs. The annual Society for Neuroscience informs scientists about available services and potential collaborations; the USA Science and Engineering Festival educates individuals every two years; and other public and scientific events will be attended as funding is available and opportunities are identified.

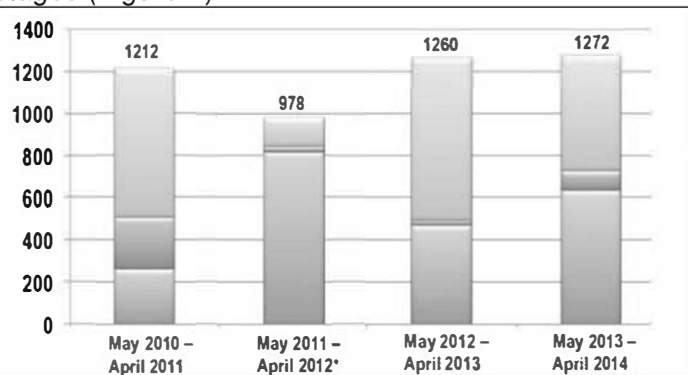
Specific Aim 2. Ensure that investigators at the local, regional, and national levels have ready access to CNPRC nonhuman primate expertise and resources.

The primary goal is to increase awareness of expertise, services, and capabilities to the broader scientific community. Information will be provided through: (1) refinements of the CNPRC website functionality; (2) enhanced marketing strategies; and (3) printed and electronic marketing materials. The scope of marketing materials will be expanded to address strategies that are targeted to attract those within the scientific community that would best be aligned to take advantage of these resources. Additionally, Core Scientists will network and share CNPRC materials at partnering exhibitions, conferences, summits, and meetings that gather industry and research services alongside scientific conferences. These mechanisms will provide growth potential with academic institutions, industry, private foundations, and philanthropy.

Specific Aim 3. Efficiently communicate information to the next generation of translational nonhuman primate investigators on the spectrum of research and training opportunities at the CNPRC.

The CNPRC website and marketing materials will be kept current with contemporary media and communication methods, attracting trainees at all career stages (Figure 7).

Figure 7. Outreach and engagement. Overall, the number of visitors has remained very high throughout the funding period (*illness limited off-site efforts in 2011-2012). The CNPRC hosts large numbers of undergraduate and graduate students and new mechanisms to further increase the number that visit will aid in building strong connections for future training opportunities and appreciation of the importance of the research. Green bar=K-12 and other educational venues at the school site; Red=K-12 students and educators at the CNPRC; blue=onsite trainees (e.g., undergraduates, veterinary students, others). Y-axis represents the number of students, trainees and visitors.



OUTREACH

BIBLIOGRAPHY AND REFERENCES CITED

Not applicable

OUTREACH

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Pilot Research Program

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename PRP_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	PRP_BibliographyandReferencesCited.pdf
10. Facilities & Other Resources	PRP_FacilitiesandOtherResources.pdf
11. Equipment	PRP_Equipment.pdf

PILOT RESEARCH PROGRAM

ABSTRACT

The objective of the California National Primate Research Center (CNPRC) **Pilot Research Program** is to spark innovative research by facilitating robust new research concepts and teams through partnerships with CNPRC Core Scientists. The CNPRC Pilot Research Program provides a mechanism for investigators new to nonhuman primate research to obtain the necessary preliminary data for NIH and related extramural grant submissions. In the next funding period, the CNPRC proposes a new approach that is based on the highly successful UC Davis Clinical and Translational Science Center (CTSC) Pilot Translational and Clinical Studies Program that was developed and thoroughly tested over 9 years of NIH funding, and has shown a high rate of return on investment. A similar format was successfully adapted to the NIH West Coast Metabolomics Center, thus the objective is to similarly enhance the CNPRC program by leveraging of funds, promoting mentoring and training of investigators and trainees, and engaging a reporting structure to capture outcomes and enhance project success. The Specific Aims for the CNPRC Pilot Research Program are to: (1) Promote partnerships and team science through a pilot program mechanism that supports innovative state-of-the-art translational research with nonhuman primates, (2) Mentor and train the next generation of investigators to ensure a pipeline of knowledgeable researchers with expertise in the use of nonhuman primate models for the study of human health and disease, and (3) Facilitate and enable cutting edge, translational pilot research studies to ensure high impact publications and successful NIH funding.

PILOT RESEARCH PROGRAM

FACILITIES AND OTHER RESOURCES

Laboratories: Pilot project recipients have the opportunity to work in the laboratories of CNPRC Core Scientists.

Clinical: Clinical care and related procedures at the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see **Primate Services**).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and Information Technology Services provides desktop support and other related services. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are available for use.

Office: Pilot awardees have the opportunity to work in shared offices and cubicles on-site at the CNPRC.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

PILOT RESEARCH PROGRAM

EQUIPMENT

Pilot awardees have the opportunity to work in the laboratories of Core Scientists and utilize equipment available for shared use in the Cores (see other sections of this application).

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Associate Director for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
						Total Salary, Wages and Fringe Benefits (A+B)	0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

C. Equipment Description	
List items and dollar amount for each item exceeding \$5,000	
Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Pilot Project Funds	300,000.00
Total Other Direct Costs	300,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	300,000.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	300,000.00	68,100.00
Total Indirect Costs			68,100.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	368,100.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PRP_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months EFFORT	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Associate Director for Research	Institutional Base Salary		0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons: File Name:											Total Senior/Key Person	
											0.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
						Total Salary, Wages and Fringe Benefits (A+B)	0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Pilot Project Funds	300,000.00
Total Other Direct Costs	300,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	300,000.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	300,000.00	68,100.00
Total Indirect Costs			68,100.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	368,100.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PRP_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Associate Director for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					0.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Pilot Project Funds	300,000.00
Total Other Direct Costs	300,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	300,000.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	300,000.00	68,100.00
Total Indirect Costs			68,100.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	368,100.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PRP_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Associate Director for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person					0.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	0.00
Total Travel Cost	0.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Pilot Project Funds	300,000.00
Total Other Direct Costs	300,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	300,000.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	300,000.00	68,100.00
Total Indirect Costs			68,100.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	368,100.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PRP_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*	
1.	Excluded by Requester				Associate Director for Research	Institutional Base Salary	EFFORT	0.0	0.0	0.00	0.00	0.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						0.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	Total Number Other Personnel					Total Other Personnel	0.00
Total Salary, Wages and Fringe Benefits (A+B)							0.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

C. Equipment Description	
List items and dollar amount for each item exceeding \$5,000	
Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	<u>0.00</u>
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	0.00
2. Foreign Travel Costs	<u>0.00</u>
Total Travel Cost	0.00

E. Participant/Trainee Support Costs	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	<u>0.00</u>
Total Participant Trainee Support Costs	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Pilot Project Funds	300,000.00
Total Other Direct Costs	300,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	300,000.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	300,000.00	68,100.00
Total Indirect Costs			68,100.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	368,100.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: PRP_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

PILOT RESEARCH PROGRAM**BUDGET JUSTIFICATION****PERSONNEL**

All effort will be committed through the Director's Office; therefore effort listed in this component does not fully demonstrate the level of commitment to these activities. Funds are dedicated to support competitive pilot research projects.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Associate Director for Research	% Effort			
Excluded by Requester	PhD, Associate Director for Research	EFFORT	months)	Excluded by Requester	is Professor in the Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine, and Core Scientist in the Respiratory Diseases Research Unit. As the Associate Director for Research, is responsible to the Director for the Pilot Research Program.
				Excluded by Requester	

EQUIPMENT

None

TRAVEL

None

SUPPLIES

\$300,000 is requested to support pilot research projects annually.

OTHER EXPENSES

None

SUBSEQUENT YEARS

Funds for pilot research projects is \$300,000 annually.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		0.00
Section B, Other Personnel		0.00
Total Number Other Personnel	0	
Total Salary, Wages and Fringe Benefits (A+B)		0.00
Section C, Equipment		0.00
Section D, Travel		0.00
1. Domestic	0.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		1,500,000.00
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	1,500,000.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,500,000.00
Section H, Indirect Costs		340,500.00
Section I, Total Direct and Indirect Costs (G + H)		1,840,500.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

PRP_SpecificAims.pdf

3. Research Strategy*

PRP_ResearchStrategy.pdf

4. Progress Report Publication List**Human Subjects Sections****5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

PRP_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

Pilot_Letters.pdf

13. Resource Sharing Plan(s)

PRP_ResourceSharing_Plan.pdf

Appendix (if applicable)**14. Appendix**

PRP_Appendix.pdf

PILOT RESEARCH PROGRAM

SPECIFIC AIMS

The overall intent of the California National Primate Research Center (CNPRC) Pilot Research Program is to provide integrated scientific, educational, administrative, and financial support for pilot projects that support the CNPRC mission. The CNPRC facilitates robust new research concepts and teams through partnerships with CNPRC Core Scientists that have a range of scientific expertise and participate in Service Cores that support studies with nonhuman primates. The CNPRC Pilot Research Program provides a mechanism for investigators new to nonhuman primate research to obtain research experiences with nonhuman primates, and to gather the necessary preliminary data to submit competitive NIH grant applications. In the next funding period, the CNPRC proposes a new approach that is based on the highly successful UC Davis Clinical and Translational Science Center (CTSC) Pilot Translational and Clinical Studies Program that was developed and thoroughly tested over 9 years of NIH funding, and has shown a high rate of return on investment. Central features of the program include leveraging funds, promoting mentoring and training, and the inclusion of an efficient reporting structure that captures outcomes. In an effort to closely monitor the success of the pilot projects, quarterly progress reports and a final report are requested which are highly effective in providing information on progress in relation to the original goals, need for additional resources, and development of new tools. This approach also ensures the appropriate documentation of presentations and publications, and new extramural grants submitted and funded. Basic concepts in this evolved structure will include a requirement for submissions to include trainees and to ensure exposure of these trainees to nonhuman primate research; active solicitation of partnerships and leveraging of funds from other UC Davis pilot programs; and linking program announcements to other translational outreach opportunities. The overriding objective is to enable cutting edge translational pilot research studies that result in high impact publications and competitive NIH grant submissions. Thus, the Specific Aims for the Pilot Research Program are as follows:

Specific Aim 1. Promote partnerships and team science through a pilot program mechanism that supports innovative state-of-the-art translational research with nonhuman primates.

Plan. The CNPRC Pilot Research Program will encourage innovation by providing essential infrastructure through key outreach efforts that cast a wide net and ensure applicants have access to the necessary expertise, resources, tools, and services for translational nonhuman primate research. Pilot project calls will be utilized to advance research in key thematic areas with a team approach. An annual pilot project retreat for funded investigators and trainees will provide further exposure to cutting edge research and collaborative opportunities.

Specific Aim 2. Mentor and train the next generation of investigators to ensure a pipeline of knowledgeable researchers with expertise in the use of nonhuman primate models for the study of human health and disease.

Plan. The program focuses on investigators new to nonhuman primate research at all career stages. The inclusion of trainees in pilot project submissions further builds a competent workforce and pipeline of investigators that will conduct nonhuman primate research at the highest quality level, taking full advantage of the wealth of mentoring and training opportunities provided through the CNPRC.

Specific Aim 3. Facilitate and enable cutting edge, translational pilot research studies to ensure high impact publications and successful NIH funding.

Plan. The CNPRC will promote research facilitation and remain flexible and forward thinking in resource development to support and enable new teams with clear paths to innovation. Through collaboration with existing university-wide resources for grant development, pilot project awardees will be encouraged to translate their findings into expanded NIH grant applications in an expeditious mentored fashion, and with the assistance of Core Scientists.

PILOT RESEARCH PROGRAM

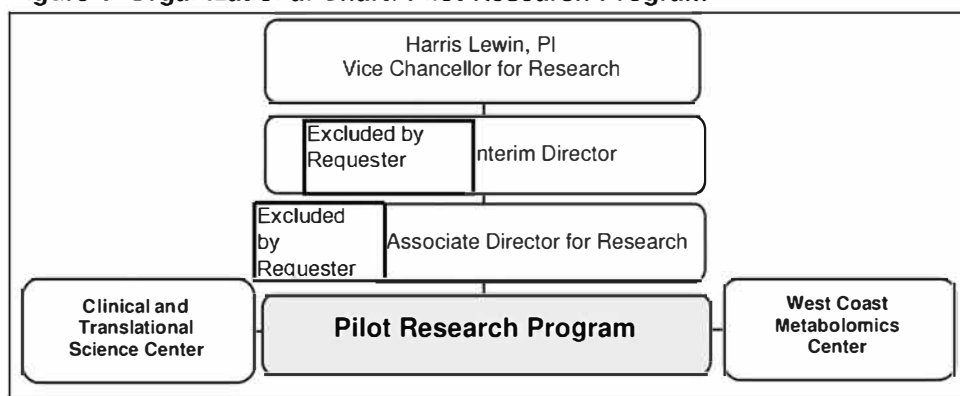
RESEARCH STRATEGY

INTRODUCTION

The primary goal of the Pilot Research Program is to provide a resource mechanism for investigators to obtain preliminary data to enhance opportunities for NIH funding using nonhuman primate models of human health and disease. Each National Primate Research Center (NPRC) is required to have a Pilot Research Program that solicits proposals from outside investigators and funds collaborative projects with NPRC Core Scientists. During the current funding period, the CNPRC administered two Pilot Research Programs; the P51-supported Pilot Research Program and an ARRA-supported Postdoctoral Pilot Research Program that was a supplement to the P51 base grant. The rationale for the ARRA Postdoctoral Pilot Research Program was to provide an opportunity for highly qualified postdoctoral fellows to conduct independent research projects utilizing nonhuman primates under the mentorship of a CNPRC Core Scientist, with the goal of facilitating the development of new investigators that will utilize NPRC resources.

In the next funding period, the CNPRC proposes a new approach that is based on the highly successful UC Davis Clinical and Translational Science Center (CTSC) Pilot Translational and Clinical Studies Program, which was successfully adapted in the NIH West Coast Metabolomics Center Outreach and Promotion Core (Figure 1).

Figure 1. Organizational Chart: Pilot Research Program



The sources of support for the last year of the current funding period (May 1, 2014 to April 30, 2015) and the first year of the proposed funding period (May 1, 2015 to April 30, 2016) per the FOA are shown in Table 1.

Table 1. Support for the Pilot Research Program

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$275,000	\$300,000
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$275,000	\$300,000

Response to Summary Statement.

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

P51 Base Grant Pilot Projects. The goal of the CNPRC Pilot Research Program is to enable investigators to obtain preliminary data that will greatly enhance the likelihood of receiving extramural funding for proposals that incorporate nonhuman primate models of human disease. During the current funding period, there was an increased emphasis on translational studies aimed at directly solving problems related to human health. Selected projects and investigators are typically junior and with no or little prior experiences with nonhuman primate research. The Pilot Research Program is a critical mechanism by which the CNPRC engages new investigators. In accordance with the National Primate Research Centers Program Guidelines (7th Edition), the following minimum criteria must be met in order to apply for CNPRC pilot funds:

- Applications can only be submitted by individuals with Principal Investigator (PI) status from any federally recognized institution.
- The project must be planned, conducted, and carried out under the supervision of at least one CNPRC Core Scientist who serves as a collaborator, and takes responsibility for overall management, coordination, and progress reports for the project.
- All activities related to the use of nonhuman primates must be conducted on-site at the CNPRC.
- Funds may not be used to provide interim support for established projects, for any projects that qualify for support from other sources, or to extend previously established nonhuman primate research.
- Conditions of funding include the submission of a progress report for inclusion in the CNPRC Annual Report, and reporting of grants and publications that develop from the pilot award on an as-requested basis. The CNPRC P51 base grant (#OD011107) must be acknowledged in any oral or written presentations of data obtained through this program.

An annual Request for Proposals is typically circulated by electronic mail in February of each year (considering each base grant funding year begins May 1), which requests a one-page Letter of Intent. The Request for Proposals is also posted on the CNPRC web page, and is disseminated to the following:

- CNPRC Core and Affiliate Scientists
- Responsible administrators for the UC Davis CTSC and Comprehensive Cancer Center for circulation through their respective listservs
- UC Davis Office of the Vice Chancellor for Research for broad distribution to the UC Davis research community and Vice Chancellors for Research at other UC campuses
- Deans of the UC Davis Schools of Medicine and Veterinary Medicine and the Colleges of Agriculture and Environmental Sciences, Biological Sciences, Engineering, and Letters and Sciences
- Deans of the Medical Schools of the other UC campuses
- Other NPRCs

The Call contains a description of the program, information on eligibility and funds availability, application procedures, review criteria, and relevant contact information for Unit Leaders, and for the Director and Associate Director for Research (see below). A link to the CNPRC web page is also included for more information about the CNPRC program. The Letters of Intent are requested to contain a short summary (no more than 1 page) with the title, aims, and goals of the project, as well as the inclusion of the names of collaborating investigators including the relevant Core Scientist(s). Following receipt, Letters of Intent are distributed to all members of the CNPRC Research Advisory Committee. Each Letter is typically ranked into one of three categories: high, moderate, or low enthusiasm. At the subsequent Research Advisory Committee meeting, there is discussion of each Letter, and a consensus is reached about which Letters merit requesting full proposals. The PI of each Letter of Intent is contacted with a request for a full proposal by a specific deadline date (about 1 month).

When a full proposal is requested, the following information is required within the standardized forms provided:

- A cover page with detailed information
- A five page application that addressed the following topics:
 - Specific Aims and Hypotheses
 - Background and Significance
 - Experimental Plan
 - Anticipated Results

- Potential Problems/Alternate Approaches
- Source of Potential Future Funding
- Relevance to Biomedical Research and Rationale for Nonhuman Primate Use
- A budget and budget justification (not to exceed two pages)
- Biographical Sketches (NIH format) for all personnel

Once the proposals have been submitted to the CNPRC, the Associate Director for Research insures the completeness of applications and requests the necessary information that might be missing. Once complete, the proposals are distributed to all members of the review committee appointed by the Director and consisting of at least three non-Core Scientists with expertise in the various disciplines represented by the applications. In the 2013 and 2014 solicitations, three different reviewers evaluated each proposal. The reviewers provide each application with an overall score, based upon the NIH scoring system, and include comments in the following areas:

- Overall Enthusiasm
- Scientific Merit (Significance, Approach, Innovation)
- Compatibility with the CNPRC Mission
- Likelihood of Subsequent Funding
- Justification for the Use of Nonhuman Primates
- Budget
- Feasibility for Conduct at the CNPRC

Final funding decisions are made by the Director in consultation with the Research Advisory Committee based upon the reviewer's critiques and availability of funds. All investigators who submit proposals are provided with a written critique. The Associate Director of Research and the Director's Office maintain the written critiques and scores. Proposals are awarded for a one-year period. In cases where a PI has not completed the project within that period, a one-year no-cost extension may be granted by the Research Advisory Committee provided that the PI describes adequate progress made to date. The progress report is discussed at the Research Advisory Committee meeting, and a decision made on whether to approve the extension. During the current funding period, the requests for a one-year no cost extension were approved.

Outcomes. During the current funding period a total of 77 Letters of Intent were received, 37 full proposals were solicited based upon selected Letters of Intent, and 14 proposals were funded (Tables 2 and 3). Funds awarded during the current funding period totaled \$183,089. The funds available were lower then anticipated and resulted from NIH mandated sequestration and cuts across all program areas of the P51 base grant.

Table 2. P51 Pilot Applications and Total Funds Allocated (May 1, 2010 to April 30, 2014)

Grant Year	Letters of Intent	Applications Solicited	Applications Funded	Total Funds Allocated (\$)
2010 - 2011	13	9	4	41,799
2011 - 2012	7	6	2	45,423
2012 - 2013	14	4	2	35,743
2013 - 2014	25	10	3	60,124
				\$183,089

Budget requests for pilot awards were typically in the range of \$20,000 per project. Pilot project recipients were also provided up to 3 animals at no additional cost in 2010-2012 (additional \$18,000 in waived animal purchase costs or use fees per project), and up to 6 animals in 2012-2014 (\$18,000 to \$36,000 in waived animal purchase costs or use fees per project), thus the pilot funds were specifically for all other animal-related activities (purchase of additional animals, per diem, Core use, and modest supplies). The provision of animals at no cost by the CNPRC added significant value to each funded pilot award. For example, in 2013, the added value provided through either animal use fees (non-terminal studies) or animal purchase costs for the three funded pilot projects totaled over \$80,000.

Table 3. P51 Funded Pilot Projects (May 1, 2010 to April 30, 2014)

Grant Year	Investigator	Institution	Funds (\$)	Project Title	Core Scientist(s)
2010 - 2011	Excluded by Requester	Private Source	20,923	Immune Modulation of the Fetus by Intra-amniotic IL-1	Excluded by Requester
			21,799	Development of Live Attenuated Vaccines against Chlamydial Genital Tract Disease	
		UC Davis	18,812	Conversion of Regulatory T-cells in the Gut During Acute SIV infection	
2011 - 2012	Excluded by Requester	UC Davis	19,789	A Nonhuman Primate Model for Autism Spectrum Disorder Treatment Discovery	Excluded by Requester
		UC San Diego	25,635	Developing a Primate Model to Investigate How Airborne Immunostimulants Regulate Development of Aeroallergen Hypersensitivity in Young Children	
2012 - 2013	Excluded by Requester	Private Source	14,872	Adeno-Associated Viral Vector Mediated Gene Silencing in Nonhuman Primate Midbrain	Excluded by Requester
			20,821	The Role of Oxytocin Biology in Primate Social Impairments	
2013 - 2014	Excluded by Requester	University of Washington	22,557	Role of Oxytocin Signaling in the Amelioration of Diet-Induced Obesity in Nonhuman Primates	Excluded by Requester
		UC Merced	20,000	Determination of Age-Related Effects on Mesenchymal Stem/Stromal Cell Function on Hematopoietic Stem Cell Engraftment and B Cell Regeneration in the Rhesus Monkey	
		UC San Francisco	17,565	Lung Regeneration Following Partial Pneumonectomy in Macaques	

A positive outcome of the Pilot Research Program is that it often leads to new project requests from additional investigators at the institution from which the Pilot Research Program awardee originates. For example, 2010 Pilot Research Program recipient [Excluded by Requester] Private Source received a [Private Source] grant in 2013. Based on [Excluded by Requester] initial contacts to the CNPRC through the Pilot Research Program, in 2012 [Excluded by Requester] (also from [Private Source]) established subcontracts with the CNPRC for other nonhuman primate studies. [Excluded by Requester] received an NIH R01 grant and [Excluded by Requester] was the recipient of a [Private Source] Grant resulting from these efforts. Dr. [Excluded by Requester] also from [Private Source] applied for an NIH R01 grant with a CNPRC subcontract, but

Unfunded Info

Pilot proposals for the last year of the current funding period have been solicited, reviewed, and selected (Table 4). Eighteen Letters of Intent were received of which 8 were solicited for full applications, and 4 selected for funding to be conducted during the May 1, 2014 to April 30, 2015 base grant year (Year 53).

Table 4. P51 Recently Selected Pilot Projects (for conduct during the 2014-2015 base grant year)

Investigator	Institution	Project Title	Core Scientist
Excluded by Requester	Private Source	A Rhesus Macaque Immunogenicity Model to Investigate the Effect of Binding of Complement Factor H on Meningococcal Factor H Binding Protein Vaccines	Excluded by Requester
	UC Davis	Identification of Neural Precursor Cells in the Fetal Macaque Brain	
	Private Source	Potential New Model for Childhood Gastroenteritis	
	UC Davis	The Fate of Inhaled Statins in the Lung and Systemic Circulation	

P51 Base Grant ARRA Supplement: Postdoctoral Pilot Projects. The transition from being a scientist “in training” to an independent investigator is typically a difficult one. In 2009, the CNPRC received an ARRA-supplement to the P51 base grant that provided four postdoctoral scholars two years of funding each to conduct an independent nonhuman primate research project under the mentorship of an established nonhuman primate investigator. The purpose of the supplement was to add depth to the existing Pilot Research Program by targeting postdoctoral researchers who would normally not be eligible for the P51-supported Pilot Research Program, with the intent of developing the next generation of nonhuman primate biomedical researchers. While applicants independently developed funded projects, a CNPRC Core Scientist also provided support for the project, and facilitated its completion. In order to target Postdoctoral Scholars, the application criteria were similar to the P51 mechanism with some critical differences. First, in order to target Postdoctoral Scholars, the application criteria required the following:

- Must have received terminal degree (PhD, DVM, MD) at the time of submission.
- Must have completed terminal degree within five years at the time of submission.
- Not previously designated as PI on an NIH grant or federally supported research project or component (except for a dissertation research grant), or have received similar support from another federal or state agency, e.g., the National Science Foundation. Previous receipt of a National Research Service Award as a trainee was permissible.
- A letter from the current mentor indicating support of the applicant’s research plan.
- Documentation that current position was in a job classification that does not normally permit PI status at the applicant’s institution.
- Commitment of at least 30% effort to the pilot project.
- Core Scientist sponsorship for the applicant research plan.

This supplement provided up to \$75,000 for each project, in addition to three animals at no cost. Two projects were supported in Year 1 and two projects were supported in Year 2. The Calls requesting Letters of Intent were posted on the CNPRC web page and disseminated via electronic mail comparable to the P51 Pilot Program. The Call contained a description of the program, information on eligibility and funds available, application procedures, review criteria, and relevant contact information as noted above. A link to the CNPRC web page was also included for more information about the program. The Letters of Intent were due in December of each year, and required a short summary (no more than 1 page) with the title, aims, and goals of the project, as well as the names of collaborating investigators (including the relevant Core Scientist). Following receipt, Letters of Intent were distributed to all members of the CNPRC Research Advisory Committee, including one non-Core Scientist member. Each Letter was ranked into one of three categories: high, moderate, or low enthusiasm. At a subsequent meeting, there was discussion of each Letter, and a consensus was reached about which Letters merited full proposals. The Letter of Intent applicants were contacted as noted and requested to submit a full proposal with the same criteria as noted above with the exception of inclusion of a letter of support from the current postdoctoral mentor and a description of the role of the CNPRC Core Scientist. Review criteria were similar to the criteria noted above, and final funding decisions were made by the Director in consultation with the Research Advisory Committee and based upon the reviewer critiques. All postdoctoral scholars who submitted full proposals were provided with a written critique.

Outcomes. The ARRA supported Postdoctoral Awards generated a total of 11 grant applications (Table 5).

Table 5. ARRA Postdoctoral Pilot Applications

Grant Year	Letters of Intent	Applications Solicited	Applications Funded	Total Funds Allocated
2009 - 2010	7	5	2	\$150,000
2010 - 2011	6	6	2	\$150,000

Of these, 4 submissions from applicants external to the CNPRC were funded (Table 6). Research funded by the Postdoctoral Pilot Program resulted in 10 publications, several new funding mechanisms (fellowships, contracts, NIH grants). Three of the recipients were successful in obtaining research appointments at UC Davis.

Table 6. ARRA Funded Postdoctoral Pilot Projects

Grant Year	Investigator	Institution	Core Scientist	Project Title	Current Position
2009 - 2011	Excluded by Requester	Lovelace Respiratory Research Institute and UC Davis	Excluded by Requester	The Contribution of Age and Environment on Establishment of Mucosal Immunity to Infectious Agents	Postdoctoral Fellow, UC Davis
		Private Source		Epigenetic Risk Following Early Life Stress in Infant Rhesus Macaques	Assistant Project Scientist, UC Davis
2010 - 2012		UC Davis		Neural Correlates of Social Buffering in Juvenile Rhesus Macaques: Friends versus Familiar Companions	Assistant Project Scientist, UC Davis
		UC Davis		Assessment of a Non-human Primate Model of Human Mammary RNA during Lactation	Assistant Professional Research Scientist, UC Davis

INNOVATION

The Pilot program represents opportunities to identify the most innovative projects using nonhuman primates and also to identify and encourage the next generation of investigators focused on such models. While progress has been made in funding high quality projects, including a novel postdoctoral program funded by a P51 ARRA base grant supplement, the CNPRC now looks to the future and innovative ways to further expand this important CNPRC program. In order to parallel the CNPRC trajectory anticipated during the next funding period, the CNPRC aims to model a highly successful pilot program where there has been a high return on investment, strengths in outreach, and opportunities for leveraging: the UC Davis CTSC Pilot Translational and Clinical Studies Program, which was integrated as a model in the Promotion and Outreach Core of the NIH-funded West Coast Metabolomics Center. As such, it has been very well received by the NIH.

The CTSC Pilot Translational and Clinical Studies Program serves as a critical tool fostering multidisciplinary translational research. Basic principles include a requirement to form new multidisciplinary teams, inclusion of trainees and exposure of these trainees to the CTSC education program; active solicitation of partnerships with other UC Davis pilot project programs; and linking CTSC pilot program announcements to translational workshops and symposia. All funded investigators and the title of their projects are posted on the CTSC website to highlight their success and innovation. In an effort to closely monitor their outcomes and identify areas where additional resources may be needed, formal quarterly progress reports are required, as well as a final report and annual updates which ensures publications, patents, presentations, and grants submitted and awarded are identified. As highlighted in the CTSC competitive renewal in 2011, the program supported 62 pilot projects spanning a wealth of translational topics resulting in 66 publications, 106 abstracts for presentation, inclusion of 94 trainees (undergraduate and graduate students, postdoctoral and clinical fellows), and extramural funding of approximately \$23 million leveraging an approximate \$414,000 CTSC investment. This pathway to success was adapted in the NIH grant application to establish the West Coast Metabolomics Center (1 of 3 in the first round and only 6 funded in the U.S.) and specifically the Promotion and Outreach Core. Similar to the CTSC, and with a focus on translational metabolomics research and services, a pilot

project funding mechanism linked to trainees and educational experiences with the goal of growing a cadre of investigators with expertise in the metabolomics field. A high level of success has been captured in this program, which has been acknowledged at the NIH level. Thus, the goal is to capitalize on and adapt this successful format in the next funding period.

APPROACH

Plans for the Next Funding Period

For the next funding period, key elements include:

- Serve as a catalyst for forging novel inter- and multidisciplinary research projects to rapidly advance knowledge and techniques with nonhuman primates pertinent to human health.
- Amplify services supporting nonhuman primate translational research and education to enhance impact and optimize utilization.
- Promote interest among trainees, junior faculty, and established investigators in utilizing nonhuman primates to conduct collaborative translational research focused on human health and disease.

Specific Aim 1. Promote partnerships and team science through a pilot program mechanism that supports innovative state-of-the-art translational research with nonhuman primates.

The CNPRC Pilot Research Program will encourage innovation by providing essential infrastructure through key outreach efforts that cast a wide net and ensure applicants have access to the necessary expertise, resources, tools, and services for translational nonhuman primate research. Pilot project calls will be utilized to advance research in key thematic areas such as lifespan health, the use of novel imaging tools and technologies, neurodevelopmental disorders, and related initiatives that advance the program and link with key NIH strategic priorities. Applicants will be required to emphasize specific plans for extramural submissions including timelines. Trainee participation will be required in all funded projects in an effort to foster a culture of team science and to encourage career choices for the next generation of scientists using nonhuman primate models. A mentoring plan for the trainee and the role of the trainee in the project will also be a requirement for submission.

Projects that involve translational research will be emphasized and increased effort will be made to establish joint pilot programs with other entities at UC Davis, such as the CTSC, MIND Institute, Metabolomics Center, Center for Molecular and Genomic Imaging, and Comprehensive Cancer Center. The intramural RISE (Research Investments in Science and Engineering) proposals funded by the Vice Chancellor for Research are examples of models for such campus-wide efforts as described in other components of this application (see **Overview**). Partnering with other pilot programs will provide mutual benefits. It will enrich the CNPRC by bringing in a wealth of research opportunities and potential partners, and it will benefit other programs by bringing in expertise in nonhuman primate models, setting the stage for durable collaborations.

The goal will be to identify promising projects that will advance the field, and recruit, mentor, and retain a broad and diverse applicant pool of investigators new to nonhuman primate research. The Pilot Research Program will support projects that will be reviewed, ranked, and selected by an external review committee with relevant expertise based on the applications submitted. CNPRC National Scientific Advisory Board (NSAB) members will also be included to ensure that key initiatives and areas of growth are considered. The Pilot Review Committee will review and rank all. Members will recuse themselves for any projects where there may be a perceived conflict of interest. Each application will be assigned to three reviewers and scored using the NIH format, with a template for the review (Table 7) using an established format with defined criteria. All submitted projects will be circulated to the Committee allowing each member the opportunity to comment on any project, and to aid in identifying those that are highly meritorious.

As described in the Progress and Major Accomplishments, the current funding period utilized a mechanism by which a limited number of colony animals were provided to pilot grant recipients at no cost along with a small budget for per diem, animal care, Service Core use, and supplies. While this approach has been successful with regards to providing the basis for new grant applications, moving forward the CNPRC is currently incorporating animal purchase/use fee costs as a component of the funds that support the pilot research project. Budgeted costs thus increase per project, and take into account animal purchase costs and use fees (which vary with age). The primary intent for this change is optimizing and clarifying the true costs that are

provided when a pilot project is awarded and to carefully determine through the reporting mechanism how the funds are being leveraged to new grant awards.

Table 7. Examples of Review Format for Pilot Project Submissions

Evaluation Criteria	Subject Content
<i>Does the PI clearly explain the significance of the proposal?</i>	<ul style="list-style-type: none"> • Does the research proposed address an important bottleneck or roadblock in a unique way? • Is the research proposed original and innovative? • Are the goals, objectives, and significance stated clearly and are they reasonable given the funds requested and the timeline? • Have potential barriers/technical difficulties been identified and alternatives presented? • Plan high risk but potentially high impact?
<i>Have the goals for the project been addressed, are there new collaborations and the inclusion of trainee(s) with roles clearly defined, and are new approaches described?</i>	<ul style="list-style-type: none"> • Is the potential impact of the research stated and justified? • Do the investigators have the expertise to carry out the project? • Has at least one Core Scientist been identified and the role explicitly stated? • Are trainees included and have the role of the trainee(s) been well defined with a mentoring plan? • Has the P.I. clearly indicated how this proposal will potentially overcome a critical research problem?
<i>Does the proposal clearly state the need for the pilot award and plans to submit an extramural grant proposal?</i>	<ul style="list-style-type: none"> • Have realistic extramural opportunities for funding been identified and will pilot support provide the necessary preliminary data? • Will support of the research provide data that will be competitive for funding at the NIH? • Does the investigator have a track record that indicates prior extramural support and publications? If a junior investigator, does the investigator have the background to ensure success? If a senior investigator, is a new concept proposed?
<i>Is the budget reasonable and well justified?</i>	<ul style="list-style-type: none"> • Has the investigator clearly detailed the funds requested for the study?

The following requirements for all funded projects will be addressed in the award letter:

- Quarterly request for an update on research progress, a final report, and an annual report for 3 years.
- Abstracts and names of investigators supported posted on the CNPRC website.
- Awardees must cite the funding source in all presentations and publications.

Specific Aim 2. Mentor and train the next generation of investigators to ensure a pipeline of knowledgeable researchers with expertise in the use of nonhuman primate models for the study of human health and disease.

The program focuses on investigators new to nonhuman primate research at all career stages. The inclusion of trainees in pilot project submissions further builds a competent workforce and pipeline of investigators that will conduct nonhuman primate research at the highest quality level, taking full advantage of the wealth of mentoring and training opportunities provided through the CNPRC. A team of Core and Affiliate Scientists will be identified for each Pilot Project recipient, based on the research focus. The team will provide a constructive mentoring environment for the recipient through direct interactions including comments for manuscripts and pre-submission reviews of grant submissions. An annual pilot project retreat for funded investigators and trainees will provide further exposure to cutting edge research and collaborative opportunities.

Specific Aim 3. Facilitate and enable cutting edge, translational pilot research studies to ensure high impact publications and successful NIH funding.

The CNPRC will promote research facilitation and remain flexible and forward thinking in resource development to support and enable new teams with clear paths to innovation. Through collaboration with existing university-wide resources for grant development, pilot project awardees will be encouraged to translate their findings into expanded NIH grant applications in an expeditious and mentored fashion, and with the assistance of Core Scientists.

PILOT RESEARCH PROGRAM

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian and the IACUC.

Excluded by
Requester

Excluded by
Requester

1. **Proposed Use of Animals.** The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. **Justification of Animal Use, Species Choice, and Numbers.** The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols, and the species choice is justified.
3. **Veterinary Care.** Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. See Primate Medicine Services section.
4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or

buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary.

5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

PILOT RESEARCH PROGRAM

BIBLIOGRAPHY AND REFERENCES CITED

Excluded by Requester

The U.S. Initiative: Clinical and Translational Science Awards – The UC Davis Perspective. *In:* (Alving B, Dai K, Chan SHH, editors) Translational Medicine-What, Why, and How: An International Perspective. Transl Res Biomed, Basel, Karger, Volume 3, pp. 18-28, 2013.

PILOT RESEARCH PROGRAM

LETTERS OF SUPPORT

Letters of support from the individuals named below are provided on the pages that follow.

1.

Excluded by Requester

 PhD, Research Associate Professor, Division of Metabolism,
Endocrinology and Nutrition, University of Washington School of Medicine
2.

Excluded by Requester

 Pharm D, PhD, Professor of Pediatrics, Division of Immunobiology, Cincinnati
Children's Hospital Medical Center



DEPARTMENT OF VETERANS AFFAIRS

Puget Sound Health Care System
1660 South Columbian Way
Seattle, WA 98108-1597

AMERICAN LAKE DIVISION
TACOMA, WA 98493-5000

SEATTLE DIVISION
SEATTLE, WA 98108-1597

In Reply Refer To:
Excluded by Requester

February 6, 2014

RE: Letter in Support of UC Davis California National Primate Research Center (CNPRC) Base Grant #OD011107 Renewal

To: Evaluation Committee

It is my distinct pleasure to strongly support the renewal of the CNPRC Base Grant #OD011107 renewal application. Through my CNPRC Pilot Project and corresponding collaboration with CNPRC Staff Scientist [redacted] (CNPRC Brain, Mind, and Behavior Unit Leader; Professor, Department of Psychology, UC Davis) and [redacted] (Professor and Vice-Chair, Department of Molecular Biosciences, UC Davis), I have been able to translate our promising findings demonstrating the effects of chronic oxytocin treatment on weight loss in diet-induced obese rodents to a diet-induced obese nonhuman primate (NHP) model. Through this CNPRC Pilot Project we found that chronic systemic oxytocin administration reduces body weight in diet-induced rhesus monkeys through a mechanism that involves reductions in food intake and increases in energy expenditure. We have since submitted [redacted]

Submitted

These findings raise interesting questions as to the extent to which oxytocin reduces food intake by enhancing the hindbrain responsiveness to satiety signals such as cholecystokinin (CCK) or inhibiting the response to feeding reward circuits in the CNS. We have successfully applied for an extension to this pilot application to examine the extent to which systemic oxytocin treatment activates specific populations of cells in the hindbrain as well as in the forebrain hypothalamus. Through my collaboration with [redacted] we also plan to create a diet-induced obesity model in titi monkeys and determine the extent to which chronic increases and reductions in oxytocin signaling alter consumption of rewarding stimuli and suppresses or facilitates the progression of diet-induced obesity in titi monkeys, respectively. These findings will provide key feasibility data to support [redacted]

Private Source

or NIH R01 funding for future larger scale and cross-sectional NHP studies. Such studies will include normal-weight and obese groups, serial monitoring of circulating satiety hormones (e.g., glucagon-like peptide-1, CCK-8), serial dosing and measurements of additional parameters (i.e. activity, increased duration, blood pressure, heart rate, core body temperature, interactive effects with CCK-8), and the use of fMRI studies to gain mechanistic insight into oxytocin's CNS effects in NHPs. Furthermore, these findings will establish key preliminary data for future Institute of Translational Health Science and NIH funding for larger clinical studies. Such studies

DEPARTMENT OF VETERANS AFFAIRS
Puget Sound Health Care System
1660 South Columbian Way
Seattle, WA 98108-1597

would test OT's ability to enhance satiety in obese persons as an early indication of its potential as a pharmaceutical intervention for the treatment of obesity. The ultimate goal is to move beyond analyses of oxytocin's chronic effects on food intake and body weight in diet-induced obese nonhuman primates to longitudinal studies examining the effect of oxytocin on body weight and body composition in obese humans.

Despite compelling evidence that oxytocin is important in the regulation of body weight, studies in humans and NHPs have primarily focused on the role of oxytocin in mood, trust, and pair-bonding.. Biological differences between rodents and primates, including humans, impede the ability to successfully identify drug targets that can ameliorate human obesity. These differences include ingestive behaviors, circadian rhythms, adipokine function, peptide hormones, responses to neurotransmitters, the predominant site of lipogenesis (liver vs. adipose tissue), and the physiology of thermogenesis. The results of metabolic studies performed in NHPs are more applicable to human physiology than those from rodent studies, emphasizing the need to develop NHP models of insulin resistance for the study of metabolic syndrome and type 2 diabetes mellitus.

Thus, my collaborations with faculty both at the CNPRC and UC Davis in addition to the established resources at the CNPRC have been extremely valuable in allowing my laboratory to translate findings from a diet-induced obese rodent model to a pre-clinical translational model of diet-induced obesity in nonhuman primates. Thus, I enthusiastically endorse the renewal to the CNPRC base Grant application.

Sincerely,

Excluded by Requester



Division of
Immunobiology

Excluded by Requester

May 7, 2014

Excluded by Requester

California National Primate Research Center
University of California

Excluded by Requester

I am writing to convey my strongest and most enthusiastic support for the renewal of the California National Primate Research Center NIH Base grant.

My close collaboration with the CNPRC started in 2010-2011, when I was awarded a pilot grant. This award allowed my colleagues from the CCHMC Perinatal Institute Excluded by Requester and me to initiate studies of how *in utero* inflammation affects fetal immune responses, as well as studying the placental inflammatory mediators in infection-associated preterm birth. These studies have since been supported by the CCHMC Perinatal Institute and have led to a published report in *The Journal of Immunology*, as well as several other manuscripts in preparation. Preliminary data also allowed us to successfully compete for support from the NIH and the Private Source Excluded by Requester with two grants awarded in 2013, which both include sub-contracts to the CNPRC.

In the last years, I have extensively used many services of the CNPRC and am therefore able to provide a testimonial of their usefulness to researchers working in other institutions such as myself. I want to particularly highlight several key aspects.

First, the nature of our research requires very close interactions with the CNPRC Research Services, which organize the logistics of our research protocols. This logistics is extremely complex, including multiple steps, from scheduling time-mated pregnancies, support for submission of IACUC protocols, coordinating multiple procedures (ultra-sound guided injections of inflammatory mediators, noise stress, newborn vaccinations, to name a few), and finally shipping biological materials when studies are completed. The constraints in this type of research are enormous, and the CNPRC Research Services have provided us with flawless support. During the preparation and execution of our experiments, we also closely interact with Pathology and Veterinary Services, and have particularly appreciated their immense knowledge and expertise, as well as their flexibility and dedication.

Second, we use CNPRC resources, such as the BioBehavioral Assessment Program led by Dr Excluded by Requester. This program is an enormously valuable and productive resource for investigators around the country and around the world. Indeed, we have recognized the value of this program for understanding the role of stress and temperament in preterm birth, and how it may influence post-natal development of immune responses. Of note, the related multi-PI NIH grant Excluded by Requester and myself from CCHMC, Excluded by Requester from the CNPRC) received Percentile Excluded by Requester attests of the recognition by the scientific community of how valuable the BBA Program is.

Third, I also want to emphasize the usefulness of CNPRC Cores such as the clinical services and the Flow Cytometry Core. As immunologists and cell biologists, we need high-end instruments for our research, and the CNPRC provides such equipment. We also greatly benefit from the many years of experience of these Cores in validating protocols and reagents for the rhesus macaque.

Finally, we deeply appreciate the fact that equipped labs are made available at the CNPRC for researchers from other institutions, which allows my colleagues and myself to perform experiments at the CNPRC for several weeks every year. During these stays, the CNPRC staff has always been extremely helpful, making our overall experience at the CNPRC highly productive and enjoyable.

Please do not hesitate to contact me for further information.

Sincerely,

Excluded by Requester

Professor of Pediatrics

Cincinnati Children's Hospital Medical Center

3333 Burnet Avenue, MLC 7038, Cincinnati, OH 45229-3039 | 513-636-0281 | Fax 513- 636-5355

www.cincinnatichildrens.org

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Letters Of Support

Page 1313

Obtained by Rise for Animals.

Uploaded to Animal Research Laboratory Overview (ARLO) on 09/19/2020

PILOT RESEARCH PROGRAM

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Brain, Mind, and Behavior Research Unit

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename BMB_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	BMB_BibliographyReferences.pdf
10. Facilities & Other Resources	BMB_FacilitiesOtherResources.pdf
11. Equipment	BMB_Equipment.pdf

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

ABSTRACT

The **Brain, Mind, and Behavior Research Unit** specializes in research on sociality, temperament, and development, with a true lifespan approach – utilizing measures from prenatal life to aged animals, including multiple time points in many studies. Increasingly, research is translational in nature with the development of many new primate models of human psychiatric disease and a focus on interventions. Research by Core Scientists includes foci on developmental models for psychiatric disease, individual differences throughout the lifespan, and social network analysis. These research agendas contribute to the training of a large number of undergraduates, graduate students, postdoctoral trainees, visiting students, and visiting scientists of many different levels. Core Scientists participate in multiple graduate programs, outreach, and summer programs for undergraduates. Unit Core Scientists also contribute significant service to the California National Primate Research Center (CNPRC) through administrative positions and committee memberships, facilitate significant research programs by external investigators, and ensure the Unit is a truly national resource. These investigators include large, well-funded groups working in behavioral neuroscience with aged monkeys, and those working in spinal cord regeneration. Core Scientists also facilitate investigators interested in the study of field cage monkeys, and those interested in working with the titi monkey colony. Pilot projects are facilitated which have been successful in attracting larger extramural funds and developing new investigators. Other contributions to colony management include enhancement of the animal colonies through evidence-based behavioral research. In summary, the Brain, Mind, and Behavior Research Unit pursues research excellence and serves as a national resource while contributing to primatological training and enhancement of animal resources at the CNPRC.

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

FACILITIES AND OTHER RESOURCES

Laboratories: The Childhood Health laboratory facility at the CNPRC is approximately [Specific Animal Location] and is fully equipped for endocrine and histological analysis (see Equipment). There is also approximately [Specific Location] animal testing space. [Excluded by Requester] has a shared laboratory space on-site with all equipment necessary to carry out stereotaxic surgery in the nonhuman primate. This includes a Kopf large animal stereotaxic apparatus with 4 microdrives (David Kopf Instruments, Tujunga, California). Since most neurosurgeries are now guided by information from a pre-surgical MRI scan, the Amaral laboratory also has two MRI-compatible stereotaxic apparatuses (Crist Instruments Co., Damascus, MD). There is also a Zeiss surgical microscope and electrophysiological equipment (preampifier, filters, oscilloscope and audio amplifier) necessary to record extracellular neuronal activity to define location of injection site.

[Excluded by Requester] laboratory is at the MIND Institute includes a wet lab suite totaling 1800 sq. ft.. These laboratories are fully equipped to carry out modern neuroanatomical studies of the primate brain. A partial list of equipment includes: five freezing, sliding microtomes (two Reichert microtomes, two Micron HM400E microtomes, and a Tetrander microtome), a vibratome, rotating platforms, cooling-heating water baths, centrifuges (Precision Scientific), three incubation-vacuum ovens (Precision Scientific), three Dialux/Laborlux microscopes (Leitz, Germany), a pipette puller (Kopf Instruments, Tujunga, CA), refrigerators, and -20°C and -70°C freezers. Common use rooms located adjacent to the laboratory house autoclaves, dish washers, ultra cold freezers and cold rooms. In addition to the lab space, five 140 sq. ft. offices, all equipped with Macintosh or PC computers with internet connections, are located adjacent to the laboratory and are used as office space for students and postdoctoral researchers.

Clinical: Clinical care and related procedures at the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see **Primate Services**).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and **Information Technology Services** provides desktop support and other related services. Biostatistics services and Biomedical Informatics support are also provided on campus and through the UC Davis CTSC. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are all available.

Office [Excluded by Requester] all occupy an office at the Primate Center. [Excluded by Requester] has an office at the MIND Institute.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

EQUIPMENT

The Childhood Health laboratory facility at the CNPRC is approximately Specific
Animal
Location and is fully equipped for endocrine and histological analysis including: Leica 3050S cryostat, shaking water baths (2), fume hood, biosafety cabinet, gamma counter, plate reader, incubators, centrifuges, and $\leq -80^{\circ}\text{C}$ (4) and $\leq -20^{\circ}\text{C}$ freezers.

Excluded by Requester

laboratory is at the MIND Institute includes: five freezing, sliding microtomes (two Reichert microtomes, two Micron HM400E microtomes, and a Tetrander microtome), a vibratome, rotating platforms, cooling-heating water baths, centrifuges (Precision Scientific), three incubation-vacuum ovens (Precision Scientific), three Dialux/Laborlux microscopes (Leitz, Germany), a pipette puller (Kopf Instruments, Tujunga, CA), refrigerators, and $\leq -20^{\circ}\text{C}$ and $\leq -80^{\circ}\text{C}$ freezers. Common use rooms located adjacent to the laboratory house autoclaves, dishwashers, ultra cold freezers, and cold rooms. Current microscopic equipment includes three Stereomicroscopes (one equipped with a Leitz digital photography system), three Dialux microscopes, one dual-headed Nikon Eclipse E600, one Nikon Eclipse E600 with a Spot digital camera, a Nikon multiphot for dark and brightfield 4X5 photomicroscopy, and a Leica DMR with infinity-corrected optics for 35 mm photomicroscopy. Our laboratory also has two computer-aided analysis systems including one Zeiss Vario microscope and one Nikon Eclipse microscope each equipped with a motorized stage and integrated with the PC-based Stereoinvestigator and Neurolucida analysis systems (MBF Bioscience, Williston VT) and one Nikon Eclipse microscope equipped with a motorized stage and integrated with the PC-based Stereoinvestigator/Neurolucida system including the Virtual Slice, MRI and Solid Modeling modules, which add the capability of performing all modern quantitative neuroanatomical analyses, such as anatomical mapping, neuron tracing, 3D-serial-section reconstruction, morphometry, image analysis, design based stereology, 3D-MRI image analysis, 3D-solid model reconstruction and the creation and analysis of high-resolution image montages. In addition, the laboratory has four MacPro and three iMAC computers connected to a variety of scanning devices including a flatbed scanner.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	20,740.00	8,272.00	29,012.00
2.					Core Scientist			0.0	0.0	18,150.00	3,957.00	22,107.00
3.					Core Scientist			0.0	0.0	15,260.00	6,086.00	21,346.00
4.					Core Scientist			0.0	0.0	11,597.00	360.00	11,957.00
5.					Core Scientist			0.0	0.0	14,397.00	5,742.00	20,139.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						104,561.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		21,461.00	11,353.00	32,814.00
1	Unit Technical Support	Excluded by Requester			26,281.00	13,903.00	40,184.00
2	TBN Core Scientists		2.4		29,841.00	9,982.00	39,823.00
4	Total Number Other Personnel				Total Other Personnel		112,821.00
					Total Salary, Wages and Fringe Benefits (A+B)		217,382.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

10,500.00

2. Foreign Travel Costs

0.00

Total Travel Cost 10,500.00**E. Participant/Trainee Support Costs**

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other:

0 Number of Participants/Trainees**Total Participant Trainee Support Costs** 0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,500.00
2. Publication Costs	7,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	10,500.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	238,382.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	238,382.00	54,113.00
Total Indirect Costs			54,113.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	292,495.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMB_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	20,948.00	8,840.00	29,788.00
2.					Core Scientist			0.0	0.0	18,150.00	4,144.00	22,294.00
3.					Core Scientist			0.0	0.0	15,412.00	6,504.00	21,916.00
4.					Core Scientist			0.0	0.0	11,712.00	363.00	12,075.00
5.					Core Scientist			0.0	0.0	14,541.00	6,136.00	20,677.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						106,750.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		21,676.00	11,990.00	33,666.00
1	Unit Technical Support	Excluded by			26,544.00	14,683.00	41,227.00
2	TBN Core Scientists	2.4			29,957.00	10,550.00	40,507.00
4	Total Number Other Personnel				Total Other Personnel		115,400.00
					Total Salary, Wages and Fringe Benefits (A+B)		222,150.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,815.00
2. Foreign Travel Costs	0.00
Total Travel Cost	10,815.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,605.00
2. Publication Costs	7,210.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	10,815.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	243,780.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	243,780.00	55,338.00
Total Indirect Costs			55,338.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	299,118.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMB_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	<div>Excluded by Requester</div>				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	20,998.00	9,173.00	30,171.00
2.					Core Scientist			0.0	0.0	18,150.00	4,280.00	22,430.00
3.					Core Scientist			0.0	0.0	15,462.00	6,754.00	22,216.00
4.					Core Scientist			0.0	0.0	11,762.00	374.00	12,136.00
5.					Core Scientist			0.0	0.0	14,591.00	6,374.00	20,965.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						107,918.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		21,726.00	12,409.00	34,135.00
Excluded by Requester	Unit Technical Support				26,594.00	15,189.00	41,783.00
2	TBN Core Scientists	2.4			30,007.00	10,928.00	40,935.00
4	Total Number Other Personnel				Total Other Personnel		116,853.00
Total Salary, Wages and Fringe Benefits (A+B)							224,771.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	11,139.00
2. Foreign Travel Costs	0.00
Total Travel Cost	11,139.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,713.00
2. Publication Costs	7,426.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	11,139.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	247,049.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	247,049.00	56,081.00
Total Indirect Costs			56,081.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	303,130.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMB_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	21,369.00	9,612.00	30,981.00
2.					Core Scientist			0.0	0.0	18,150.00	4,407.00	22,557.00
3.					Core Scientist			0.0	0.0	15,722.00	7,072.00	22,794.00
4.					Core Scientist			0.0	0.0	11,948.00	392.00	12,340.00
5.					Core Scientist			0.0	0.0	14,922.00	6,712.00	21,634.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						110,306.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			23,387.00	13,756.00	37,143.00
1	Unit Technical Support	Excluded by Requester			27,076.00	15,926.00	43,002.00
2	TBN Core Scientists	2.4			30,195.00	11,328.00	41,523.00
4	Total Number Other Personnel					Total Other Personnel	121,668.00
Total Salary, Wages and Fringe Benefits (A+B)							231,974.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

11,473.00

2. Foreign Travel Costs

0.00

Total Travel Cost 11,473.00**E. Participant/Trainee Support Costs**

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other:

0 Number of Participants/Trainees**Total Participant Trainee Support Costs** 0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,824.00
2. Publication Costs	7,649.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	11,473.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	254,920.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	254,920.00	57,867.00
Total Indirect Costs			57,867.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	312,787.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMB_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*	
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	21,582.00	10,007.00	31,589.00
2.					Core Scientist			0.0	0.0	18,150.00	4,534.00	22,684.00
3.					Core Scientist			0.0	0.0	15,880.00	7,363.00	23,243.00
4.					Core Scientist			0.0	0.0	12,067.00	408.00	12,475.00
5.					Core Scientist			0.0	0.0	16,204.00	7,513.00	23,717.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						113,708.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		24,155.00	14,638.00	38,793.00
1	Unit Technical Support	Excluded by Requester			30,744.00	18,631.00	49,375.00
2	TBN Core Scientists		2.4		30,727.00	11,866.00	42,593.00
4	Total Number Other Personnel				Total Other Personnel		130,761.00
					Total Salary, Wages and Fringe Benefits (A+B)		244,469.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	11,817.00
2. Foreign Travel Costs	0.00
Total Travel Cost	11,817.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,939.00
2. Publication Costs	7,878.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	11,817.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	268,103.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	268,103.00	60,860.00
Total Indirect Costs			60,860.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	328,963.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: BMB_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by R equester	Core Scientist, Unit Leader	% Effort			
	Core Scientist				
	Core Scientist				
	Core Scientist				
	Core Scientist				
TBN	Core Scientist	10	0	90	100
TBN	Core Scientist	10	0	90	100
Excluded by R equester	Administrative Assistant	% Effort			
	Unit Safety Coordinator				

TBN=to-be-named

Excluded by R equester **PhD, Core Scientist and Unit Leader** EFFOR T months % Effort Excluded by is Professor and Vice Chair, Department of Psychology, College of Letters and Sciences. Her research interests are in the field of behavioral neuroendocrinology. Specifically, she studies the hormones oxytocin and vasopressin, and how they are related to the formation and maintenance of social bonds. She examines this question in a developmental and a comparative fashion, using both rodent (prairie vole) and primate (titi and rhesus monkey) models.

Excluded by R equester **PhD, Core Scientist** EFFOR T months % Effort Excluded by R equester is Distinguished Professor of Psychiatry and Behavioral Sciences, School of Medicine, and the Research Director of the UC Davis MIND Institute. Excluded by was trained as a neuroscientist and psychologist. His research involves studies of the structure and function of the hippocampal formation and amygdaloid complex in the nonhuman primate model and in humans. For the last 18 years he has also carried out behavioral studies in the rhesus monkey, with a focus on analyses of the "social brain", and studied the monkey model of autism.

Excluded by R equester **PhD, Core Scientist** EFFOR T months % Effort Excluded by Requester is Research Professor, Department of Psychology, College of Letters and Sciences. Excluded by Requester research program is focused on the causes and consequences of individual differences in biobehavioral organization, a term that encompasses temperament, hypothalamic-pituitary-adrenal (HPA) regulation, and emotionality. He developed the BioBehavioral Assessment (BBA) Program which is based on more than three decades of psychobiological research documenting the existence of stable, individual differences in patterns of adaptation to the environment. Excluded by Requester is a member of the Behavioral Research Services Core where he oversee the BBA services.

Excluded by R equester **PhD, Core Scientist** EFFOR T months % Effort Excluded by Requester is Professor Emeritus, Department of Psychology, College of Letters and Sciences. Excluded by Requester is interested in primate biobehavioral development, and has been studying this phenomenon throughout his career. He has been a collaborator on the BBA project since its inception in 2001. He focuses on the examination of the role of prenatal experience, as well as of the role of different early experiences on biobehavioral outcomes.

Excluded by R equester **PhD, Core Scientist** EFFOR T months % Effort Excluded by R equester is Professor, Department of Population Health and Reproduction, School of Veterinary Medicine. Her research program focuses on the large matrilineal social groups of rhesus macaques unique to the CNPRC as well as captive and wild macaque groups in both Europe and Asia. Patterns of health and well-being within human and animal societies and across different multispecies communities represent emergent global patterns whose underlying dynamics must be understood to better tackle complex health issues. She is the lead for the Behavior

Management Services in Primate Services and she leads the cooperative training and management services in the Behavioral Research Services Core.

TBN Core Scientists (2) (1.2 calendar months – 10% each Core Scientist). The commitment of the Provost and respective Dean's of the Schools of Medicine and Veterinary Medicine, and the Colleges of Biological Sciences, Engineering, and Letters and Sciences (see **Overview**) to new faculty positions includes two Unit Core Scientist positions (see Research Strategy). One of the new faculty recruitments is proposed at the junior investigator level and one with a more established research program.

Excluded by Requester	Administrative Assistant	EFFORT	months	% Effort	Excluded by Requester	provides administrative support for CNPRC-related activities and programs.
Excluded by Requester	Unit Safety Coordinator	EFFORT	months	% Effort	Excluded by Requester	serves as the Unit Safety Coordinator, provides assistance in the training of staff and students, coordinates and prepares sample shipments to investigators, and maintains the required documentation associated with these activities.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None requested

TRAVEL

\$10,500 total is requested for each Core Scientist to attend a national meeting in their respective area(s) of expertise (7 x \$1,500).

SUPPLIES

\$3,500 in general supplies is requested to support activities with new investigators and sharing of resources.

OTHER EXPENSES

\$7,000 is requested for manuscript preparation and submission (7 x \$1,000).

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		543,243.00
Section B, Other Personnel		597,503.00
Total Number Other Personnel	20	
Total Salary, Wages and Fringe Benefits (A+B)		1,140,746.00
Section C, Equipment		0.00
Section D, Travel		55,744.00
1. Domestic	55,744.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		55,744.00
1. Materials and Supplies	18,581.00	
2. Publication Costs	37,163.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,252,234.00
Section H, Indirect Costs		284,259.00
Section I, Total Direct and Indirect Costs (G + H)		1,536,493.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

BMB_SpecificAims.pdf

3. Research Strategy*

BMB_ResearchStrategy.pdf

4. Progress Report Publication List

BMB_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

BMB_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

BMB_lettersofsupport.pdf

13. Resource Sharing Plan(s)

BMB_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

SPECIFIC AIMS

The Brain, Mind, and Behavior Research Unit specializes in research on sociality, temperament, and development, with a true lifespan approach – utilizing measures from prenatal life to aged animals, including multiple time points in many studies. Increasingly, research is translational in nature with the development of many new primate models of human psychiatric disease. Core Scientists head vibrant individual research agendas that contribute to the training of a very large number of undergraduates, graduate students, postdoctoral trainees, visiting students, and visiting scientists of many different levels. Our Core Scientists also contribute significant service to the California National Primate Research Center (CNPRC) through administrative positions, and committee memberships. The Research Unit also facilitates significant research programs by outside investigators, especially those interested in working in behavioral neuroscience with aged monkeys; those working with field cage monkeys; and those interested in working with the titi monkey colony. Unit Specific Aims for the next funding period include:

Specific Aim 1. Advance the CNPRC resource through scientific contributions directed at understanding normal and abnormal function, and at developing interventions to remediate abnormal function, at the levels of brain, mind, and behavior (both individual and social behavior).

Plan. In pursuit of this Specific Aim, we will conduct mechanistic and interventional studies using the nonhuman primate as a laboratory animal model for human neural systems, psychopathologies, and behavioral abnormalities; contribute towards the understanding of lifespan health by investigating the role of chronologic age in the structure and function of brain, mind, and behavior; develop nonhuman primate models of neurological and psychiatric disorders such as autism and schizophrenia with the goal of more rapidly advancing therapeutic interventions for human patients; continue to explore the role of brain, mind, and behavior on other physiological systems within the organism; and advance next generation technologies for molecular modification of the functioning primate brain.

Specific Aim 2. Contribute unique expertise and service towards utilization of the CNPRC resources at both regional and national levels.

Plan. The Unit will provide technological and collaborative expertise for the investigation of structure and function of brain, mind, and behavior through collaborations and support of affiliate research; through development of methodologies using the nonhuman primate as a laboratory animal model; and through serving as a biological specimen repository for catalogued nonhuman primate samples (behavioral and tissue) obtained through NIH funded studies in brain, mind, and behavior.

Specific Aim 3. Train and mentor the next generation of nonhuman primate scientists in research focusing on the brain, mind, and behavior.

Plan. The Unit will provide training and mentoring opportunities for undergraduates, graduate students, postdoctoral fellows, visiting students, and junior investigators through a variety of opportunities. These include involvement of students receiving research credit in cutting-edge research on brain, mind, and behavior including social network theory, biobehavioral assessments, and work with the outdoor rhesus and titi monkey colonies. We will also continue a formal internship program with Brigham Young University students as well as opportunities for visiting students and scientists.

Specific Aim 4. Enhancement of CNPRC colony resources.

Plan. The Unit will provide expertise on rhesus and titi monkey behavior and physiology to enhance their well-being, behavioral management, and continued colony success. Core Scientists will continue to enhance the CNPRC rhesus monkey colony resource by obtaining and making available new data on naturally occurring variation in social roles in a marker of inflammation.

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

RESEARCH STRATEGY

INTRODUCTION

The Brain, Mind, and Behavior (BMB) Research Unit specializes in research on sociality, temperament, and development, with a true lifespan approach – utilizing measures from prenatal life to aged animals, including multiple time points in many studies. Increasingly, research is translational in nature with the development of many new primate models of human psychiatric disease and a focus on interventions. Core Scientists head vibrant individual research agendas that contribute to the training of a very large number of undergraduate students,

graduate students, postdoctoral trainees, visiting students, and visiting scientists of many different levels. Our Core Scientists also contribute significant service to the CNPRC through administrative positions and committee memberships. Research Unit Core Scientists facilitate significant research programs by external investigators, making the BMB Unit a truly national resource. These investigators include large, well-funded groups working in behavioral neuroscience with aged monkeys (University of Arizona, Excluded by Requester, Mount Sinai); and those working in spinal cord regeneration (UC San Diego). The Unit also facilitates the needs of investigators interested in the study of field cage monkeys, and those interested in working with the titi monkey colony.

Figure 1. Organizational Chart: Brain, Mind, and Behavior

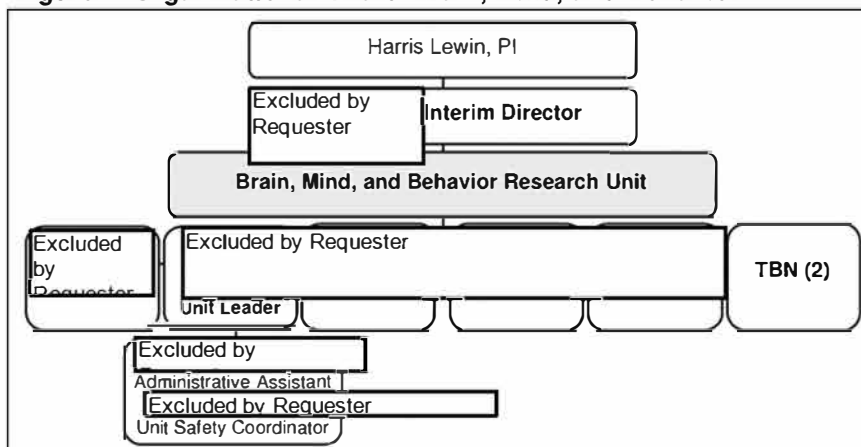


Table 1. Brain, Mind, and Behavior Research Unit Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Psychology, College of Letters and Sciences	• Core Scientist, Unit Leader • Colony Management Committee
	Department of Psychiatry and Behavior Sciences, School of Medicine	• Core Scientist • Team member of a UC Davis RISE project
	Department of Psychology, College of Letters and Sciences	• Core Scientist • Behavior Research Services Core • Lead, Analytical and Resource Core (to 2013) • Associate Director for Research (to 2011)
	Department of Psychology, College of Letters and Sciences	• Core Scientist • Colony Management Committee
	Department of Population Health and Reproduction, School of Veterinary Medicine	• Core Scientist • Lead, Behavior Management Services • Lead, Behavior Research Services Core
TBN (2)	Based on joint recruitments	Core Scientists
Excluded by Requester	CNPRC	Administrative Assistant
	CNPRC	Unit Safety Coordinator

RISE=Research Investments in Science and Engineering; TBN=to-be-named

Table 2 shows the support for the BMB Unit per the FOA. A small component of salary is supported on the P51 base grant (see budget justification), and represents the commitment to the mission, outreach, and services. Extramural grant funding is shown in Table 3, below.

Table 2. Support for the Brain, Mind, and Behavior Research Unit (does not include research grants per FOA. See Unit grant funding Table 3, below)

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$216,079	\$238,302
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$216,079	\$238,302

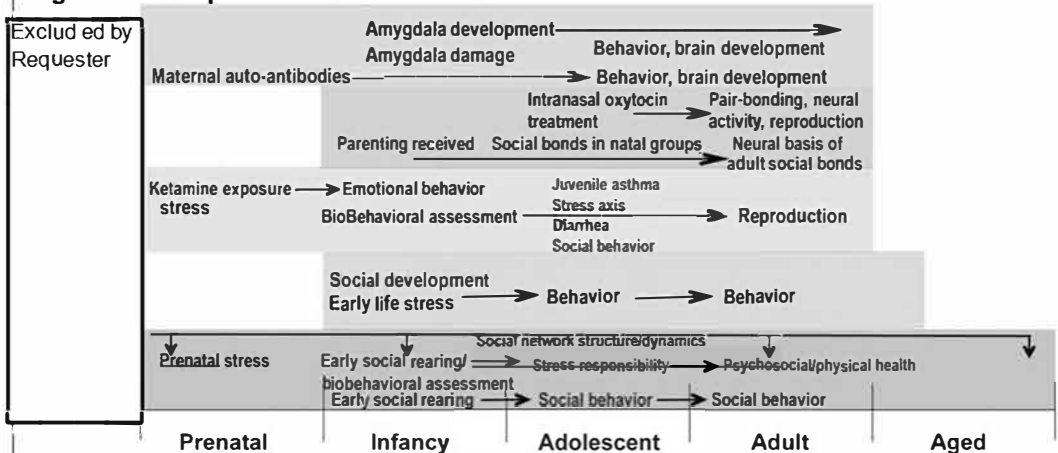
reviewers' comments

Response to Summary Statement.

reviewers' comments

SIGNIFICANCE

The BMB Unit currently consists of five Core Scientists, all of which are addressing aspects of behavior relevant to lifespan health. Specifically Unit research programs focus on animal models of neurodevelopmental disorders, the role of individual differences throughout the lifespan, and social network theory applied to the advancement of human and animal health

Figure 2. Lifespan health research in the BMB Unit

(Figure 2). In addition, the Unit supports the research of many national investigators (Unit Affiliates

Excluded by Requester

who carry out extensive research programs, particularly in aging monkeys. Major areas of expertise include:

- 1. Animal Models of Neurodevelopmental Disorders.** A major research focus area in the Unit is neurodevelopmental disorders, particularly disorders including social deficits, such as autism. The effects of social development on lifespan health has been a central theme of the BMB Unit from its inception by Dr. [Excluded by Requester] whose early work on attachment in monkeys, and its effects on later behavior, was central to the field. All of the current Unit members work on some aspect of sociality and its relationship to whole body health and physiology. The translational potential of this work is increased by the research performed

Excluded by Requester

in Core Scientists' laboratories – including human subjects research by [Excluded by Requester] rodent research by Dr. [Excluded by Requester] and collaborations by all Unit members [Excluded by Requester] serves as MIND Institute Director of Research at the (focuses on human developmental disorders), accelerating the translation of this research to the clinic.

In addition to focusing on lifespan health (Figure 2), the BMB Unit Core and Affiliate Scientists emphasize research on interventions. Examples include findings that chronic intranasal oxytocin, currently in clinical trials for children with autism, may have long-term, potentially detrimental effects on social behavior; however, these effects appear to depend on the developmental stage at administration [Excluded by Requester] Current ongoing studies by Unit Affiliates [Excluded by Requester] (in collaboration with [Excluded by Requester] Reproductive Sciences and Regenerative Medicine Unit) are looking at the “critical window hypothesis” in a monkey model, providing an experimental test of the idea that efficacy of estrogen treatment is impacted by timing post-menopause. These monkey data directly inform clinicians researching hormone effects on cognition in women as well as decisions by physicians to recommend (or not) post-menopausal hormone therapy. In addition, Unit Affiliates are also investigating the efficacy of a cyclooxygenase inhibitor to reduce depressive responses to social loss [Excluded by Requester] the role of embryonic stem cells and induced neural progenitors in spinal cord injury repair [Excluded by Requester] and use of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) to increase neuronal survival and improve memory and executive functioning in a monkey model of Alzheimer's Disease [Excluded by Requester]

The BMB Unit utilizes, and facilitates the use of, several unique resources for the study of social development and neurodevelopmental disorders. A small titi monkey (*Callicebus cupreus*) colony (~86

Figure 3. Titi monkey family with infant carried by father.



animals) located at the CNPRC is a perfect example of a unique primate resource – it is the only laboratory colony of these monkeys in the world (Figure 3). While *Callicebus cupreus* are not considered endangered,

they are a CITES Appendix II species in which trade is closely controlled. The CNPRC is thus the only readily available source for this species for researchers. Because of their strong monogamous pair-bonds, titi monkeys are an ideal primate model for the neurobiology of social bonds and are used as such in research by [Excluded by Requester] While this colony is currently supported by two R01s (one to [Excluded by Requester] the other [Excluded by Requester] collaborators from the MIND Institute and University of Minnesota), plans for expanding the investigators utilizing the colony is detailed under the Future Directions section, below.



Another unique resource in the BMB Unit is the half-acre field cages containing large, stable social groups of rhesus monkeys (Figure 4). These groups are well-characterized by our **Behavior Management Services** team (see **Primate Services**), by our BioBehavioral Assessment (BBA) Program (see below), and are utilized by the individual research programs of several BMB Core Scientists. These data have been leveraged to support the research of new Affiliate Scientists such as [Excluded by Requester]

Figure 4. Rhesus monkeys in outdoor social groups.

2. Role of Individual Differences throughout the Lifespan. The development of the field of personalized medicine has brought the idea of individual differences to the forefront. The BBA Program is a resource unique to the NRC system. **(Note that this is a research program distinguished from the Behavior Research Services Core, which is a fee-for-service Core that offers assessment capability).** The program is based on more than three decades of psychobiological research documenting the existence of stable, individual differences in patterns of adaptation to the environment, referred to as biobehavioral organization (encompassing a variety of related processes including emotionality, temperament, and behavioral and physiological reactivity). Different patterns of biobehavioral organization are detectable at an early age and are remarkably persistent across the lifespan. In primate colonies, such differences arise naturally, as well as from specific husbandry practices. The BBA Program involves quantification of individual differences in biobehavioral organization, and since its inception in 2001, more than 3,800 animals have been assessed. Data are made available on the internal CNPRC website, and data sets are available from [Excluded by Requester] (PI, R24-OD010962). Data have been used (1) to better understand colony-

strategy

relevant outcomes (papers are published or in preparation showing how biobehavioral organization is related to display of abnormal behavior, prevalence of diarrhea, ease of learning through positive and negative reinforcement, and reproductive outcomes); (2) to demonstrate how maternal, environmental, and genetic factors, as well as routine colony management practices, separately and together, affect variation in biobehavioral organization (e.g., nursery-rearing, prenatal exposure to ketamine, polymorphisms for specific candidate genes, birth timing, degree of Chinese ancestry, energy content of mother's milk); and (3) for animal selection and for hypothesis testing by both internal and external scientists – for example, in the current funding period, 69 separate datasets were provided to 34 individuals. Recipients of these datasets included scientists, postdoctoral fellows, and graduate and undergraduate students from multiple institutions across the U.S. Also during this period, the BBA Program was a component of 38 proposals (21 funded, 1 under review) including CNPRC Pilot Projects, Foundation grants, and NIH grant applications to multiple institutes or centers (NHLBI, NIAAA, NICHD, NIDA, NIEHS, NIMH, NCRR, OD). The focus of these grants covered a broad range, in terms of both scientific questions, and in terms of the subject age; while the BBA Program assesses animals in the infancy period, data are used to identify temperament patterns that are linked to behavioral and health outcomes at later ages – funded projects have examined asthma in juveniles, social motivation in young adults, and preterm labor in adult females. Examples of funded projects that used BBA data are noted with an asterisk in the funded grant table at the end of this section.

3. Social Network Theory Applied to the Advancement of Human and Animal Health. A new focus of the Unit includes using the tool of social network theory to advance human and animal health. Rhesus monkeys have complex hierarchical family-structured social networks that are analogous to human social structures and thus can be used as a translational model for the importance of the social environment on a variety of health outcomes in humans. A recent publication [2014] discusses the use of novel network analysis techniques to decipher monkey societal collapse as a model for investigating systemic risk assessment in financial and other human societal systems. The idea is that one can use these new computational network approaches to predict and prevent systemic collapse at multiple organizational levels in social and other biological systems and the effects of social or biological instability on health outcomes. Another significant finding is that dominance or status uncertainty is more important than absolute rank in influencing negative health outcomes in rhesus macaques. This finding suggests that the certainty of ones' relationships within and across socioeconomic classes, rather than socioeconomic class alone (low, middle, high income; e.g., rank), may be predictive of positive or negative health in human societies. Future directions of this program will be to continue the multi-level multi-disciplinary study of socioecological effects on health and well-being in the macaque as a translational model for humans as well as to enhance the welfare of captive and wild macaques world-wide. This includes expansion of current studies on how social networks influence infant development and the inclusion of brain structure and function as both a health outcome and as predictors of other health metrics.

Progress and Major Accomplishments: Contributions to the CNPRC Mission

The BMB Unit continues to be at the forefront of behavior and neuroscience research, as demonstrated by the Unit publication and funding record. During the current reporting period (May 1, 2010 through April 30, 2014), BMB Core and Affiliate Scientists published 131 articles in peer-review journals and garnered a total of \$28.3 million in extramural funds (Table 3). BMB Research Unit Core Scientists support the role of the CNPRC as a resource by our Affiliate program (Figure 5), our facilitation of access to data and tissue by outside investigators, and other CNPRC services.

Table 3. Extramural Funding for the BMB Unit (May 1, 2010 to April 30, 2014)

May 2010 - April 2011	May 2011 - April 2012	May 2012 - April 2013	May 2013 - April 2014	TOTAL*
\$7,077,905	\$6,346,358	\$7,503,281	\$7,408,565	\$28,336,109*

*Does not include currently funded grants May 1, 2014 to April 30, 2015, to date, of \$6,280,952

Affiliate Scientists and the BMB Unit. A major focus of the BMB Core Scientists is the facilitation of research by Affiliates. Affiliate Scientists may identify research opportunities at the CNPRC through interactions with Core Scientists at conferences and in other venues; through identification of research resources on our website; and through applications to the CNPRC pilot program (see below). Core Scientists then work with Affiliates for preparation of animal protocols and for applications for grant funding. In some cases, these associations are true collaborations (see Table 4). In other cases, the Core Scientist facilitates the Affiliate's research as a service to the CNPRC, including supervision of on-site personnel, animals, and study conduct.

Table 4. Affiliates, Publications with Affiliates, and Grants led by Affiliate Scientists (May 1, 2014-April 30, 2014)

Institution	Number of Affiliates	Total Publications	Total Grant Funding (\$)
CNPRC	23	26	3,044,265
UC Davis	27	17	2,893,516
Outside UC Davis	28	56	11,768,045
TOTAL	78	99	\$17,705,826

The BMB Unit has many active Affiliates across UC Davis. For instance, [Excluded by Requester] research (MIND Institute) has produced a monkey model of maternal autoimmunity which shows symptoms (behavioral,

[Excluded by Requester]

neural, and in eye-tracking) similar to those in human autism and schizophrenia. She plans to use positron emission tomography (PET) imaging data to develop novel diagnostic biomarkers and targeted treatments for schizophrenia. In addition, she has an R21 to evaluate a potentially neuroprotective compound in monkeys.

[Excluded by Requester]

research (Affiliate Scientist) on iron deficiency in monkey models led to a clinical study that supported the specific finding of lengthened red blood cell half-life associated with prenatal iron deficiency [et al., 2014].

[Excluded by Requester]

Figure 5. BMB Unit Core Scientists maintain a large number of collaborations throughout the UC Davis campus, and the world. In this social network analysis the size of the nodes represents the number of collaborations for each Core Scientist, and the width of the line represents the number of collaborations with other scientists. Green=CA, blue=national, red=international

The I-CAN SZ (Interdisciplinary Collaborative Analysis of Neuroimmune-based Schizophrenia) program is led by Affiliate Scientists [Excluded by Requester] Center for Neuroscience, and includes Core Scientists [Excluded by Requester] and [Excluded by Requester] Reproductive Sciences and Regenerative Medicine Research Unit), and Affiliate Scientist [Excluded by Requester]

[Excluded by Requester] brings together eight research groups. The program tests the idea that maternal infection during pregnancy contributes to the development of SZ, a disabling brain disorder that affects 1% of the population by altering immune molecules in the brains of offspring, resulting in changes in cellular connections. This is the first study to characterize changes in immune responses, brain inflammation, brain anatomy, and behaviors simultaneously in high-risk individuals as well as in two nonhuman model systems. This RISE program (see **Overview**) highlights ongoing efforts on brain disorders.

As noted, the Pilot Program is a useful tool for recruitment of new scientists interested in initiating research at the CNPRC. The application and review process is described elsewhere (see **Pilot Research Program**); it is important to note that each project requires the guidance and participation of a Core Scientist (Table 5).

Table 5. P51 Pilot Research Projects in the BMB Unit

Recipient	Dates	P51 Type	Title of Project	Outcomes
[Excluded by Requester]	2009-2011	Supplement Postdoctoral	Epigenetic Risk Following Early Life Stress in Infant Macaques	<ul style="list-style-type: none"> • NIH R03 • 2011 Janssen Fellowship in Translational Neuroscience
	2010-2012	Supplement Postdoctoral	Neural Correlates of Social Buffering in Juvenile Rhesus Macaques: Friends vs. Familiar Companions	<ul style="list-style-type: none"> • Private foundation funding [Excluded by Requester]
	2011-2012	Pilot Program	A Nonhuman Primate Model for Autism Spectrum Disorder Treatment Recovery	<ul style="list-style-type: none"> • Publication in progress
	2012-2013	Pilot Program	The Role of Oxytocin Biology in Primate Social Impairments	<ul style="list-style-type: none"> • NIH R21 • SFARI Pilot Award
	2013-2014	Pilot Program	Role of Oxytocin Signaling in the Amelioration of Diet-Induced Obesity in Nonhuman Primates	In progress

Facilitating Access to Data and Tissue Samples. BMB Core Scientists responded to many requests for data and tissue samples during the current funding period. The BBA Program filled 34 requests, while BMB investigators also filled two requests for rhesus brain tissue and seven requests for titi monkey tissue and blood samples.

Training and Mentoring. The BMB program is extremely active in training and mentoring at all levels (Figure 6). Undergraduates in particular are heavily recruited, usually from classes taught by Core Scientists (Table 6). These undergraduates are primarily from Psychology; Animal Biology; and Neurobiology, Physiology, and Behavior, and they receive course credit for their participation in BMB research programs. Active research is balanced with laboratory meetings and journal clubs where they obtain the theoretical basis for their internship.

Figure 6. BMB Unit trainees during 2010-2014.

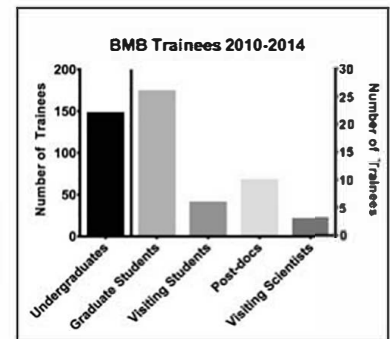


Table 6. Outcome Measures for 147 BMB Unit Undergraduates (21 under-represented minorities)

Current Undergraduate	Graduate School	Professional School	Employment	Internships / Volunteer	Lost to Follow-up
54	18	16	20	4	35

During the prior funding period, [Excluded by Requester] served as the facilitators for a yearly summer internship program associated with [Excluded by Requester] of Brigham Young University (BYU). BYU supports approximately 8 students every summer for internships in the BMB Unit for a 2-month period. During that time, the interns work in multiple laboratories and learn skills including behavioral observation, sample collection, and tissue slicing. Each summer the BMB Unit organizes a research seminar series – originally for these students – but open to others as well – which has become very well attended by faculty, students, and staff from throughout the CNPRC. This program has resulted in numerous research presentations by the students at scientific conferences, as well as publications [Excluded by Requester] et al., 2014).

All BMB Core Scientists also participate in one or more graduate groups on the UC Davis campus [Excluded by Requester]. [Excluded by Requester] Animal Behavior, Neuroscience, Psychiatry and Behavioral Sciences [Excluded by Requester] Animal Behavior and Psychology; [Excluded by Requester] Psychology; [Excluded by Requester] Psychology; [Excluded by Requester] Animal Behavior, Ecology, Anthropology, Animal Biology, Preventive Veterinary Medicine). Graduate students from the BMB Unit have distinguished themselves in recent years, winning many nationally competitive fellowships and dissertation awards. Graduating BMB students from the last five years have gone on to postdoctoral positions at Columbia University, UCLA, and OHSU, among others; more advanced graduates hold faculty positions at University of Arizona, Cambridge University, Bucknell University, University of Pennsylvania, and Virginia Institute of Technology. Unit postdoctoral fellows have been similarly successful. Recently [Excluded by Requester] (laboratory) was awarded a K99 Career Transition Award from NIH and [Excluded by Requester] (laboratory) is now a tenure-track assistant professor at Harvard University.

Enhancement of Colony Resources. BMB Core Scientists serve the CNPRC in many other capacities that enhance both the animal colonies and the CNPRC as a national resource [Excluded by Requester] leads **Behavior Management Services** at the CNPRC (see **Primate Services**), while [Excluded by Requester] (who served as Associate Director for Research until 2011) was the head of the Analytical and Resource Core until late 2013, and is a current member of the **Behavior Research Services Core**. The Core offers behavioral phenotyping services, positive reinforcement training, and assessments similar to those in the BBA Program, on a recharge basis. [Excluded by Requester] is the Unit Leader for BMB and represents BMB on the Research Advisory Committee in her role as Unit Leader.

In the current funding period, BMB Core Scientists were also members of many standing and ad hoc committees at the CNPRC, for instance [Excluded by Requester] serve on the Colony Management Committee [Excluded by Requester] participated in search committees for both the senior and associate veterinarian positions; [Excluded by Requester] served as chair of the Academic Personnel committee at the CNPRC, as well as a member of the search committee for the Information Technology Services Assistant Director [Excluded by Requester] is a team member of a multidisciplinary campus RISE initiative. Finally, all BMB Core Scientists are active in their home departments, in service to their college or school and at the University level, and in service to their fields.

INNOVATION

BMB has advanced innovation in several areas:

- **Technological innovation.** The BMB Unit has piloted techniques including reversible neural lesioning, advances in sophisticated, non-invasive eye-tracking technology, and development of a robotic device to assess impaired hand function. Many research programs use non-invasive imaging (microPET, MRI).
- **Innovation in the field of individual differences/personalized medicine.** The use of natural variation in the large field cage populations to study the effects of temperament on health including asthma, SIV infection, and chronic diarrhea.
- **Innovation in treatments.** Studies in titi monkeys are examining the long-term effects of intranasal oxytocin in humans; long-term results from clinical trials with autism will not be known for years. Studies have also resulted in improved immunosuppressive treatments for monkeys with stem cell grafts. Other interventions developed in the BMB Unit include a cyclooxygenase inhibitor to reduce depressive responses to social loss injury, the role of both embryonic stem cells and induced neural progenitor cells in repair of spinal cord injury, and the use of neurotrophic factors such as NGF and BDNF to increase neuronal survival as well as improve memory and executive functioning in Alzheimer's Disease.
- **Innovation in monkey models.** BMB Core Scientists, in collaboration with other CNPRC Core Scientists and outside Affiliate Scientists, have developed monkey models for autism, loneliness, spinal cord injury, and the effects of temperament on asthma, preterm labor, and response to social loss.
- **Innovation in social network theory.** Core Scientists used social network theory in innovative ways, including using primate social systems as a model for banking collapse, and investigating the dynamics of rhesus monkey social systems in relationship to biomarkers of stress and other health outcomes.

APPROACH

Plans for the Next Funding Period

Going forward, the BMB Unit will continue to support the Specific Aims of **Research Excellence** and **Resource Enhancement** within our specific spheres of excellence, which include the study of lifespan health, with a focus on neurodevelopment, individual differences, and social network theory. Key to advances in these areas will be the recruitment of additional junior faculty, as well as further development of the value of our research resources such as the titi monkey colony and rhesus monkeys in the field cages.

Specific Aim 1. Research excellence.

The BMB Unit has a hiring plan which includes the following two positions, in order of importance:

- **Primate Behavioral Genetics and Epigenetics.** This is a critical position for expansion of BMB research into important new scientific areas. The candidate would have an appointment in the Biological Psychology area of the Psychology department. This scientist will strengthen links between the Psychology department and the CNPRC, and would contribute to generate a critical mass for behavioral genetics and epigenetics in Psychology, providing opportunities for program project or training grant submissions.
- **Social Neuroscience.** There is growing interest in understanding how components of the social environment get "under the skin" to affect behavior and health. A new Core Scientist in this position would strengthen the existing focus on social neuroscience within the BMB Unit, and could help replace some of the scientific and collaborative expertise of [Excluded by Requester]. Possibilities include the departments of Psychiatry or Psychology.

Specific Aim 2. Contribute unique expertise and service.

BBA Program [Excluded by Requester] has applied for an NIH renewal of the BBA Program, which will continue to enhance the value of the field cage resource, and attract biobehavioral researchers from across the U.S. The program provides behavioral and neuroendocrine characterization of the majority of the infants born at the CNPRC in the field cages. One goal for the next funding period for this R24-supported program is to include a measure of inflammation (e.g., C-reactive protein, measured by the Clinical Pathology Laboratory in the **Anatomic and Clinical Pathology Services**), to provide new data which will be pertinent to immune- and health-related outcomes, and likely make this resource attractive to individuals studying infectious disease.

Titi Monkey Colony. A goal for the next funding period is to increase the multi-user base of the titi monkey colony. The **CNPRC Pilot Program** provides opportunities to attract PIs to work with this species. One such collaboration, with [Excluded by Requester] from the University of Washington, is already planned.

Technological Innovations to Advance Neuroscience. Recently, Core Scientist [Excluded by Requester] and his team have developed advanced technologies for carrying out behavioral neuroscience. With colleagues from the University of North Carolina [Excluded by Requester] team is the first to employ Designer Receptors Exclusively Activated by Designer Drugs (DREADDs). Using an adeno-associated viral vector, the gene for the DREADDs can be introduced into any brain system and the receptor is produced and inserted into neuronal membranes. When

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Requester

the agonist clonazapine-N-oxide is introduced (either through intravenous or oral administration), the receptors are activated and the transfected neurons are either inhibited or activated depending on the form of the DREADD. With R21 funding [Excluded by Requester] is investigating the effectiveness and behavioral consequences of this technique for transiently inactivating structures such as the amygdala or hippocampus.

Specific Aim 3. Training and mentoring.

The BMB Unit provides hands-on scientific training to large numbers of undergraduates, graduate students, visiting students, and postdoctoral fellows. In the next funding period, the BMB Unit plans to:

- **Additional post-training assessments.** While students in the BYU internship program currently present final reports for their internship, we plan to request these from all students participating in BMB research. In addition, we will develop a standardized form such as those used for more formal course evaluations.
- **Mentoring of new faculty.** It has been some years since the Unit has had junior faculty, and we plan to add several during the next five-year period. UC Davis has an NSF ADVANCE program that provides an excellent model of formal mentoring for new faculty. A LAUNCH committee includes the new faculty member, the department chair, a senior person whose field is related within the department, a senior person whose field is related outside the department, and a committee convener, who schedules and leads meetings, and ensures they are on track. Here, we would include members from the CNPRC and the home department.

Specific Aim 4. Enhancement of Animal Colonies.

The BMB Unit currently contributes to enhancement of the animal colonies through active participation in colony management activities (participation in committees; providing rank information on the outdoor field cages), involvement in the **Behavior Management Services**, and providing expertise on behavior. Dr.

Excluded by
Requester

[Excluded by Requester] will continue to be at the forefront of use of evidence-based management practices and techniques which lend themselves to enhanced well-being, such as positive reinforcement training. For example, Dr.

Excluded by
Requester

[Excluded by Requester] will collaborate with [Excluded by Requester] on a study investigating indoor-housed rhesus macaque pairing and the effect of pairing status changes on research outcomes, as well as a study investigating the influence of subject personality on animal training for research projects. [Excluded by Requester] is also planning a new project, using a social network approach, investigating how the complex interplay between developing systems within an individual and the social environment impacts biomarkers of health outcomes.

Summary: The BMB Unit is a thriving Unit with a strong focus on lifespan health and interventions. The Core Scientists have a history of excellence in publications and grant funding, and support large programs by Affiliate Scientists. In addition, they provide significant training opportunities, especially to undergraduates. Plans for the next five years will further enhance the resources available within the Unit.

CORE SCIENTIST NARRATIVES

Core Scientist: [Excluded by Requester] PhD, Distinguished Professor of Psychiatry and Behavioral Sciences, School of Medicine; Director of Research, UC Davis MIND Institute

Research Program: [Excluded by Requester] laboratory pursues research programs dealing with the neurobiology of primate social behavior and emotion and with the development and neuroanatomical organization of the primate and human amygdala and hippocampal formation. He has also carried out a longstanding program designed to understand the organization of brain regions involved in memory. Since becoming Research Director of the MIND Institute, his research with nonhuman primates has become increasingly translational. Over the last 10 years he has fostered efforts to establish nonhuman primate models of autism spectrum disorder and schizophrenia. Both of these models explore neuroimmune interactions in the etiology of psychiatric disorders. For autism, [Excluded by Requester] and colleagues have examined whether unusual brain-directed antibodies found in a substantial proportion of mothers of children with autism may be pathogenic. Pregnant rhesus monkeys are treated with purified IgG antibodies derived from mothers of children with autism or mothers of typically developing children. As Research Director of the MIND Institute, he is currently coordinating a comprehensive and multidisciplinary analysis of children with autism called the Autism Phenome Project to define biomedical characteristics of different types of autism. This research with children with autism has informed his translational attempts at developing promising primate models of the disorder.

Contributions to the CNPRC Mission: [Excluded by Requester] has been a CNPRC collaborator on a multidisciplinary campus RISE initiative which is led by Affiliate Scientist [Excluded by Requester] recently completed a collaborative NIH Blueprint project with scientists at the Allen Brain Institute that evaluated gene expression in the developing rhesus monkey brain. [Excluded by Requester] has 33 publications (May 1, 2010 to April 30, 2014).

Table 7. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Neurobehavioral Relationships in Senescent Hippocampus	Collaborator
	Autism studies	Collaborator

Core Scientist: Excluded by Requester PhD, Professor and Vice-Chair of the Department of Psychology, College of Letters and Sciences, and Unit Leader of the Brain, Mind, and Behavior Research Unit

Research Program: Excluded by Requester research program focuses on the neurobiology of social behavior, and how human manipulations of the hormone oxytocin (OT) may affect the long-term ability to form social bonds. In addition, she studies the ways in which OT and the closely related hormone arginine vasopressin (AVP) subserve these social bonds. In studies of OT and AVP, she works with two socially monogamous species, prairie voles (*Microtus ochrogaster*) and titi monkeys (*Callicebus cupreus*). Studying socially monogamous species allows for the examination of strong social attachments in adult males, as well as male parenting, which are not behaviors typically observed in other common biomedical models such as rats, mice, and rhesus monkeys. Current research, which is funded by two R01s and a grant from a private foundation, has two main foci. The first R01 has examined the development of titi monkeys as a nonhuman primate model for the neurobiology of social bonding. The second R01 focuses on the effects of exposure to chronic intranasal OT in prairie voles, titi monkeys, and BTBR mice.

Contributions to the CNPRC Mission: Unit Leader; CNPRC Research Advisory Committee and Colony Management Committee; Scientific Manager of Titi Monkey Colony; Co-host for BYU intern program; President, American Society of Primatologists (ASP); Associate Editor, American Journal of Primatology; Host, 2012 meeting of ASP. Excluded by Requester has 11 *primate* publications (May 1, 2010 to April 30, 2014).

Table 8. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Neurobehavioral Relationships in Senescent Hippocampus	Core Scientist for grants
	Role of Oxytocin Signaling in the Amelioration of Diet-Induced Obesity in Nonhuman Primates	Core Scientist for pilot, collaborator, co-author on meeting abstract
	Estrogen and the Aging Brain	Core Scientist for grants

Core Scientist: Excluded by Requester PhD, Research Psychologist, Department of Psychology, College of Letters and Sciences, and Behavior Research Services Core

Research Program: Excluded by Requester research program is focused on the causes and consequences of individual differences in biobehavioral organization, a term that encompasses temperament, hypothalamic-pituitary-adrenal (HPA) regulation, and emotionality. This interest stems from two overlapping perspectives. The first is an "animal model" perspective, which has grown out of the recent interest in "personalized medicine" in humans. The research asks, what are the enduring characteristics of individuals that shape their responses (either behavioral or physiological) to the situations they encounter? The second perspective that informs the work is applied. How can we use quantitative information on biobehavioral organization to better manage our colony? We know that particular situations (e.g., frequent exposure to ketamine) are risk factors for poor health or behavioral outcomes. But not all individuals that experience those situations develop those outcomes. What individual-level biobehavioral characteristics serve as additional risk factors, either alone or through interaction with more traditional risk factors, for such outcomes? He has been conducting a BBA Program since 2001 and accumulated data on more than 3,800 animals. These data are available on the internal CNPRC website, and are being used to understand animals that might be at risk for outcomes such as motor stereotypy, self-biting, and chronic diarrhea.

Contributions to the CNPRC Mission: Associate Director for Research (2002-2011); Member, Behavior Research Services Core (2010-present); Lead, Analytical and Resources Core (2008-2013); Chair, CNPRC Academic Personnel Committee (2009-2010); PI, BBA Program (2000-present); Co-host for BYU intern program (2010-present). Excluded by Requester has 25 peer-reviewed publications (May 1, 2010 to April 30, 2014).

Table 9. Examples of Affiliates and Collaborations (out of 11 projects)

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Social Regulation of Gene Expression	Co-Investigator
	Neurodevelopmental Profiling of the Epigenome and Transcriptome in Human and Rhesus Monkeys	Co-Investigator

Excluded by Requester	Plasticity and Regeneration in the Primate Spinal Cord	Core Scientist for grants
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Core Scientist: Excluded by Requester **PhD, Professor Emeritus Psychology, and Research Scientist**
Research Program: Throughout his professional career, Excluded by Requester has been interested in the biology of primate behavior, particularly the effects of environmental conditions on social development. He carried out the first studies of the effects of a nursery environment on social and emotional behavior of rhesus monkeys. He also completed the first field study of the monogamous titi monkeys and established the first captive breeding colony of the species. Following his transition to emeritus status, he received a part time appointment at the CNPRC that allows continued involvement in research. He has participated in many projects consistent with his interests and expertise, usually as collaborator or co-investigator. During the current funding period, he has been included as author on more than 80 publications and as sole or first author on more than 30.
Contributions to the CNPRC Mission: Excluded by Requester has contributed as a former BMB Unit Leader and through extensive mentoring activities. He has received recognition from the American Association for the Advancement of Science (Fellow), American Society of Primatologists (President, Distinguished Primatologist Award), International Primatological Society (President), and the American Psychological Association (Distinguished Scientific Contribution Award) which have contributed indirectly to the importance of the CNPRC as a research venue. Excluded by Requester has 11 peer-reviewed publications (May 1, 2010 to April 30, 2014).

Table 10. Examples of Affiliates and Collaborators

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Neurobiology of Primate Social Behavior	Grant, papers
	Neurobiological Mechanisms of Social Bonding in a Monogamous Primate	Grant, papers

Core Scientist: Brenda McCowan, PhD, Professor of Population Health and Reproduction, School of Veterinary Medicine Behavior Management Services, and Behavior Research Services Core

Research Program: As Core Scientist in the Brain, Mind, and Behavior Unit, Excluded by Requester program focuses on the large matrilineal social groups of rhesus macaques unique to the CNPRC as well as captive and wild macaque groups in both Europe and Asia. Patterns of health and well-being within human and animal societies and across different multispecies communities represent emergent global patterns whose underlying dynamics must be understood to better tackle complex health issues. One important goal of this program is to employ evolutionary and social network theories for practical applications at the human-animal interface using an interdisciplinary framework comprised of computational biology, genomics, epidemiology, and behavioral ecology. Her team seeks to understand how spatial and mathematical relations of networks relate to the content and quality of relationships and how such variation influences a diversity of health outcomes. This program also trains a multitude of undergraduate, graduate, and postdoctoral students among a diversity of collaborations that spans from within the CNPRC across an international scale.

Contributions to the CNPRC Mission: Leader of the Behavioral Management Service; Member of Colony Management Committee, Enrichment Committee, and Titi Monkey Management Committee; Member of Behavior Research Services Core; UC Davis IACUC; NRC Behavioral Management Consortium. Dr. Excluded by Requester has 18 peer-reviewed publications during the current funding period.

Table 11. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Rhesus Model for Proinflammatory Influences on Depression	Collaborator, co-author on publication

Table 12. Brain, Mind, and Behavior Research Unit Funded Grants *Grants that relied on BBA data

PI (Core Scientist)	Institution	Type	Title	Description
Excluded by Requester	UC Davis	NIH R37 (MH057502)	Neurobiology of Primate Social Behavior	Effects of lesioning in the amygdala, hippocampus, and cingulate on social behavior in rhesus monkeys
		NIH R01 (NS016980)	Functional Organization of the Hippocampal Formation	Maturation of the hippocampus from fetal through adult life in rhesus monkeys
		NIH R01 (MH041479)	Anatomy of the Primate Amygdala Complex	Postnatal development of the primate amygdala
		Private Source	Creating a Developmental Gene	Creating atlas of gene expression during rhesus monkey development

Excluded by Requester	UC Davis	NIH R01 (HD053555)	Expression Atlas Neurobiology of Social Bonding in a Monogamous Primate	Basic neurobiology of social bonding in titi monkeys, with relevance to neurobiology of autism
		NIH R01 (HD071998)	Effects of Chronic Intranasal Oxytocin <i>Supplement also received</i>	Long-term effects of intranasal oxytocin, which is being used to treat autism, on behavior and neural systems in titis
		Private Source	Neurobiology of Social Behavior in Titi Monkeys	Pharmacology of prosocial behavior in a monogamous primate
	University of Arizona	NIH R01 (AG003378)	Neurobehavioral Relations in Senescent Hippocampus	Understand the basis of memory impairments
	UC Davis	NIH R01 (MH080218)	Primate Models of Autism	Primate model of maternal auto-antibodies and social impairment
		NIH R21 (NS081487)	Efficacy of a Novel Neuroprotective Compound	Effects of P7C3A20 on hippocampal neurogenesis in rhesus monkey
	UC San Francisco	Private Source	Gene Therapy for Treatment of Spinal Cord Injury	Develop new tasks assessing limb and hand function in monkeys with spinal cord injury
			Neuroprotection in a Contusion Spinal Cord Injury Model	Develop a contusion model of spinal cord injury and test various treatment modalities to encourage recovery
	Private Source	NIH R37 (AG033590)	Social Regulation of Gene Expression	Explore functional genomics and inflammation in a naturalistic model of loneliness in rhesus monkeys
	UC Davis	NIH R24 (OD010962)	Biobehavioral Characterization of Rhesus Monkeys*	Individual differences in patterns of behavioral, neuroendocrine, and immunological organization in rhesus
		NIH R01 (DA024441)	Methamphetamine, Stress, and SIV <i>Supplement also received</i>	Methamphetamine use and stress on blood-brain barrier and gene expression patterns in SIV-infected rhesus monkeys
		NIH R21 (HL089148)	Temperament as a Risk Factor in Asthma Susceptibility*	Examine animals that show an inhibited temperament on measures of physiology relevant to the development of asthma
	UC Davis	NIH R01 (EY003991)	Development and Reorganization of Prenatal Visual System	Prenatal studies on the retina
	Private Source	NIH P50 (MH090966)	Serotonergic Modulation of Brain Development*	Examine serotonin transporter (SERT) effects on brain maturation and behavior
	UC Davis	NIH R01 (HD065826)	Fluoxetine: Sensitive Ages and Genotypes for Adverse Effects*	Effects of fluoxetine treatment on cognition, hippocampal, and cortical development
	Private Source	NIH R01 (MH094774)	Neurodevelopmental Profiling of the Epigenome*	Cross-sectional study of gene expression and methylation patterns in various brain regions in monkeys vs. human
		NIH R21 (MH099361)	Rhesus Model for Proinflammatory Influences in Depression*	Explore a rhesus monkey model for studying the link between social stress, depression, and proinflammatory factors
		NSF (0921978)	Maternal Influences on Infant Outcomes*	Consequences of lactational performance on infant growth and other parameters
	UC Davis	NIH R03	Developing a	Track the effects of maternal care on

Excluded by Requester		(HD069600)	Translational Model of Maternal Care*	infant neurobehavioral development, in biological and cross-fostered infants
		UCD Academic Fed Award	Transgenerational Effects of Paternal Early Stress*	Investigate the biological vs. social mechanisms for transgenerational effects of paternal early stress
	UC Davis	NIH R01 (NS035103)	Somatosensory Cortex and Thalamus	Investigate the role of posterior parietal cortex in coordinated activities using a microfluidic cooling device
	Univ of Michigan	NIH P01 (HD039386)	Iron Deprivation and Brain Development	Role of prenatal iron deprivation in inhibition and impulsivity
	UC Davis	NIH R24 (RR024396)	Behavioral Management of Deleterious Aggression*	Investigate predictors of social instability in group-housed macaques
		NIH R21 (RR02486)	Innovative Nursery-Rearing for Rhesus Monkeys	Interactive surrogate peer-rearing design for nursery-reared monkeys
		NIH R01 (HD068335)	Expanding the Utility of Social Network Analysis	Advance theory and methodology of social network analysis in health
		Private Source	Understanding Non-Pathogenic Diarrhea	Improving animal well-being and reduce morbidity through reduction of diarrhea
		Private Source	NIH R01 (AG010606)	Cognitive Function in the Aging Monkey
	Private Source	NIH P01 (AG016765)	Estrogen and the Aging Brain	Effects of estrogen replacement on cognition in aged monkeys
		NIH R01 (HD078127)	Maternal Temperament, Stress, and Inflammation*	Examine factors creating elevated risk for preterm birth
		Private Source	Biomarker Discovery for Low Sociability*	Contrast low- and high-sociable monkeys on behavior and cerebrospinal fluid/blood biomarkers
		NIH R21 (HD079095)	A Monkey Model of Naturally Occurring Low Sociability*	Test whether abnormal neurochemical signaling is associated with naturally occurring social deficits
		UCSD	Transplantation of Human Neural	Evaluate the use of human neural stem cells to improve functional recovery after spinal cord injury
	UC San Diego	UCSD	SCI Consortium Study	Investigate therapeutic treatments for monkeys with spinal cord injury
		NIH R01 (NS042291)	Plasticity and Regeneration in the Primate	Augment CNS plasticity and regeneration after experimental spinal cord injury
		NIH P01 (AG010435)	Gene Delivery and Environment	Optimize <i>in vivo</i> vectors for gene therapy in primates
		CIRM	Neural Stem Cells as a Developmental	Using a monkey model of Alzheimer's, test candidate stem cell treatments
	UC Davis	NIH R01 (EY016182)	Functional Properties of Neural Circuits for Vision	Studies functional relationship of thalamus and cortex in vision
		NIH R01 (EY016182)	Prenatal Development of Visual System	M and P cell differentiation of retinal ganglion cells in rhesus monkey
	UC Davis	Private Source	Manipulation of Oxytocin in Juvenile Rhesus Macaques	Effects of oxytocin and antagonists on affiliative preferences in juvenile rhesus
	University of Alabama	NSF	Primate-based Heterogeneous Mobile and Static Sensor Networks	Translation of primate social systems via agent-based modeling for use in computing and communications

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT**PUBLICATIONS (May 1, 2010 to April 30, 2014)**

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SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC. [Excluded by Requester]

1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal] of indoor animal space. The outdoor animal housing area includes [Specific Animal] field corrals, [Specific Animal] corn cribs, [Specific Animal]. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLIV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester]. Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations.

Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT**BIBLIOGRAPHY AND REFERENCES CITED**

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SCIENTIFIC UNITS: BRAIN, MIND AND BEHAVIOR RESEARCH UNIT**LETTERS OF SUPPORT**

Letters of support from the individuals named below are provided on the pages that follow.

1. Excluded by Requester PhD. Regents' Professor, Psychology, Neurology, and Neuroscience; Evelyn F. McKnight Chair for Learning and Memory in Aging; Director, Evelyn F. McKnight Brain Institute; Director, ARL Division of Neural Systems, Memory and Aging; Associate Director, BIO5 University of Arizona
2. Excluded by Requester PhD, Tiffany and Margaret Blake Distinguished Professor of Psychology and of Psychiatry and Behavioral Neuroscience; Director, Center for Cognitive and Social Neuroscience, The University of Chicago
3. Excluded by Requester PhD, Dean of Basic Sciences and the Graduate School of Biomedical Sciences; Professor, Arthur M. Fishberg Department of Neuroscience, Friedman Brain Institute; W.T.C. Johnson Professor of Geriatrics and Palliative Medicine, Icahn School of Medicine at Mount Sinai
4. Excluded by Requester AS, LATg, Center for Neuroscience, University of California, Davis
5. Excluded by Requester MD, PhD, Professor, Department of Neurosciences; Director, Center for Neural Repair; Director, Translational Neuroscience Institute, University of California, San Diego



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FAX: (520)626-2618

May 2, 2014

Brain, Mind & Behavior Unit
California National Primate Research Center
c/o Karen L. Bales
University of California
Davis, CA 95616

Dear Colleagues,

I am writing this letter to express my strong and enthusiastic support for renewal of the base grant for the California National Primate Research Center. This center serves as a national resource, such that investigators such as myself, who are not on-site, are able to run large non-human primate research programs from remote. I am a Regents' Professor at the University of Arizona, Director of the Evelyn K. McKnight Brain Institute, and former President of the Society for Neuroscience. Since 2001, I have carried out research on aging and the hippocampus at the CNPRC. This research has been supported by the National Institute for Aging for 32 years. The existence of the NIA-supported aged rhesus macaque colony at the CNPRC, as well as the extensive support services for outside scientists, have made this research possible. Excluded by Requester Our local core scientist liaison, supervises on-site personnel, participates in meetings with veterinary staff, facilitates space requests and generally aids in helping the research run smoothly.

In summary, the CNPRC is a critical national resource whose excellent facilities, animal colonies, scientific expertise, and services deserve continued funding and support from NIH.

Sincerely,

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Evelyn F. McKnight
Brain Institute



THE UNIVERSITY OF CHICAGO

CENTER FOR COGNITIVE AND SOCIAL NEUROSCIENCE

Excluded by Requester

May 29, 2014

Dear Colleagues,

I have been asked to write a letter of support for the renewal of the P51 base grant for the California National Primate Research Center, and I am happy to do so. I am on the faculty in the Department of Psychology and the Department of Psychiatry and Behavioral Neuroscience at the University of Chicago. Recently, I have served as a member of the National Institutes of Health Center for Scientific Review (CSR) Advisory Council (2011-2013) and as a member of the Department of Health and Human Services National Advisory Council on Aging (2004-2007). I believe I have a good sense of NIH goals and standards.

My personal research interests are focused on exploring the fundamentally social nature of humans – how our biology has been shaped by our sociality, and how, in turn, our embeddedness in social groups affects our biology, including our gene expression, and through these processes our health. One individual attribute that I have been studying for more than two decades is perceived social isolation, or loneliness, a psychological disposition that involves the perception that one is on the social perimeter and a disposition that confers significant risk for morbidity and mortality. Our understanding of the biological mechanisms that mediate the loneliness-health relationship – and potential treatments to affect both the psychological as well as biological dysfunction in loneliness -- has been hampered by the lack of a valid animal model. Rodents, for example, may be suitable for some questions but do not possess the elaborate sociality that characterizes our species. A better model is the rhesus monkey, which shares significant similarities in social, as well as immune, endocrine, and central nervous system functioning.

With a MERIT award from the National Institute on Aging, I have been collaborating with

Excluded by R equ at CNPRC (and Excluded by R equester at UCLA) on a comparative study of loneliness (operationalized behaviorally as a discrepancy between an animal's preferred and actual social environment), with a special focus on underlying endocrine, inflammatory, and genomic correlates. The work that we proposed in this grant was possible only because of the resources available at CNPRC. These resources included not only the collaborative expertise of Dr.

Excluded by Requester but also the field cage resource and the staff resources at the Center.

At its base, loneliness involves a discrepancy between social interest and social attainment. To identify animals that are lonely in a way that is most similar to loneliness in humans, we needed to study individuals that are in large, naturalistic, year-round social groups – and because there are 24 field cages of rhesus monkeys at CNPRC and world experts in primatology such as

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Requester

we had the opportunity to investigate the *behavioral* concept of loneliness in nonhuman primates. Loneliness, like pain, is not a particularly common disposition, so a large number of socially living animals needed to be screened to identify such animals, and to distinguish them from animals that also show low social attainment but are presumably satisfied with that status (paralleling what we have found in humans when distinguishing between introversion, where being alone is pleasant and preferred, and loneliness, where being with others or alone is dysphoric because neither is the preferred social environment). The field cage environment was a remarkable resource to accomplish this task. Also important was the expertise of staff at CNPRC who understand social behavior and who can observe and record social behavior accurately, and staff that can perform blood sampling and animal capture and relocation for the additional behavioral testing that we required. In short, CNPRC had all of the pieces in place to enable someone with no prior experience with nonhuman primates to establish a research presence to investigate a psychobiological phenomenon that has the potential for enormous translational impact.

I believe that the unique resources at CNPRC make it well-positioned to contribute to our own research program, but more importantly, the resources and expertise at the CNPRC make it well positioned to contribute to the programs of many others scientists who are seeking to understand the relationship between social functioning and mechanisms that influence health and well being. I am fully supportive of the renewal of the CNPRC's P51 base grant.

Sincerely,

Excluded by Requester



Icahn
School of
Medicine at
Mount
Sinai

Excluded by Requester

April 24, 2014

Excluded by Requester

Department of Psychology
UC-Davis
Davis, CA 95616

Dear Excluded by Requester and Colleagues,

I am happy to write this letter in support of continued funding for the California National Primate Research Center (CNPRC). I am Dean of Basic Sciences and the Graduate School of Biomedical Sciences at the Icahn School of Medicine at Mount Sinai, Professor in the Fishberg Department of Neuroscience and the Friedman Brain Institute, and the Willard T.C. Johnson Professor of Geriatrics and Palliative Medicine (Neurobiology of Aging). I have a long collaborative history with the CNPRC, where I have carried out studies on estrogen replacement and its effects on cognition and cortical circuitry in rhesus macaques, funded by a P01 from the National Institute of Aging for the last 13 years. This grant has been renewed twice and contains a fairly large subcontract to the CNPRC, since all of the live animal experiments are done at CNPRC. It would not be possible to have received the initial grant or the renewals without the resources provided by the aging colony of rhesus monkeys housed at the CNPRC as well as the expertise of colleagues such as Excluded by Requester

Excluded by Requester

Excluded by Requester In addition to all aspects of animal husbandry and geriatric veterinary care, the CNPRC has provided endocrine assays, supervision of on-site employees, help with animal protocols, and many other services which have facilitated work for off-site PIs. Excluded by Requester as our Core Scientist liaisons for the last five years, have been invaluable in facilitating the logistics of this complex research project. The CNPRC is a unique institution of national importance that provides resources and expertise such as those associated with the aged macaque colony that just are not available anywhere else. I enthusiastically support full renewal of the base grant funding for the CNPRC.

Excluded by Requester

-----Original Message-----

From: Excluded by Requester

Sent: Wednesday, April 23, 2014 12:17 PM

To: Excluded by Requester

Subject: Thank you!

Excluded by
Requester

I just wanted to write you and thank you endlessly for the time you have allowed a couple of employees from CNPRC to come out and give us some guidance on chair training and establishing successful pairs at CNS.

Excluded by Requester took some time to come out and give me some chair training tips for an animal I was having some difficulty with. His expertise is priceless! He is extremely helpful, patient, and down right amazing. The things he taught me in just a small amount of time have been vital and invaluable to my learning and teaching process here with my primates, as well as, the personnel and primates from the other labs here. Excluded by Requester such an important factor in the primate world. His humane and safe training techniques make all aspects of working with primates less stressful to both the animal and the handler. We are so lucky to have him at the Primate Center!!!

Excluded by Requester has also been an extremely valuable resource for us over at CNS. She is promptly available with advice and guidance via email and has visited 2-3 times to help improve my assessment skills of primate social behavior and assist in first time pairing. Assessing possible pairs is extremely detailed and takes a lot of skill and expertise. Excluded by Requester knowledge has played an integral role in guiding me on what to look for, as well as, allowing me to train other laboratory personnel here at CNS. Prior to Excluded by Requester help, CNS had one intermittent pair established. Now out of the 27 animals housed at CNS, 12 of them are successfully paired. I appreciate the ability to have CNPRC as a resource and hope the relationship can be reciprocated continuously.

Sincerely,

Excluded by Requester

UNIVERSITY OF CALIFORNIA, SAN DIEGO

UCSD

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SANTA BARBARA • SANTA CRUZ

Excluded by Requester

9500 GILMAN DRIVE
LA JOLLA, CALIFORNIA 92093-0626

June 3, 2014

Excluded by Requester

Dear Colleagues,

I strongly support the renewal of the P51 base grant for the California National Primate Research Center at the University of California, Davis. I am the Director of the Center for Neural Repair and a Professor of Neurosciences at University of California, San Diego. The goal of my lab is to discover and evaluate treatments to restore function following spinal cord injury (SCI).

While our experiments in rats and mice have identified promising approaches for the treatment of spinal cord injury and Alzheimer's disease, successful translation to humans is greatly assisted by non-human primate testing. Rodents and primates differ greatly in immune function, as well as CNS anatomy, function, and size. The corticospinal tract, for example, is critical for fine hand motor function in primates, but not in rodents, making non-human primate models critical for the assessment of hand function after SCI. In addition, my lab has identified spontaneous sprouting of neurons in the corticospinal tract as a novel target for therapeutic intervention; this spontaneous sprouting had not been revealed in our rodent studies. Finally, our pilot work in stem cell transplantation in the non-human primate has revealed both promising results and multiple challenges not observed in rodents (and probably present in humans). The availability of the non-human primate model will therefore greatly enhance these studies' predictive value for human translation.

My non-human primate research program in spinal cord injury repair has remained exclusively at the CNPRC for the last 20 years due to the unique resources available there. For example, our project makes extensive use of the surgical resources at CNPRC, and the facilities are superb for the kind of work we do. More important, perhaps, is the skill of the technical staff that assists with the surgeries – from anesthesia techs to staff veterinarians, everyone knows the background of the project, and performs at very high levels to support the program. In addition, the CNPRC has the resources to collect and process tissue samples, prepare budgets for grant proposals, and manage animal use protocols. Finally, the large breeding colony at CNPRC ensures that there will be a sufficient number of animals available that meet our strict inclusion criteria.

Moreover, based on our work at the primate center we have translated growth factor gene therapy to human clinical trials in Alzheimer's disease. One of our programs is in Phase 2 multicenter clinical trials across the United States, and this program was heavily dependent on studies we performed at the CNPRC. We will soon translate a second gene therapy program

for Alzheimer's disease to clinical trials, also heavily dependent on preclinical studies performed at the CNPRC.

In all our translational studies, the non-human primate model has been essential for determining dosing and scaling of therapies. We learned things that we simply could not learn in any model other than the non-human primate model. For our human translational programs, the resources of the CNPRC have been essential and, we believe, have directly had a positive impact on translation to the clinic.

In conclusion, as a frequent user of CNPRC's surgical and support services, I enthusiastically support this renewal application. CNPRC's resources are critical to advance a translational agenda in spinal cord research.

Sincerely,

Excluded by Requester

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

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 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Infectious Diseases Research Unit

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename ID_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	ID_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	ID_FacilitiesOtherResources.pdf
11. Equipment	ID_Equipment.pdf

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

ABSTRACT

The mission of the **Infectious Diseases Research Unit** is to develop nonhuman primate models for investigating host-pathogen interactions and thereby build a foundation for intervening against a wide range of infectious diseases. The Research Unit is composed of six Core scientists drawn from the Schools of Medicine and Veterinary Medicine who maintain a high level of extramural grant funding for nonhuman primate research and conduct studies on a broad range of infectious pathogens, including bacteria and viruses causing acute or chronic/persistent infections. The Unit is well-integrated into the prominent theme of comparative medicine at UC Davis, and each of its members maintain robust extramural collaborations on projects involving infectious disease research in macaques. Basic and translational research efforts in the Infectious Diseases Research Unit focus on mechanisms of infectious agent transmission and pathogenesis, protective immunity and vaccinology, and testing and development of therapeutic approaches. The Infectious Diseases Research Unit is leading investigations on the role of the host microbiome in health and disease in nonhuman primates. In addition, members of the Unit directly contribute to the major theme of lifespan health at the California National Primate Research Center through studies spanning fetal to aged rhesus macaques. Outcomes of such studies will aid in understanding mechanisms of inflammatory diseases and promote the development of novel countermeasures that maintain and/or restore healthy immune function throughout life.

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

FACILITIES AND OTHER RESOURCES

Laboratories:

Excluded by Requester [Proprietary Info] main laboratory [Proprietary Info] The laboratories are fully equipped for all molecular and immunologic analyses. All of the work is conducted according to Biosafety Level 2 guidelines. The room also includes two biological safety cabinets for non-infectious tissue culture work, CO₂ incubators, microscope, and centrifuge. The room is equipped with an inspected chemical fume hood. Two $\leq -20^{\circ}\text{C}$ and a $\leq -80^{\circ}\text{C}$ freezers are within this space in addition to two 4° refrigerators. Larger pieces of equipment are located within shared equipment rooms. Tissue culture work with infectious agents is conducted in shared facilities located within the CCM and CNPRC, and tissue culture work is conducted according to Biosafety Level 2 guidelines.

Excluded by Requester [Proprietary Info] has dedicated laboratory space [Proprietary Info] Included are fully equipped laboratory areas, tissue culture rooms, microscopy room, BSL-2 and BSL-3 laboratories that total 2,500 sq. ft.

Excluded by Requester [Proprietary Info] occupies laboratories at the Primate Center encompassing [Proprietary Info] Additional laboratory space is associated with the Immunology and Pathogen Detection Resources Core (see Core).

Excluded by Requester [Proprietary Info] occupies laboratories at the [Proprietary Info] which support this infectious disease studies. The shared [Proprietary Info] accommodate work on viruses in primary and cell line cultures, as well studies of bacteria (*M. tuberculosis*, BCG, *H. pylori*). These laboratories contain ducted biosafety cabinets, refrigerators and freezers, tissue culture incubators, microscopes, tabletop centrifuges, and automatic pipetors.

Excluded by Requester [Proprietary Info] occupies laboratories at the CNPRC encompassing 900 sq. ft. equipped for all aspects of cell and molecular biology with an adjacent 150 sq. ft. laboratory equipped for tissue culture [Proprietary Info] also occupies [Proprietary Info]

Excluded by Requester [Proprietary Info] occupies 1,600 sq. ft. of assigned space at the CCM and has all necessary microbiology laboratory equipment for studies of *H. pylori*. His research personnel have direct access to large shared equipment items and procedure rooms at CCM.

Clinical: Clinical care and related procedures at the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see **Primate Services**).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and **Information Technology Services** provides desktop support and other related services. Biostatistics services and Biomedical Informatics support are also provided on campus and through the UC Davis CTSC. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are all available.

Office [Excluded by Requester] have offices at the CNPRC [Excluded by Requester] each have an office [Proprietary Info] and [Proprietary Info] A Senior Administrative Officer and five administrative staff support the faculty (total of 8) [Proprietary Info]

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

Microbiome and gene expression analyses will be performed through the [Proprietary Info]

[Proprietary Info]

[Proprietary Info] This facility has successfully leveraged the existing strengths in gene expression and microbiota analyses for nonhuman primate studies. The HMSB Core is designed to provide researchers with easily accessible, customized, and cost-effective resources for integrating analyses of microbial community structure and host-microbe interactions in health and disease. The services from the Core include, nucleic acid extraction and sample processing for library construction and next-generation sequencing (NGS), functional analysis of NGS data sets, and microarray-based gene expression profiling using the Affymetrix GeneChip system. The NGS analytical services offered utilize state-of-the-art open source software platforms and other customized scripts developed by fellow HMSB Core Associate-Director [Excluded by Requester] PhD. The HMSB Core has developed and optimized methodologies for processing and analyzing small size tissue and fluid samples from nonhuman primates and for the evaluation of gene expression and the microbiota from fecal, mucosal, and body fluid samples of rhesus macaques.

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

EQUIPMENT

Excluded by Requester Microcentrifuges (5), agarose mini-gel apparatus (5)/power supply (3), acrylamide gel apparatus (BIORAD Mini-Protean II) (2), western blot apparatus (3) (1-Hoeffer and 2 Immunetics Miniblotter 28), 3000V power supply (Fisher #FB-600) (2), Eppendorf Gradient Thermocycler, Refrigerator/Freezer, Belco hybridization oven; microplate reader (BIORAD model 550), Slab gel dryer (BIORAD model 483, laminar flow biological cabinet (Forma) (3), ultralow Cryostar freezers (3), liquid nitrogen tanks for long-term storage of cells (3), CO₂-humidified incubators (Forma Scientific) (4), 2 TJ-6 centrifuges (Beckman) (2).

Excluded by Requester The laboratory is equipped with centrifuges, tissue sectioning apparatus, incubators, freezers, gel electrophoresis equipment, microfuges, microscopes with cameras and computers, tissue culture hoods, chemical safety hoods, a cytospectrophotometer, and immunoblot apparatus. Two BSL-2 laboratories with tissue culture and chemical safety hoods are available to perform monkey sample processing. A BSL-3 laboratory is available for infectious sample processing work. Two separate closed laboratories are available for immunohistochemistry work and for non-infectious tissue culture work. A small closed laboratory is available for real-time PCR. Core Facilities and general laboratory support services with autoclaves, glass washing, medical waste disposal, dry ice, and ice machines are available. Through the shared laboratories on the same floor, laser-capture microdissection (Arcturus XT Laser Capture Microdissection System), frozen or fixed tissue sectioning equipment, lyophilizer, flow cytometers, ultracentrifuges, bacterial culture room, bioanalyzer, confocal microscope, Fluidigm, realtime PCR equipment (ABI Viia 7 – The Viia 7 System), ELISA readers, preparatory centrifuges, etc. are available. In addition, electron microscopy and histopathology services, FACS analysis and a Cell sorter and laser scanning cytometer available. Complete availability to the equipment is available for performing cellular, molecular, immunological and pathological analyses of the monkey samples.

Excluded by Requester Temperature controlled CO₂ incubators (4), ≤-20°C (2) and ≤-80°C (2) freezers, liquid nitrogen tanks for cellular cryopreservation (1), Zeiss inverted microscopes (2), biosafety cabinets (4), temperature-controlled table top centrifuges (2), microfuges (2), heatblocks, gel and immunoblot apparatus, Perkin-Elmer GeneAmp 9600/9700 thermal cyclers (1), Omni Bead Mill homogenizer used in preparation of tissue samples for microbiome work.

Excluded by Requester Chemical hoods (2), ≤-20°C freezers, deli-type refrigerators, computers (4), a laser printer, table-top centrifuges, a microplate reader, autoblot, gel electrophoresis systems, water bath incubator, bacterial incubator, rotator, rocker, vortexes, automatic pipetors, hotplate, microgram and gram scales, a clean air workstation, a PCR thermocycler, and a Luminex system (detection instrument, vacuum manifold plate washer, dedicated computer) for multiplex immunoassay.

Excluded by Requester Equipment located in the CNPRC and CCM labs or shared by all CNPRC investigators: Perkin-Elmer GeneAmp 9600 thermal cyclers (4), automated ELISA plate washer (1), biosafety cabinets (10), Wallac 96-well format scintillation counters (2), ELISA readers (3), rotary shakers (2), tissue culture incubators (16), gel apparatus (8), immunoblot apparatus (4), preparatory centrifuges (6), cytocentrifuge (1), Omicron cryostat (1), Zeiss Axioimager-1 automated microscope with an Apotome Imager for brightfield and 5 color fluorescence optics connected to an Axiovision digital imaging workstation (1); Zeiss Axioplan 2 photomicroscope with a motorized stage and brightfield and fluorescence optics connected to a Zeiss Axioacam camera interfaced with an Pentium computer which runs Axiovision software; Adobe Photoshop (1); Becton-Dickinson FACSCalibur flow cytometer with 2 lasers capable of 4 color analysis (1), FACSaria cell sorter with 3 lasers capable of 10-color analysis and 4 way sorting (1) has a Zeiss KS ELISPOT Reader System (1), and access to two ABI 7900 HT sequence detection system with robotic plate manipulation (Real-time PCR machine) (2) at the CNPRC and a H.L. Shephard Cesium irradiator (1) at the CCM.

Excluded by Requester Includes a laminar flow hood, fume hoods (2), CO₂ incubators (3), standard incubators (2), a microscope and an inversion microscope, thermocyclers (3) (including 1 BioRad real time thermocycler), 4° refrigerators (2), ≤-20° freezers (2), ≤-80° freezers (2) (located in common space), microcentrifuges (3),

balances (2), pH meter, bench top centrifuge, Genepix 4100A scanner, protein and DNA electrophoresis equipment, NanoDrop 2000c, MiniBeadbeater-16 cell disruptor, and waterbaths (2).

Laboratories in the CCM are equipped with multiple light, phase, dark and fluorescent microscopes, photomicroscopes, dissecting microscopes, inverted microscopes, macrophotography unit, multiple class II biohazard containment cabinets, vented stainless steel tissue cutting table, rotary shakers, adjustable temperature incubators, analytical balances, multiple $\leq -80^{\circ}\text{C}$ freezers, ice machines, scintillation counters, orbital shaking incubators, electrophoresis equipment, electroporation apparatus, water baths, shaking water baths, assorted ≤ -20 freezers, high speed refrigerated centrifuges, ultracentrifuges, spectrophotometers, pH meters, DNA thermal cyclers, ELISA readers, bench top centrifuges, autoclaves, survey meters, exhaust hoods, microwave ovens, UV view boxes, gel photography apparatus, liquid nitrogen refrigerator, and other general laboratory equipment. Core laboratories at CCM contain two instruments for Taqman assay (ABI Prism 7700 Sequence Detector, Perkin Elmer; ABI Prism 7900HT Sequence Detection System, Applied Biosystems) that are available for shared use. All CCM equipment and laboratory space is available for general use.

Specific Animal Location

Specific Animal Location

BSL-2 and BSL-3 with laminar flow biosafety cabinets, tissue culture incubators, and microscopes. CCM also has a 300 sq. ft. fully equipped research histopathology laboratory with automated tissue processing and embedding equipment.

The HMSB Core also oversees the use and maintenance of a number of shared equipment resources for the School of Medicine. The list of equipment includes an Arcturus XT Laser Capture Microdissection system, a Leica RM2255 Microtome, and an ABI Viia 7 RT-PCR system that can be used for more defined and targeted gene expression studies. Shared equipment also includes a LICOR Odyssey Infrared Imager for fluorescence scanning and quantitation, a Qiagen Pyromark Q24 for real-time sequence analysis for epigenetics research and genetic analysis, and a Qiagen QIAcube system for integrating automated, low-throughput sample preparation into the workflow. The HMSB Core utilizes 2 Illumina MiSeq Systems that are operated by the Genome Center's DNA Technologies Core and also conveniently located in the same building (GBSF).

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2015

End Date*: 04-30-2016

Budget Period: 1

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	33,172.00	11,096.00	44,268.00
2.					Core Scientist			0.0	0.0	18,150.00	6,071.00	24,221.00
3.					Core Scientist			0.0	0.0	18,150.00	3,957.00	22,107.00
4.					Core Scientist			0.0	0.0	7,605.00	2,544.00	10,149.00
5.					Core Scientist			0.0	0.0	18,150.00	7,239.00	25,389.00
6.					Core Scientist			0.0	0.0	18,150.00	3,957.00	22,107.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

148,241.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
Excluded by Requester 2	Unit Technical Support		EFFORT		33,270.00	17,600.00	50,870.00
	TBN Core Scientists	2.4			29,841.00	9,982.00	39,823.00
3	Total Number Other Personnel					Total Other Personnel	90,693.00
					Total Salary, Wages and Fringe Benefits (A+B)		238,934.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	12,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	12,000.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	4,000.00
2. Publication Costs	8,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	12,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	262,934.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	262,934.00	59,686.00
		Total Indirect Costs	59,686.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	322,620.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ID_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	33,504.00	11,799.00	45,303.00
2.					Core Scientist			0.0	0.0	18,150.00	6,392.00	24,542.00
3.					Core Scientist			0.0	0.0	18,150.00	4,144.00	22,294.00
4.					Core Scientist			0.0	0.0	7,681.00	2,705.00	10,386.00
5.					Core Scientist			0.0	0.0	18,150.00	7,659.00	25,809.00
6.					Core Scientist			0.0	0.0	18,150.00	4,144.00	22,294.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

150,628.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Unit Technical Support	Excluded by Requester	EFFORT		33,603.00	18,588.00	52,191.00
2	TBN Core Scientists	2.4			29,957.00	10,550.00	40,507.00
3	Total Number Other Personnel					Total Other Personnel	92,698.00
					Total Salary, Wages and Fringe Benefits (A+B)		243,326.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

12,360.00

2. Foreign Travel Costs

0.00

Total Travel Cost 12,360.00**E. Participant/Trainee Support Costs**

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other:

0 Number of Participants/Trainees**Total Participant Trainee Support Costs** 0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	4,120.00
2. Publication Costs	8,240.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	12,360.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	268,046.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	268,046.00	60,846.00
Total Indirect Costs			60,846.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	328,892.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ID_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	33,604.00	12,237.00	45,841.00
2.					Core Scientist			0.0	0.0	18,150.00	6,610.00	24,760.00
3.					Core Scientist			0.0	0.0	18,150.00	4,280.00	22,430.00
4.					Core Scientist			0.0	0.0	7,846.00	2,857.00	10,703.00
5.					Core Scientist			0.0	0.0	18,150.00	7,929.00	26,079.00
6.					Core Scientist			0.0	0.0	18,150.00	4,280.00	22,430.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

152,243.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Unit Technical Support	Excluded by Requester	EFFORT		35,685.00	20,382.00	56,067.00
2	TBN Core Scientists	2.4			30,672.00	11,170.00	41,842.00
3	Total Number Other Personnel					Total Other Personnel	97,909.00
					Total Salary, Wages and Fringe Benefits (A+B)		250,152.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	12,731.00
2. Foreign Travel Costs	0.00
Total Travel Cost	12,731.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	4,244.00
2. Publication Costs	8,487.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	12,731.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	275,614.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	275,614.00	62,564.00
		Total Indirect Costs	62,564.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	338,178.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ID_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2018

End Date*: 04-30-2019

Budget Period: 4

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	36,248.00	13,599.00	49,847.00
2.					Core Scientist			0.0	0.0	18,150.00	6,809.00	24,959.00
3.					Core Scientist			0.0	0.0	18,150.00	4,407.00	22,557.00
4.					Core Scientist			0.0	0.0	8,310.00	3,118.00	11,428.00
5.					Core Scientist			0.0	0.0	18,150.00	8,164.00	26,314.00
6.					Core Scientist			0.0	0.0	18,150.00	4,407.00	22,557.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

157,662.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
Excluded by Requester	Unit Technical Support:		EFFORT		37,424.00	22,012.00	59,436.00
2	TBN Core Scientists	2.4			31,300.00	11,742.00	43,042.00
3	Total Number Other Personnel					Total Other Personnel	102,478.00
						Total Salary, Wages and Fringe Benefits (A+B)	260,140.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	13,113.00
2. Foreign Travel Costs	0.00
Total Travel Cost	13,113.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	4,371.00
2. Publication Costs	8,742.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	13,113.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	286,366.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	286,366.00	65,005.00
Total Indirect Costs			65,005.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	351,371.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ID_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2019

End Date*: 04-30-2020

Budget Period: 5

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	37,335.00	14,418.00	51,753.00
2.					Core Scientist			0.0	0.0	18,150.00	7,009.00	25,159.00
3.					Core Scientist			0.0	0.0	18,150.00	4,534.00	22,684.00
4.					Core Scientist			0.0	0.0	8,560.00	3,306.00	11,866.00
5.					Core Scientist			0.0	0.0	18,150.00	8,416.00	26,566.00
6.					Core Scientist			0.0	0.0	18,150.00	4,534.00	22,684.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

160,712.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Unit Technical Support	Excluded by Requester	EFFORT		38,921.00	23,586.00	62,507.00
2	TBN Core Scientists	2.4			31,826.00	12,290.00	44,116.00
3	Total Number Other Personnel					Total Other Personnel	106,623.00
					Total Salary, Wages and Fringe Benefits (A+B)		267,335.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	13,506.00
2. Foreign Travel Costs	0.00
Total Travel Cost	13,506.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	4,502.00
2. Publication Costs	9,004.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	13,506.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	294,347.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	294,347.00	66,817.00
Total Indirect Costs			66,817.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	361,164.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: ID_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist, Unit Leader	% Effort			
	Core Scientist				
	Core Scientist				
	Core Scientist				
	Core Scientist				
	Core Scientist				
TBN	Core Scientist	10	0	90	100
TBN	Core Scientist	10	0	90	100
Excluded by Requester	Unit Safety Coordinator	% Effort			

TBN=to-be-named

Excluded by Requester **PhD, Core Scientist and Unit Leader** EFFORT months – % Effort Excluded by Requester is Professor, Department of Pathology and Laboratory Medicine, School of Medicine. Excluded by Requester has studied molecular mechanisms of pathogenesis in rhesus macaques experimentally infected with SIV/SHIV clones and has collaborated with extramural investigators to test anti-HIV vaccine and drug therapy approaches in simian AIDS models. In the SHIV/macaque model, he studies highly active antiretroviral therapy (HAART) and viral reservoirs.

Excluded by Requester **PhD, Core Scientist** EFFORT months – % Effort Excluded by Requester is Professor, Department of Pathology and Laboratory Medicine, School of Medicine, Director of the Center for Comparative Medicine (CCM), and CNPRC Interim Director. Excluded by Requester has characterized the natural history of RhCMV infection in the breeding corrals of rhesus macaques in which RhCMV is endemic, and his laboratory develops key reagents and techniques to investigate molecular, virological, and immunological parameters of RhCMV infection for use at the CNPRC and at other institutions.

Excluded by Requester **PhD, Core Scientist** EFFORT months – % Effort Excluded by Requester is Professor and Chair, Department of Medical Microbiology and Immunology, School of Medicine. Excluded by Requester research program focuses on gastrointestinal (GI) tract pathogenesis and defenses in the SIV/macaque model for simian AIDS. This includes studies of the effects of SIV infection on the magnitude and nature of the gut mucosal immune response to incoming pathogens or co-infections, specifically *Salmonella typhimurium*, role of gut mucosal innate immunity by characterizing functional defects in key immune cells, and impact of initiating early antiretroviral therapy in reversing GI tract mucosal damage and restoring the mucosal immune functions.

Excluded by Requester **MD, PhD, Core Scientist** EFFORT months total; EFFORT months – % Effort Excluded by Requester shared with the Reproductive Sciences and Regenerative Medicine Research Unit). Excluded by Requester is Assistant Professor, Department of Medical Microbiology and Immunology, School of Medicine, and leads the Immunology and Pathogen Detection Resources Core. Excluded by Requester studies the interplay of host-microbe interactions in relation to immune system development. His studies are also examining the impact of microbial colonization on maturation of the immune system.

Excluded by Requester **DVM, PhD, Core Scientist** EFFORT months – % Effort Excluded by Requester is Professor, Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine. Excluded by Requester has maintained a long-standing research program in AIDS vaccine development and immunology in macaques. He has studied correlates of protective immunity of live-attenuated SIV vaccines, developed the mucosal membrane transmission models for SIV infection via vaginal mucosa and penile membranes, and tested prophylactic microbicides.

Excluded by
Requester

EFFORT

% Effort

Excluded by
Requester**MD, PhD, Core Scientist**

months

Excluded by
Requester

is Professor, Department of Medical Microbiology and Immunology, School of Medicine. is a microbiologist and infectious diseases physician with a longstanding interest in the pathogenesis of *Helicobacter pylori*, which he studies in mice and nonhuman primates, as well as humans.

TBN, Core Scientists (2) (1.2 calendar months – 10% each Core Scientist). The commitment of the Provost and respective Dean's of the Schools of Medicine and Veterinary Medicine, and the Colleges of Biological Sciences, Engineering, and Letters and Sciences (see **Overview**) to new faculty positions includes two Unit Core Scientist positions (see Research Strategy). One of the new faculty recruitments is proposed at the junior investigator level and one with a more established research program.

Excluded by Requester

EFFORT

% Effort

Excluded by
Requester**Unit Safety Coordinator**

months

serves as the Unit Safety Coordinator, provides assistance in the training of staff and students, coordinates and prepares sample shipments to investigators, and maintains the required documentation associated with these service activities.

Administrative support for four of the six Core Scientists who are also faculty in the Center for Comparative Medicine (CCM) is provided through CCM. Administrative support for the other two Core Scientists is provided through their home department (Medical Microbiology and Immunology, School of Medicine).

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None requested

TRAVEL

\$12,000 total is requested for each Core Scientist to attend a national meeting in their respective area of expertise (8 x \$1,500).

SUPPLIES

\$4,000 in general supplies is requested to support activities with new investigators and sharing of resources.

OTHER EXPENSES

\$8,000 is requested for manuscript preparation and submission (8 x \$1,000).

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		769,486.00
Section B, Other Personnel		490,401.00
Total Number Other Personnel	15	
Total Salary, Wages and Fringe Benefits (A+B)		1,259,887.00
Section C, Equipment		0.00
Section D, Travel		63,710.00
1. Domestic	63,710.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		63,710.00
1. Materials and Supplies	21,237.00	
2. Publication Costs	42,473.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,387,307.00
Section H, Indirect Costs		314,918.00
Section I, Total Direct and Indirect Costs (G + H)		1,702,225.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)Inventions and Patents*: ☒ Yes ☐ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☒ No**7. Change of Investigator / Change of Institution Questions**☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

ID_SpecificAims.pdf

3. Research Strategy*

ID_ResearchStrategy.pdf

4. Progress Report Publication List

ID_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

ID_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

ID_LettersofSupport.pdf

13. Resource Sharing Plan(s)

ID_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

SPECIFIC AIMS

The Infectious Diseases (ID) Unit at the California National Primate Research Center (CNPRC) continues to advance nonhuman primate models of acute and chronic infectious diseases on a wide range of both viral and bacterial pathogens and to use these models for studies of pathogenesis and development of novel vaccines and therapies. Taking together individual member's expertise and collaborative activities, the Unit is very well poised for basic and translational research on infectious disease pathogenesis, vaccine and drug interventions, and studies of mechanisms of host-pathogen interactions. Such studies are performed with well-established analytical methods as well as emerging "-omics" approaches and technologies. Several members of the Unit are conducting "lifespan"-related research through studies of the effects of aging on infection, pathogenesis, and vaccine efficacy. Importantly, the Unit's research is also contributing to the management and health of the nonhuman primates housed at the CNPRC through development of infectious disease diagnostics used for maintaining Specific Pathogen Free (SPF) animals and through pathogenesis studies, thus ensuring availability of high-quality subjects for many biomedical research applications. Members of this Unit also engage the expertise of other CNPRC Scientific Research Units and Service Cores as well as existing campus resources and programs to facilitate basic host-pathogen research studies in nonhuman primates and to seek opportunities for potential translation of these studies into clinical application. Importantly, this Unit is well integrated into the prominent theme of comparative medicine at UC Davis through appointments in the Center for Comparative Medicine, the Schools of Medicine and Veterinary Medicine, and the use of resources in the Clinical and Translational Sciences Center (CTSC). Major accomplishments over the current funding period are grouped according to three inter-related investigational themes: (1) infectious disease models and mechanisms of pathogenesis, (2) immunology and vaccines, and (3) therapy for infectious pathogens and disease. Many of these host-pathogen studies in macaques have direct translational significance, and several Unit members either hold IRB approval for research involving human subjects or are conducting nonhuman primate studies that will be translated to clinical trials. The current ID Unit investigators, interacting with other CNPRC Scientific Research Units and Service Cores as well as collaborating with UC Davis and extramural investigators, are very well positioned to contribute to nonhuman primate research and provide essential services as described in the following Specific Aims:

Specific Aim 1: Advance the CNPRC resource through scientific contributions to understanding host-pathogen interactions and treatment of infectious diseases across the age spectrum.

Plan. The ID Unit will advance the CNPRC resource through scientific contributions towards the understanding of host-pathogen interactions and treatment of infectious diseases. Accordingly, Unit members fulfill several functions: (1) conduct mechanistic and interventional studies using the nonhuman primate as a laboratory animal model for infectious diseases, (2) contribute towards the understanding of lifespan health by investigating immune ontogeny and aging, particularly in relation to host responses to pathogen infection, the role of persistent infections on immune function, and age-related changes in vaccine responses, and (3) provide scientific expertise to advance the development of novel rhesus macaque microbiome resources.

Specific Aim 2: Provide nonhuman primate expertise and services to investigators at the regional and national levels to advance NIH-supported research excellence.

Plan. The ID Unit provides unique expertise and service towards enhancement of the CNPRC resources, as related to infectious diseases, at both a regional and national level. This includes development of methodologies and reagents using the nonhuman primate as a laboratory animal model.

Specific Aim 3: Mentor and train the next generation of translational nonhuman primate investigators.

Plan. A central mission is to mentor and train new investigators at all career stages in the development of expertise in primatology, the design and study of nonhuman primate models of human health and disease, team science, and the conduct of multidisciplinary translational investigations.

Specific Aim 4. Ensure the highest standards of research and animal care for the CNPRC resource.

Plan. ID Unit Core Scientists will continue to play an active role in maintaining the health of CNPRC colony animals through participation in the Colony Management Committee, Infection Control Committee, and other key infrastructure and administrative functions related to immunology and infectious diseases.

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

RESEARCH STRATEGY

INTRODUCTION

The Infectious Diseases (ID) Unit studies a variety of host-pathogen interactions in nonhuman primates through multidisciplinary collaborations that make mechanistic discoveries, establish new disease models, and provide a basis for clinical interventions. Members of the Unit (Figure 1) are integrated into other centers and programs at UC Davis and thus can draw on many state-of-the-art resources for biomedical research. Basic and translational research activities in the Unit are organized into three investigational themes: (1) infectious disease models and mechanisms of pathogenesis, (2) immunology and vaccines, and (3) therapy for infectious pathogens and disease. Furthermore, Unit members contribute service activities, based on their infectious disease expertise that benefit the health and management of the macaque colony (Table 1).

Figure 1. Organizational Chart: Infectious Diseases

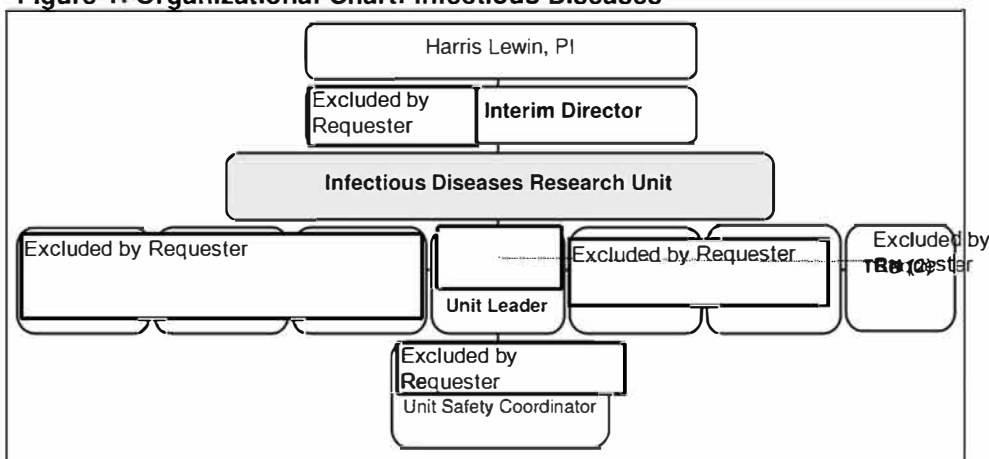


Table 1. Infectious Diseases Research Unit Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Pathology and Laboratory Medicine, School of Medicine	• Interim Director, Core Scientist • Infection Control Committee
	Department of Medical Microbiology and Immunology, School of Medicine	• Core Scientist • Colony Management
	Department of Medical Microbiology and Immunology, School of Medicine	• Immunology and Pathogen Detection Resources Core • Colony Management
	Department of Pathology and Laboratory Medicine, School of Medicine	• Unit Leader • Research Advisory Committee
	Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine	• Colony Management Committee
	Department of Medical Microbiology and Immunology, School of Medicine	• Colony Management
TBN (2)	Based on joint recruitments	Core Scientists
Excluded by Requester	CNPRC	Unit Safety Coordinator

*Joint appointment in Reproductive Sciences and Regenerative Medicine Research Unit; TBN=to-be-named

Table 2 shows the support for the ID Unit per the FOA. A small component of salary is supported on the P51 base grant (see budget justification), and represents the commitment to the mission, outreach, and services. Extramural grant funding is shown in Table 3, below.

Table 2. Support for the Infectious Diseases Research Unit (does not include research grants per the FOA. See Unit grant funding Table 3, below)

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$244,847	\$262,934
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$244,847	\$262,934

Response to Summary Statement

reviewers' comments

reviewers' comments

reviewers' comments

SIGNIFICANCE

Because of genetic, physiologic, and immunologic similarities with humans, macaques are directly relevant for developing models of human diseases used to investigate mechanisms of pathogenesis and to discover, test, and develop novel interventions. During the current funding period, Unit Core Scientists were successful in obtaining extramural grants that totaled approximately \$32.6 million (Table 3). Productivity of the ID Unit is also shown by 104 publications in peer-review journals (May 1, 2010 to April 30, 2014).

Table 3. Extramural Grant Funding for the ID Unit (May 1, 2010 to April 30, 2014)

May 2010 - April 2011	May 2011 - April 2012	May 2012 - April 2013	May 2013 – April 2014	TOTAL*
\$9,604,958	\$8,172,049	\$6,833,928	\$8,000,326	\$32,611,261*

*Does not include currently funded grants May 1, 2014 to April 30, 2015, to date, of \$6,608,127

Progress and Major Accomplishments: Contributions to the CNPRC Mission

Scientific Accomplishments. The combined research expertise of the ID Unit has expanded during the current funding period beyond its historic focus on nonhuman primate models of viral infections to include studies of bacterial pathogens and an emphasis on mucosal immunology. The expanded focus has resulted in a broader knowledge base and augmented extramural funding support to enable investigations of a wider range of pathogens and interventional strategies through intra- and inter-unit interactions at the CNPRC as well as through extramural collaborations (Figure 2). Letters of support from extramural scientists are included in the Appendix. Selected host-pathogen studies are described for each of the three investigational themes to highlight important accomplishments and the highly interactive nature of the members of the ID Unit.

1. Infectious Disease Models and Mechanisms

Figure 2. Social Network Analysis for the ID Unit

Excluded by Requester

of Pathogenesis

Cytomegalovirus (CMV) Infection. To establish the macaque model of rhesus CMV (RhCMV) infection and disease at the CNPRC, [Excluded by Requester] has defined the natural history of the virus in breeding corrals of rhesus macaques in which RhCMV is endemic [Excluded by Requester] et al., 1994]. These studies, conducted in collaboration with [Excluded by Requester] (Reproductive Sciences and Regenerative Medicine Unit) and other investigators, are critical not only for the health and management of colony macaques, but also for testing novel vaccine approaches based on CMV vectors [Excluded by Requester] 2003]. Key reagents and techniques to investigate molecular, virological, and immunological features of RhCMV infection have been developed. Notable examples include fibroblast-adapted and epitheliotropic strains of RhCMV, development of serological assays for IgA, IgM, and IgG antibody responses to RhCMV infection, real-time PCR assays to quantify RhCMV genomes in rhesus macaque tissues and bodily fluids, and development of the fetal pathogenesis model of RhCMV [Excluded by Requester] 2006; [Excluded by Requester] 2011].

***H. pylori* Colonization and Pathogenesis.** The gastric pathogen, *H. pylori*, which is prevalent in many developing countries, was shown for the first time by [Excluded by Requester] in collaborative studies involving Dr. [Excluded by Requester] a CNPRC pathologist, to induce expression of antimicrobial peptides (defensins) in the gastric mucosa of rhesus macaques [Excluded by Requester] 2013; [Excluded by Requester] 2006]. [Excluded by Requester] is also using this model to examine the interplay between expression of host glycans that serve as receptors for *H. pylori*, and expression of bacterial outer membrane proteins that serve as adhesins; results of these studies demonstrate crosstalk of bacterium and host and provide a basis for additional studies of mechanisms of *H. pylori* colonization and disease, highly relevant to human health.

***M. tuberculosis* Infection** [Excluded by Requester] collaborated with [Excluded by Requester] (Respiratory Disease Unit) in a project that used the macaque model for *M. tuberculosis* infection and disease progression to demonstrate the feasibility of stereologic sampling principles for the quantitation of bacterial burden and lesions (granulomas) in lung of experimentally infected animals. In addition, a computerized tomography (CT) imaging method was tested in a pilot study to monitor disease progression; the results showed that CT could be used to assess the impact of anti-*M. tuberculosis* drugs and vaccines during the live-phase of preclinical trials [Excluded by Requester] 2011]. These findings offer significant promise with regard to the considerable challenges to global human health by *M. tuberculosis* infections.

Immunomodulatory Mechanisms. [Excluded by Requester] a member of both the ID and the Reproductive Sciences and Regenerative Medicine Units, has used the macaque model for AIDS to show that regulatory T cells (Tregs) from young but not old macaques were associated with disease progression in SIV infected macaques [Excluded by Requester] 2012]. In an interventional study, Th17 and T-reg populations were pharmacologically altered to evaluate the impact of induced changes on disease progression; this work was performed in collaboration with [Excluded by Requester] (UCSF) and CNPRC Affiliates [Excluded by Requester]. Reduction in the size of the Th17 cell compartment was associated with increased bacterial translocation, higher viral loads, and less robust CD4+ T cell responses to SIV. These findings have significant implications for understanding immune-mediated protection against HIV. In comparative analysis of the gut and lung mucosae in SIV infection [Excluded by Requester] has identified protective mucosal innate immune networks including defensins [Excluded by Requester] UC Irvine) and innate anti-viral restriction factors [Excluded by Requester] 2011]. Experimental CD8+ T cell depletion studies [Excluded by Requester] UCSF) highlighted the importance of non-cytolytic T cell activity in anti-viral protection [Wong et al., 2010]. Current studies of microbiota and metabolomics with other Core and Affiliate Scientists show changes in the microbiota diversity at the mucosal sites during viral infection and inflammation.

2. Immunology and Vaccines

Novel CMV Vaccine Strategies. In studies with direct translational potential for human CMV infection, Dr. [Excluded by Requester] has shown that immunization of macaques with viral IL-10 elicited immune responses protective against RhCMV challenge; this result could fundamentally change the paradigm for human CMV vaccines [Excluded by Requester] et al., 2014]. In studies of vaccine safety, a collaboration between [Excluded by Requester] genetic modifications in RhCMV-based vaccine vectors have been demonstrated to result in significantly reduced pathogenesis in the exquisitely sensitive fetal macaque model. This work has set the basis for a new collaboration with [Excluded by Requester] (Oregon Health Sciences University) aimed at testing the safety of RhCMV vectors for vaccination against other viral and bacterial pathogens.

HIV/AIDS Vaccines and Genital Tract Immunity [Excluded by Requester] has shown that immunization with a chimeric live-attenuated simian/human immunodeficiency virus (SHIV) results in a systemic infection that induces a moderate population of SIV-specific CD8+ T and CD4+ T cells with cytolytic potential in the vaginal mucosa [Excluded by Requester] et al., 2012]. This study provides proof that vaccines can prevent infection after vaginal SIV

inoculation and suggests that a clinically relevant prophylactic vaccine for HIV can be developed. The results of additional vaccine studies using adenovirus (Ad) vectors in macaques recapitulated the lack of protection against HIV acquisition in the HIV STEP clinical trial. In collaboration with Merck Research Laboratories, Ad5 seropositive macaques immunized with the Ad5 vector SIV vaccine were shown to be at greater risk of challenge infection [Excluded by Requester et al., 2012]. [Excluded by Requester] has also studied mechanisms of sexually transmitted pathogens, including HIV/SIV and HSV-2. A full set of immune cells (B cells, plasma cells, T cells, dendritic cells) were identified in the penile tissues, and IgG and antiviral antibodies were detected on foreskin secretions [Excluded by Requester 2011]. This is the first description of antiviral effector immune responses in the foreskin of primates; next steps include eliciting antiviral immunity at this and other mucosal sites by immunization.

Innate Immune and Vaccine Mediated Control of Influenza A Virus Replication [Excluded by Requester] has also shown that treatment with IFN- α significantly reduced influenza A virus replication in the trachea of experimentally infected macaques [Excluded by Requester 2011]. Antibody present at the time of challenge, and not anamnestic B cell responses, conferred protection from the re-challenge. Novel proprietary adjuvants were shown to enhance immune responses to FluZone®, a commercial vaccine, and these enhanced responses improve vaccine-mediated control of virus replication in elderly and juvenile animals with important practical implications for humans [Excluded by Requester 2014].

3. Therapy for Infectious Pathogens and Disease

Viral Reservoirs in the SHIV/Macaque Model of Antiretroviral Therapy. In collaborative studies involving [Excluded by Requester] (Emory University), antiretroviral therapies based on either 3 or 4 drug combinations have been shown to suppress virus loads to very low levels in RT-SHIV infected macaques [Excluded by Requester et al., 2010; 2014]. Comprehensive analysis of the tissue and organ distribution of vRNA and vDNA demonstrated widespread persistence of residual virus in tissues during therapy. This model is very useful for testing pharmacologic therapies aimed at eliminating latent virus or establishing a “functional” cure.

Novel Therapies for Idiopathic Chronic Diarrhea (ICD). ICD is a significant problem at the NPRCs. Dr. [Excluded by Requester] (Project Scientist mentored by [Excluded by Requester]) and collaborators at UCSF have shown that treatment of macaques displaying ICD with helminths ameliorated colitis by restoring mucosal barrier functions and reducing overall bacterial attachment [Excluded by Requester 2012]. In addition, helminth colonization was associated with changes in the community of attached colonic bacteria. These results also defined ICD in macaques as a tractable preclinical model for ulcerative colitis in which these clinically beneficial effects can be further investigated. In studies with [Excluded by Requester] treatment of ICD with prebiotics (inulin) was associated with changes in GI microbiota and resolution in some animals.

Service Activities. Core Scientists actively engage in a variety of services that enhance the nonhuman primate resource. These include model and assay development, colony management, diagnostics, training, and committee work. Members of the ID Unit have developed many key reagents and techniques to investigate host-pathogen interactions for several viral and bacterial agents (see below). These efforts are critically important for establishing specific colony management practices and infrastructure improvements. The Unit has the expertise needed to enhance the quality of macaques in the colony through studies of the microbiome and its influence on health and disease in a wide age-range of animals. Four Unit members have also served as reviewers of CNPRC pilot project proposals, and two have served as collaborators:

- [Excluded by Requester] Department of Microbiology and Immunology, UC Davis, with CNPRC Core Scientist [Excluded by Requester] “Conversion of Regulatory T-cells in the Gut during Acute SIV Infection”
- [Excluded by Requester] PhD, Genome Center, UC Davis with CNPRC Core Scientist [Excluded by Requester] “Assessment of a Nonhuman Primate Model of Human Mammary RNA during Lactation” [Excluded by Requester et al., 2013]

Members of the Unit have contributed extensively to services in the **Immunology and Pathogen Detection Resources Core**. In particular, [Excluded by Requester] has developed assays and reagents for detecting RhCMV (antibody and PCR assays for virus) and played a key role in establishing the SPF Level 2 macaque colony [Excluded by Requester 2008]. For immunological studies, validated assays have been developed by [Excluded by Requester]

for quantitation of functional Treg cells, IL-17-producing cells such as Th17 and Tc17 cells, and comprehensive panels for phenotyping antigen-presenting cells [Excluded by Requester] expertise in detection and epidemiology of *H. pylori* is valuable for collecting data on the prevalence of this agent in different age groups of macaques. His laboratory has developed culture, PCR, and serological (ELISA) assays that are used for monitoring transmission and seroprevalence of *H. pylori* in different SPF groups [Excluded by Requester] (Affiliate Scientist, prior Core Scientist) has developed a novel and sensitive antibody neutralization assay for measles virus to test monkey samples for surveillance studies and for monitoring efficacy of vaccination in the colony. In addition, the ID Unit has facilitated the testing of a commercial measles virus vaccine for use by the **NPRC Consortium**

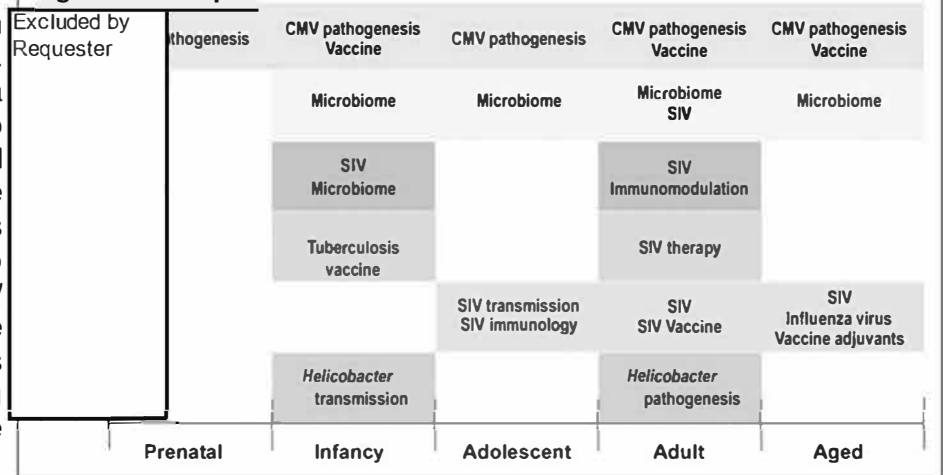
by participating in experimental design and data analysis. ID Unit members maintain inventories of various reagents and specimens obtained during the course of their research projects. This material (i.e., cryopreserved cells, cryopreserved and fixed tissues, histology slides, plasma samples, antibodies), as well as relevant data (e.g., clinical information) is available upon request. Each member has shared various items and protocols with both intramural and extramural investigators.

INNOVATION

Facilitating Use of Macaque Models of Human Disease. The ID Unit has the expertise and capability to contribute to new studies of infection and immunity over the entire age-range of macaques. Accordingly, the Unit is fully aligned with the

overarching theme of lifespan health research at the CNPRC (Figure 3). The human immune system is in a state of flux from birth onward due to developmentally regulated events and the host's responses to a wide range of beneficial and pathogenic infectious agents. Repeated exposure to antigens, particularly chronic/persistent infections, may shape the immune system such that deleterious long-term effects, including inflammation and immune senescence, become manifest later in

Figure 3. Lifespan Health Research in the ID Unit



life. Rhesus macaque models, closely reflecting human conditions, are being used to investigate if, and to what extent, the immunological environment differs between juvenile and adult monkeys infected with persistent infectious agents, including RhCMV and *H. pylori*. These studies aim to study the interplay of immunomodulatory functions of the agent and maturation of host immune responses at the molecular and cellular levels. The Unit is well positioned for new studies aimed at defining the impact of the microbiome in health and disease and for exploring new interventional strategies against infectious pathogens as part of the broader emphasis on lifespan research. Examples of original investigations in macaques include studies of HSV-2 transmission and its role as a cofactor for infection with other pathogens, ligated intestinal loop model for investigating pathogen interactions and disease mechanisms, effects of *H. pylori* infection on the gastric microbiota, and development of a vaccine against RhCMV.

Forefront of Nonhuman Primate Research. In support of the highly translational nature of this research, several Unit members have IRB approval for studies involving human subjects or are currently involved in nonhuman primate studies that serve as a preclinical venue for subsequent clinical trials. Several Unit investigators have initiated studies using genomics and transcriptomics technologies with an emphasis on analyzing both microbial flora (microbiomics, viromics) and host responses (pathways and networks of innate and adaptive immunity, stress responses, and regulatory and metabolic responses). In keeping at the forefront of biomedical research, members of the ID Unit are investigating infection and immunity in relation to aging (Figure 3). As mentioned above, the ID Unit has played a major role in the development of new diagnostics for macaques that directly detect infectious agents (e.g., RhCMV, *H. pylori*, measles virus) and host responses; these methods have been used to study transmission and define prevalence in colony macaques at the CNPRC. New studies on the microbiome at multiple anatomic sites (i.e., GI tract, vagina, oral cavity, lung) position the ID Unit at the forefront of nonhuman primate microbiome research.

APPROACH

Specific Aim 1. Advance the CNPRC resource through scientific contributions to understanding host-pathogen interactions and treatment of infectious diseases across the age spectrum.

Members of this Unit seek opportunities for basic infectious disease studies with potential for translation into clinical application through intra- and extramural interactions (Figure 2). Importantly, this Unit is well integrated into the prominent theme of comparative medicine and animal modeling at UC Davis and within the emerging theme of lifespan health research (Figure 3). Examples of specific future research activities of ID Unit members, and their collaborators, are highlighted for each of the three investigational themes.

1. Infectious Disease Models and Mechanisms of Pathogenesis

HSV-2 Model

Excluded by Requester is collaborating with Excluded by Requester (University of Washington) to define the pathobiology of vaginal HSV-2 infection in nonhuman primates and the effect of HSV-2 infection on vaginal SIV transmission. He has established the HSV-2 infection model in rhesus macaques and made progress defining the virology and immunology of HSV-2 infection. After optimization, this model will enable the testing of candidate prophylactic HIV-1 and HSV vaccines and microbicides in a biologically relevant context.

CMV in Neurodevelopmental Disease.

In a collaborative project with researchers at the UC Davis MIND Institute, Excluded by Requester aims to determine whether congenital CMV infection significantly increases the risk for postnatal development of autism spectrum disorder (ASD). This collaboration includes Excluded by Requester (Department of Public Health Sciences) and Core Scientist Excluded by Requester (Brain, Mind, and Behavior Unit) who studies ASD-like disease in rhesus macaques. Substantiation of a potential role of CMV in humans will lead to novel avenues of investigation.

H. pylori Pathogenesis. Expression of the *H. pylori* type IV bacterial secretion system (T4SS), involving a pathogenicity island, is being analyzed during colonization and infection in rhesus macaques. Excluded by Requester studies the role of CagY as a molecular switch that alters the function of the T4SS and “tunes” the host inflammatory response so as to maximize persistent infection. Because immune tolerance early in life may alter selection of CagY variants, he will also examine the effects of age on CagY on T4SS function through collaboration with Excluded by Requester (Respiratory Diseases Research Unit).

2. Immunology and Vaccines**AIDS and Mucosal Immunology/Vaccines.**

Excluded by Requester have developed a model to characterize the role of vaginal inflammation and its relationship to the vaginal microbiome; these efforts will investigate the mechanism by which bacterial vaginosis enhances HIV-1 transmission. Additional studies are aimed at determining if the antiviral immune response found in the foreskins of SIV-infected macaques are also present in men. Excluded by Requester has obtained IRB approval in collaboration with Excluded by Requester (Department of Medicine), for studies to determine how best to elicit antiviral immunity in the foreskin by vaccination.

GI Tract Mucosal Immunology

Excluded by Requester focuses on the effects of SIV infection on immune sensing and the subsequent responses of the gut mucosal immune system to bacterial pathogens versus non-pathogenic commensal bacteria in the GI tract. Assays for the measurement of changes in the gut microbiota of rhesus macaques are being established in the UC Davis Host-Microbe Systems Biology Core (see Aim 2). The novel intestinal loop model will be utilized to analyze molecular and immunologic aspects of early gut mucosal responses to pathogens compared to responses to commensal microbiota during SIV infection.

CMV Vaccines.

In collaboration with Excluded by Requester (Oregon Health and Science University), Drs. Excluded by Requester are evaluating the pathogenic potential of modified RhCMV-based SIV vaccine vectors. They will determine whether genetic modifications in the RhCMV genome reduce intrauterine pathogenesis.

Vaccines against Acute Viral Pathogens

Excluded by Requester aims to determine the nature of the immune responses that protected influenza virus H3N2-immunized macaques from challenge with the heterosubtypic H1N1 virus. In collaboration with the NIH Vaccine Research Center, he will define immune correlates to develop an anti-influenza virus vaccine that can reliably elicit appropriate responses. With the veterinary staff at the CNPRC (see **Primate Medicine Services**), Excluded by Requester is testing a new live-attenuated measles virus vaccine and ways to establish rapid diagnosis of viral exanthem in colony animals. In addition, he plans to study improved methods and adjuvants for infant vaccination against measles virus infection.

3. Therapy for Infectious Pathogens and Disease**Anti-Latency Therapy for HIV/AIDS.**

As members of the NIH-supported Collaboratory of Antiviral Researchers for Eradication (CARE) of HIV-1, Excluded by Requester (Affiliate Scientist) have begun to test novel pharmacologic approaches for inducing (reactivating) virus from latent cell reservoirs in the SHIV/macaque model. Novel “anti-latency” compounds that regulate viral transcription are being tested for safety and efficacy at either reducing or eliminating virus from reservoirs.

Treatment for ICD.

Serum-derived bovine immunoglobulin (SBI) is composed primarily of concentrated bovine IgG. Excluded by Requester mentored by Excluded by Requester plans to study the effects of SBI treatment on ICD in macaques. The hypothesis is that SBI consumption can alter the microflora composition as well as neutralize the toxins (e.g., immunopotent TLR ligands) of colonic bacteria. The results of such studies on mitigating ICD will impact the health and well-being of colony macaques.

Contribute towards the understanding of lifespan health by investigating immune ontogeny and aging.

A major area of study focuses on the long-term effects of persistent pathogens on the immune system which is in a dynamic state from birth onward due to developmentally regulated events and the host's responses to a

wide range of beneficial and pathogenic infectious agents. The SPF Level 2 colony is approaching 12 years of existence and thus provides a uniquely valuable resource for investigators to study the indigenous viral flora in relation to development and maturation of the immune system as well as susceptibility to various pathogens.

Immune System Development Impacted by Persistent Infection [Excluded by Requester] aim to characterize the immunological differences between juvenile and adult monkeys infected with persistent viruses, notably RhCMV. Statistical analyses reveal significant differences between age and SPF cohorts in: percentages and absolute numbers of peripheral lymphocyte subsets, concentration of cytokines secreted by peripheral blood mononuclear cells in response to mitogen and RhCMV antigen, and the percentage of animals shedding RhCMV. Importantly, these results provide a basis for further studies that will test the hypothesis that early exposure to CMV imparts a long-term impact on host immune function that, coupled with an aging immune system, restricts the generation of protective levels of vaccine-induced immunity.

Immune System Maturation and Microbiota. Recent studies by [Excluded by Requester] and Ardeshir have shown that breast-fed infants develop robust populations of memory T cells, as well as Th17 cells within the memory pool, while bottle-fed infants do not. These findings may partly explain the variable human susceptibility to conditions with an immune basis, as well as variable protection against certain infectious diseases. These investigators also characterized differences in the microbiota of the breast- and bottle-fed groups, thus setting the stage for analyzing microbial components in immune system maturation and for testing diets and other interventions that modulate immunologic development.

Provide scientific expertise to advance the development of novel macaque microbiome resources.

There is increasing recognition that the composition of the primate microbiome may have far-reaching implications for health and disease. Developments in “-omics” methods offer important new opportunities to enhance infectious disease research in nonhuman primates and thereby enhance translation.

Microbiome Resources. Several Unit investigators have initiated studies that use genomics and transcriptomics technologies to analyze interactions of the microbial flora and host responses. The campus Host-Microbe Systems Biology Core in the School of Medicine [Excluded by Requester] (Affiliate Scientist in the Department of Microbiology and Immunology), as well as other -omics facilities and bioinformatics capabilities at UC Davis, will be essential for these activities (see **Overview**). The partnership with BGI will enable high volume DNA and RNA sequencing. Further expansion and coordination of -omics research at the CNPRC will be important for implementing a “systems biology” approach to understand the complexities of infectious diseases, particularly chronic infections in outbred species such as rhesus monkeys.

Macaque Microbiome. Several CNPRC investigators have initiated studies of macaque microbiomes found in healthy animals and in association with certain diseases. [Excluded by Requester] uses the SIV/macaque model for HIV transmission to investigate the vaginal microbiome in relation to the potential increased risk of viral acquisition. [Excluded by Requester] has developed the intestinal loop model to analyze molecular and immunologic aspects of early gut mucosal responses to pathogens versus commensal microbiota during SIV infection.

[Excluded by Requester] have generated data supporting the hypothesis that neutralization of proinflammatory bacterial antigens will resolve colonic inflammation. Accordingly, the role of the microflora composition in ICD will be studied, and therapies will be tested to neutralize toxins.

Specific Aim 2. Provide nonhuman primate expertise and services to investigators at the regional and national levels to advance NIH-supported research excellence.

Unit Core Scientists fulfill their roles by providing a variety of services that enhance the nonhuman primate resource. For example: (1) **Colony management** in the oversight and serological/molecular analyses of the SPF colonies; (2) **Infrastructure improvements** in the development of BSL3 housing and extramural funding; (3) **CNPRC Committees** including the Colony Management, Research Advisory, and Infection Control Committees, as well as University committees such as the Institutional Animal Care and Use Committee; (4) Core Services such as the **Immunology and Pathogen Detection Resources Core**.

The composition of the nonhuman primate microbiome may have far-reaching implications for health. Accordingly, the ID Unit is taking the lead in a comprehensive characterization of the microbiome in various macaque SPF populations at the CNPRC in different age groups. Studies of the microbial flora will be integrated with studies of host responses. A biological specimen repository, consisting of rectal swabs and fecal samples from macaques, has been established and will be expanded to several age groups. Plans include making portions of these samples available to other investigators pursuing microbiomics and metabolomics investigations. Future plans also include the creation of a digital repository of freely accessible experimental protocols to facilitate expanded studies of various pathogens in macaques; depositing viral and

bacterial strains with American Type Culture Collection (or equivalent) to facilitate distribution of key reagents; and increase outreach to investigators who plan to translate nonhuman primate studies into clinical trials.

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

All members of the ID Unit have been actively involved in teaching, training, and mentoring as well as in various research communication activities and outreach. Core scientists provide didactic lectures at the graduate and undergraduate levels, actively participate in graduate programs and teaching, maintain leadership roles in seminars and symposia, and serve as research mentors for veterinary students through the Students Training in Advanced Research (STAR) program, and for CNPRC staff, fellows, junior faculty, and visiting scientists. Graduate group membership (leadership roles) for ID Unit Core scientists includes: Comparative Pathology (Academic Advisor, Executive Committee, Chair of Educational Policy committee), and Microbiology (Academic Advisor). Participation in teaching includes (*Instructor of Record): PMI270 (Advanced Immunology), PMI128* (Animal Virology), PMI290* (Graduate Seminar), MMI210 (Animal Models of Infectious Diseases), MMI480A (Medical Immunology), MMI480B (Medical Microbiology), MIC162 (Virology), and MIC262* (General and Molecular Virology). Specific examples of ID Unit mentoring of individuals supported by NIH training grants include [Excluded by Requester] in the Animal Models of Infectious Diseases Training Program [Excluded by Requester] in the CTSC T32 Predoctoral Clinical Research Training Program, and [Excluded by Requester] in the NIH Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Training Program.

Infectious disease research in nonhuman primates will benefit from interactions with several new university-wide biomedical research activities that are described in the overall section including the CTSC, Data Science Institute, Human Genomics Initiative, Center for Mucosal Health, and the West Coast Metabolomics Center (see **Overview**). An important example of a new program that highlights integration of the CNPRC with the UC Davis campus is the Research Investments in Science and Engineering (RISE) Program. A major project in the RISE program, "Protecting the Fragile Intestine: Integrating Microbiota and Mucosal Health", is led by ID Unit

Core Scientist [Excluded by Requester] with key faculty drawn from several other departments. Since funding of the RISE proposal, several new NIH grants have been submitted by CNPRC Core and Affiliate Scientists that address the microbiome from a variety of anatomical perspectives; this is anticipated as another area of research growth during the next funding period. The Center for Comparative Medicine, located immediately adjacent to the CNPRC, promotes the concept of "One Medicine" through interdisciplinary comparative medical research, teaching, and model development. Its research mission is to investigate the pathogenesis of human disease, using experimental animal models and naturally occurring animal diseases. Importantly, four CNPRC Core Scientists are members of the CCM faculty [Excluded by Requester]

Two new Core Scientists in the ID Unit will be an excellent complement to the basic and translational research activities in the Unit and will contribute to the management of the resource. Candidates will have PhD, MD, DVM, or combined degrees and will enter at the Assistant or Associate Professor level. These individuals will have strong accomplishments in infectious disease research and animal modeling. Examples of research activities include development of new nonhuman primate models of infectious pathogens, immunology and vaccinology studies, development of novel therapies for infectious diseases, and analysis of the microbiota in health and disease. Such studies can be conducted in a wide age-range of animals and thus will enhance the theme of lifespan research at the CNPRC. Through studies of host-pathogen interactions, new Core Scientists can contribute to the animal resource, for example by characterization of the infectious agents and microbiota in colony macaques and development of new assays for infectious agents and host responses. Appointments may be in the School of Medicine (e.g., Microbiology or Pathology, Division of Infectious Diseases) or in the School of Veterinary Medicine (Pathology, Microbiology, and Immunology).

Specific Aim 4. Ensure the highest standards of research and animal care for the CNPRC resource.

ID Unit Core Scientists will continue to play an active role in maintaining the health of CNPRC colony animals through participation in the Colony Management and Infection Control Committees, and other key infrastructure and administrative functions related to immunology and infectious diseases.

CORE SCIENTIST NARRATIVES

Core Scientist [Excluded by Requester] Professor, Department of Pathology and Laboratory Medicine, School of Medicine, CCM Director, Interim CNPRC Director

Research Program [Excluded by Requester] has characterized the natural history of RhCMV infection in the breeding corrals of rhesus macaques in which RhCMV is endemic, and his laboratory develops key reagents and techniques to

investigate molecular, virological, and immunological parameters of RhCMV infection for use at the CNPRC and at other institutions. In collaboration with [Excluded by Requester] (Oregon Health and Science University) [Excluded by Requester] are evaluating the pathogenic potential of modified RhCMV-based SIV vaccine vectors. In studies in macaques directly related to lifespan health [Excluded by Requester] is conducting a comprehensive analysis of the immune system. These studies may identify novel approaches to deal with problems associated with immune senescence, such as poor responses to vaccines in elderly individuals.

Contributions to the CNPRC Mission: CNPRC Interim Director; Research Advisory Committee; Infection Control Committee; development of the macaque model for studies of RhCMV pathogenesis and vaccination; mentor trainees pursuing research in nonhuman primates; 18 publications (May 1, 2010-April 30, 2014).

Core Scientist: [Excluded by Requester] **PhD**, Professor and Chair, Department of Microbiology and Immunology, School of Medicine

Research Program: [Excluded by Requester] research program focuses on GI tract pathogenesis and defenses in the SIV/macaque model for simian AIDS. This includes studies of the effects of SIV infection on the magnitude and nature of the gut mucosal immune response to incoming pathogens or co-infections, specifically *Salmonella typhimurium*, role of gut mucosal innate immunity by characterizing functional defects in key immune cells, impact of initiating early antiretroviral therapy in reversing GI tract mucosal damage and restoring the mucosal immune functions, and development of novel assays for measuring cytokine responses at the single-cell level.

Contributions to the CNPRC Mission: Leadership in mucosal immunology and microbiome research; Director, Host-Microbe Systems Biology Core; Collaborations with Affiliates studying innate immunity and the microbiome, mentorship of trainees and junior faculty interested in nonhuman primate research; intra- and inter-Unit collaborations and synergy for projects focused on mucosal immunity; 18 publications (May 1, 2010-April 30, 2014).

Core Scientist: [Excluded by Requester] Assistant Professor, Department of Microbiology and Immunology, School of Medicine, Immunology and Pathogen Detection Resources Core

Research Program: [Excluded by Requester] studies the interplay of host-microbe interactions in relation to immune system development. His work on immune regulation, with an emphasis on Th17 and Treg cells, sets the stage for exploring the role of the microbiome in setting the balance of T cell subsets with implications for inflammation in the GI tract, particularly in the SIV/macaque model of simian AIDS. He participates in research on defining mechanisms of pathogenesis of ICD and testing novel immunomodulatory treatment modalities. His studies are also examining the impact of microbial colonization on maturation of the immune system.

Contributions to the CNPRC Mission: Lead, Immunology and Pathogen Detection Resources Core; leadership within the CNPRC on microbiome and metabolome projects; collaborations with Affiliate investigators studying the interplay of the microbiome and host immune development; mentoring trainees interested in nonhuman primate research; intra- and inter-Unit collaborations and synergy for projects focused on tolerance and microbial trafficking; 7 publications (May 1, 2010-April 30, 2014).

Core Scientist: [Excluded by Requester] **PhD**, Professor, Department of Pathology and Laboratory Medicine, School of Medicine, Unit Leader

Research Program: [Excluded by Requester] has studied molecular mechanisms of pathogenesis in rhesus macaques experimentally infected with SIV/SHIV clones and has collaborated with extramural investigators to test anti-HIV vaccine and drug therapy approaches in simian AIDS models. In the SHIV/macaque model, he studies highly active antiretroviral therapy (HAART) and viral reservoirs [Excluded by Requester] is using this model to test novel therapeutic approaches, based on small-molecule viral inducers that aim to eliminate virus from these reservoirs in a multidisciplinary collaboration supported by a U19 grant from NIH which involves 17 principal investigators from 12 research institutions and industry. Additional related studies aim to analyze pharmacologic properties of viral activators and the penetration of antiretroviral drugs and in the RT-SHIV/macaque model.

Contributions to the CNPRC Mission: Unit leader; Research Advisory Committee; development of protocols for sensitive detection of SIV/SHIV RNA and DNA in tissues and body fluids; leadership on HAART and novel approaches for treating latent HIV infection; multiplex serological detection of *M. tuberculosis* and pathogenesis/vaccine model of TB in macaques; 17 publications (May 1, 2010-April 30, 2014).

Core Scientist: [Excluded by Requester] **DVM, PhD**, Professor, Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine

Excluded by
Requester

Research Program has maintained a long-standing research program in AIDS vaccine development and immunology in macaques. He has studied correlates of protective immunity of live-attenuated SIV vaccines, developed the mucosal membrane transmission models for SIV infection via vaginal mucosa and penile membranes, and tested prophylactic microbicides. This includes pioneering studies of innate immunity and both cellular and antibody responses in these mucosal tissues. He has expanded his research into studies of influenza virus A infection and immunity to this virus in macaques and has shown the importance of adjuvants for eliciting protective immunity in elderly populations. He has begun to develop a macaque model for HSV-2 transmission and pathogenesis and is characterizing the vaginal mucosal microbiome in relation to inflammation and potential effects on viral transmission.

Contributions to the CNPRC Mission: Development of protocols for analysis of adaptive and mucosal immune responses; leadership in viral transmission *via* mucosal membranes; 29 publications (May 1, 2010-April 30, 2014).

Excluded by
Requester

Core Scientist MD, PhD, Professor, Department of Medical Microbiology and Immunology, School of Medicine

Excluded by
Requester

Research Program is a microbiologist and infectious diseases physician with a longstanding interest in the pathogenesis of *Helicobacter pylori*. About 5 years ago he made the interesting observation that the functionality of the *H. pylori* type IV secretion system (T4SS), encoded on the *cag* pathogenicity island (*cagPAI*), is lost during experimental infection of rhesus macaques. This is a strategy used by the bacterium to modulate the host inflammatory response to its own purposes. He discovered that the key protein is CagY, an essential component of the *H. pylori* T4SS that has an unusual sequence structure. He aims to analyze this novel strategy by which a bacterial secretion system alters the host immune response, identify the mechanisms where the T4SS and host immunity intersect, and thereby develop a broader understanding of the relationship between chronic infection and inflammation.

Contributions to the CNPRC Mission: Characterization of the prevalence of *H. pylori* in macaques, development of immunological and PCR-based assays; 16 publications (May 1, 2010-April 30, 2014).

Table 4. Infectious Diseases Research Unit Externally Funded Grants

PI (Core Scientist PI)	Institution	Type	Title	Description
Excluded by Requester	University of North Carolina	NIH R21 (AI077373)	A Rhesus Macaque Model of SIV-Malaria Co-Infection	Goal is to develop a macaque model to study malaria infection and test interventions
		NIH R21 (HD056051)	A Nonhuman Primate Model of Infant CMV Infection	Evaluates immune responses to primary RhCMV infection in neonatal macaques
		NIH R01 (DE019064)	A Novel Oral Combination Pediatric HIV and TB Vaccine to Prevent Breast Milk Transmission	Adjuvanted DNA/ MVA vaccines will be tested for SIV Infection in infant macaques
	UC Davis	NIH R01 (AI049342)	A Nonhuman Primate Model for Cytomegalovirus Vaccines	Evaluates RhCMV viral IL-10 as a vaccine antigen
		NIH R01 (AI063356)	Evaluation of Protective CMV Vaccines in Rhesus Macaques	Tests RhCMV vaccines-based immunization with DNA and whole inactivated virus
		NIH R01 (AI097629)	Vaccine-Mediated Targeting of Viral IL10 to Control HCMV Shedding and Reinfection	Studies post-exposure vaccination of macaques with RhCMV-encoded viral IL-10 protein for reduced shedding and protection
		NIH R01 (AI049342)	Prevention of Primary HCMV Infection by Vaccinating Against HCMV Encoded-IL10	Goal is to produce and purify RhCMV gB as a vaccine antigen to be used with vIL-10
	University of New Mexico	Private Source	Assessment of HCMV Vaccine Strategies in Rhesus Macaques	Evaluates proposed human CMV (HCMV) vaccine modalities in macaques
			Evaluation of a CCR5 Vaccine for HIV Infection in the SIV/Macaque Model	Immunization with CCR5 co-receptor will be tested as a vaccine against SIV infection

Excluded by Requester	UC Davis	NIH R01 (DK043183)	Pathogenesis of Intestinal Dysfunction in Simian AIDS	The cellular basis of intestinal effects of SIV infection will be analyzed
		NIH R01 (AI043274)	Intestinal Cytokine and T Cell Homeostasis in SIV Infection	Uses an intestinal loop model in SIV infected macaques to study host-microbe interactions
		NIH R01	HIV Reservoir and CD4 Repopulation in Gut Lymphoid Tissue	Effects of immune activation in GALT on HIV replication and pathogenesis are studied
	UC Irvine	NIH R56 (AI093953)	Evaluation of a Subunit Chlamydia Trachomatis Vaccine in Rhesus Macaque	Evaluates the efficacy of a new vaccine for chlamydia
	Private Source	NIH R01 (AI103960)	HCMV Vaccine Produced from BAC-MVA that blocks Epithelial and Fibroblast Entry	Evaluates MVA constructs of HCMV vaccine antigens for immunogenicity in rhesus monkeys
		NIH U01 (AI074512)	Adjuvant Enhanced Antiviral Immunity	Evaluate the usefulness of adding a CLDC adjuvant to influenza vaccines
	UC Irvine	NIH R01 (AI102715)	The Impact of Antibody and pH on Female-to-Male SIV Infection	Goal is to determine infectivity of immune-complexed viral particles in macaques exposed by foreskin inoculation of SIV
	UC Davis	Private Source	Oral Drug Treatment for Enhanced Immune Control Over HIV Replication	Oral antiretroviral drug regimens will be tested for inhibition of SIV in the SIV/macaque model
	UCSF	NIH R21 (EY018559)	Aberrant T Cell Function and Immunopathogenesis of CMV Immune Recovery Uveitis	Aberrant T cell function in CMV IRU is linked to differential restoration of inflammatory and regulatory T cell subsets
	Private Source	NIH U01 (AI070976)	A Novel Systemic and Mucosal Adjuvant for Biodefense	Evaluate the usefulness of adding a VEE replicon adjuvant to influenza vaccines
	University of Wash	NIH R01 (AI078229)	Evolution and Emergence of Simian Retroviruses in South Asia	Evaluates the presence of SFV and SRV in humans in Bangladesh
	University of North Carolina	NIH R01	Drug Bio-Distribution in HIV Tissue Reservoirs	Use a novel mass spectrometry approach to assess levels of antiretroviral drugs in tissues
	UC Davis	Private Source	Pharmacologic Properties of Viral Inducers	Define the pharmacologic properties of anti-HIV latency agents in macaques
			Evaluation of Novel Anti-TB Vaccines in Nonhuman Primates	This project tests new anti-TB vaccines based on attenuated <i>M. tuberculosis</i> vectors
	UC Davis	NIH U19 (AI096113)	Martin Delaney Collaboratory to Eradicate HIV Infection	Develop novel pharmacologic approaches to induction of HIV/SIV from latent reservoirs
	UC Davis	Private Source	Meningococcal Vaccines in Infant Rhesus Macaques	New meningococcal vaccines will be tested for immunogenicity
	UCSF	NIH U19	Bay Area Hepatitis C Cooperative Research Center	Examine differential effectiveness of anti-HCV drug regimens and effects on NK cells and APC
	UC Davis	NIH P01 (AI082278)	Mechanisms of Protection from and Enhanced Susceptibility to HIV Infection and Vaccination	This project models the HIV STEP vaccine trial where adenovirus responses may have enhanced HIV infection
		NIH R01 (AI094620)	SIV Transmission in Male Nonhuman Primate	Define the virology and immunology of penile SIV transmission

Excluded by Requester		Dept of Defense	Effect of FGI-101-1A6 on SIV Transmission	Evaluate the ability of a monoclonal antibody to block SIV transmission or suppress virus
		NIH R01 (AI098488)	Modeling Inflammation in HIV Transmission	Define local cellular immunity in macaques inoculated with HSV-2 on reactivation and SIV infection
	Private Source	NIH R01 (RR025996)	Primate Model Towards HIV Eradication Strategies	A combination of 5 anti-retroviral drugs will be tested in the SHIV/macaque model
		NIH R01 (AI095113)	Development and Characterization of Safety-Enhanced RhCMV/SIV Vectors	Study RhCMV vectors for attenuation and induction of protective anti-SIV immunity
		NIH P01 (AI094417)	Development of an Effector-Memory T Cell AIDS Vaccine (Core B)	Study RhCMV vectors for attenuation and induction of protective anti-SIV immunity
		Private Source	Development of an attenuated CMV vector for an HIV/AIDS vaccine	Test the safety of attenuated RhCMV vaccine vectors after inoculation into macaques
	UC Davis	NIH R01 (DE021273)	Attenuated RhCMV Delta 10 SIV Oral Vaccine Vectors Encoding TLR5 Ligands	Determine if a TLR2 agonist can augment the protection immune responses from an RhCMV vector
		NIH R21 (AI088471)	Development and Immunogenicity of Attenuated RhCMV Delta 10 Vaccine	Evaluates whether deletion of RhCMV-encoded viral IL-10 improves immunogenicity of RhCMV vectors for SIV
	UC Davis	NIH R01 (AI081037)	Role of <i>H. pylori</i> Outer Membrane Proteins in Colonization and Host Response	Studies the role of outer membrane Bab proteins in <i>H. pylori</i> colonization and host response
		NIH RC1 (AI086597)	Defensin Gene Copy Number and Primate Innate Immunity	Examines the role of number of defending genes in innate immunity
		NIH R21 (AI080788)	<i>Helicobacter pylori</i> and the Gastric Microbial Community in Rhesus Macaques	Examine the effects of <i>H. pylori</i> on the gastric microbial community, and in turn study the effect that this community has on <i>H. pylori</i> colonization
		NIH R01 (AI070803)	Modulation of Outer Membrane Protein Expression in <i>Helicobacter pylori</i>	Analyzes changes in OMP expression and bacterial colonization
	University of Tennessee	NIH RC1 (AI078514)	Development of a Novel Gastrointestinal Radiomitigator	Preclinical development of a GI radiation countermeasure
		NIH RC2 (AI087550)	Preclinical Development of a GI Radiation Countermeasure	Preclinical development of a GI radiation countermeasure
	UC Davis	Private Source	Evaluation of Long-term Efficacy and Safety of Anti-Viral Drugs in Monkey Models	Testing of efficacy of antiretrovirals in SIV-infected rhesus monkeys
			Preclinical Safety, Toxicity, and Immunogenicity of ContreVir	Testing a proprietary intervention for viral infection in macaques
	Private Source	NIH P01 (AI058708)	Molecular Mechanisms of HIV Post-Integration Latency	Uses the SHIV/macaque model to test novel anti-latency compounds

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

PUBLICATIONS (May 1, 2010 to April 30, 2014)

- Excluded by Requester
- Excluded by Requester Vaccine-induced control of viral shedding following rhesus cytomegalovirus challenge in rhesus macaques. J Virol 85:2878-2890, 2011. PMCID: PMC3067943
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- Excluded by Requester
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- Excluded by Requester
- Excluded by Requester Protein arginine methyltransferase 1-directed methylation of Kaposi sarcoma-associated herpesvirus latency-associated nuclear antigen. J Biol Chem 287:5806-5818, 2012. PMCID: PMC3285351
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- Excluded by Requester
- Excluded by Requester Efficacy of influenza vaccination of elderly rhesus macaques is dramatically improved by addition of a cationic lipid/DNA adjuvant. J Infect Dis 209:24-33, 2014. PMCID: PMC3864389
- Excluded by Requester
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PPAR γ -

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SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, and the IACUC.

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1. **Proposed Use of Animals.** The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal] of indoor animal space. The outdoor animal housing area includes [Specific Animal] field corrals, [Specific Animal] corn cribs, [Specific Animal] [location]. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. **Justification of Animal Use, Species Choice, and Numbers.** The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.
3. **Veterinary Care.** The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian), [Excluded by Requester] Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations.

Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

- 4. Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
- 5. Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

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SCIENTIFIC UNITS: INFECTIOUS DISEASES RESEARCH UNIT**LETTERS OF SUPPORT**

Letters of support from the individuals named below are provided on the pages that follow.

1.

Excluded by Requester

 MD, Principal Investigator, HIV Vaccine Trials Network, Fred Hutchinson Cancer Research Center
 2.

Excluded by Requester

 MD, PhD, Professor, Department of Pathology and Laboratory Medicine, University of California, Irvine
 3.

Excluded by Requester

 MD, Professor, Department of Medicine, Division of Hematology/Oncology, University of California, San Francisco
 4.

Excluded by Requester

 PhD, Professor, Department of Molecular Cell Biology, University of California, Merced
 5.

Excluded by Requester

 MD, PhD, Professor of Medicine; Chief, Division of Experimental Medicine, University of California, San Francisco
 6.

Excluded by Requester

 MD, Associate Director, Vaccine and Gene Therapy Institute, Oregon Health and Science University – West Campus
- and
- Excluded by Requester

 PhD, Senior Scientist, Vaccine and Gene Therapy Institute, Oregon Health and Science University – West Campus



HIV VACCINE TRIALS NETWORK

April 28, 2014

Excluded by Requester

Director
California National Primate Research Center (CNPRC)
University of California
Davis, CA 95616

Dear

Excluded by Requester

I am delighted to provide a letter of support for the renewal of the NIH Base Grant that supports the CNPRC. As you know, my personal research has been on STI infections in HIV-1; having made the initial observation that prevalent HSV-2 increases the rate of HIV-1 acquisition. Hence, our work together with Excluded by Requester a recently awarded R01 grant to determine how herpes simplex virus enhances SIV/HIV transmission is of direct relevance and importance. Ultimately, the goal of the grant is to test strategies to blunt HSV associated inflammation and lower HIV transmission. We must use Herpes B virus negative multiparous rhesus macaques for this study of vaginal SIV transmission. It is possible to obtain enough of these animals for these studies at only two primate facilities in the world, one of which is the CNPRC.

The relatively large size of the macaque population at the CNPRC and the rigorous approach to managing the colony provides investigators with unique animal populations that can be used to more accurately model human clinical conditions. Our HSV project is one example of how the large CNPRC colony supports important studies that may translate into important clinical advances.

Lastly, as head of the HIV Vaccine Trials Network, I have found the group's work in HIV vaccine development to be invaluable. In summary, the CNPRC offers a unique, large and well-characterized colony of NHP that has produced important nonhuman primate models of human diseases. I very much look forward to utilizing the resources of the CNPRC in our future work.

Sincerely yours,

Excluded by Requester

Principal Investigator, HIV Vaccine Trials Network

Fred Hutchinson Cancer Research Center
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UNIVERSITY OF CALIFORNIA, IRVINE

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Department of Pathology & Laboratory Medicine
School of Medicine

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FAX (949) 824-2160

July 1, 2014

Excluded by Requester

Interim Director – California National Primate Research Center
University of California, Davis

Dear

Excluded by Requester

It is with great pleasure that I offer my support for your P51 submission for the California National Primate Center (CNPRC) and to emphasize the critical need for the nonhuman primate model to advance studies of discovery in small animals to relevant hosts that recapitulate the human condition. I can directly attest to the vital importance of the CNPRC because I was able to leverage the results generated by a pilot project awarded to me by the CNPRC in 2010 to an R56 award from NIH (AI093953; 04/01/11-03/31/13). The work evaluated the immunogenicity of the native form of the Major Outer Membrane Protein (MOMP) of *Chlamydia trachomatis* in a relevant primate host. This study was predicated on our prior work demonstrating the immunogenicity of MOMP in a mouse model. However, since results in mice are often poor predictors of results in humans, we chose to take advantage of the opportunity provided by the call for Pilot Projects from the CNPRC to use the monkey model as a preclinical venue prior to potentially moving to human clinical trials. The results from the CNPRC Pilot project resulted in one manuscript (Vaccine, 29:3456-64, 2011), and the R56 award was conducted in rhesus macaques at the CNPRC with a collaborator. The value added conducting studies in macaques was evident by the results we have been able to generate following conducting vaccine/challenge studies with *C. trachomatis*. We are currently finishing the final *in vitro* studies and plan to submit this work for publication.

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Pending Support

Pending Support

The CNPRC is an invaluable resource that broadly serves outside investigators who would not otherwise have access to this model. In sum, I strongly endorse the macaque and intellectual resources available at the CNPRC as critical for translating animal studies to better diagnostic, prevention, and treatment modalities in humans.

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Professor, Department of Pathology and Laboratory Medicine

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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DIVISION OF HEMATOLOGY/ONCOLOGY
SAN FRANCISCO, CALIFORNIA 94143-1270

April 25, 2014

Excluded by Requester

California National Primate Research Center (CNPRC)
University of California
Davis, CA 95616

Dear

Excluded by Requester

This letter is written in support of the renewal of the NIH Base Grant that funds the CNPRC. Because of my long-standing research program on HIV/AIDS, I will address primarily the importance of nonhuman primates for studies of pathogenesis of AIDS and for anti-HIV interventions. Certainly, the physiological and immunological similarities to humans make rhesus macaques a highly relevant species for studying this pathogen as well as many other infectious diseases. The work of several investigators at UC Davis (e.g.,

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has advanced macaque models of SIV (and SHIV) infection for elucidating mechanisms of pathogenesis, vaccine development, and development of anti-viral therapies (including analysis of viral reservoirs). Because of the relatively large size of the macaque population at the CNPRC, this resource offers unique opportunities to conduct disease studies in a wide age range of animals. This fact is exemplified by previous and ongoing work on HIV infection and drug development in pediatric settings as well as in juvenile and adult animals. In addition, it is very important to recognize that this primate center has a highly trained veterinary staff and has optimized clinical care procedures that enable investigators to conduct comprehensive studies of acute and chronic infections.

The collective scientific and veterinary expertise at CNPRC is also particularly important for new efforts on the theme of lifespan health research and toward the investigation of the role of the microbiome in health and disease. As an example of my respect for the UC Davis Center and the importance of work with nonhuman primate models, I convene a meeting 2-3 times a year as part of the Bay Area Targeted Action Group for HIV Vaccines, sponsored by the AIDS Research Institute at UCSF. This meeting rotates through different locations in Northern California and is often held at UC Davis with attendance of about 50 scientists.

In summary, the CNPRC offers a robust environment for a wide range of disease studies in nonhuman primate models. I very much look forward to witnessing future accomplishments in both basic and translational biomedical research at the CNPRC.

Sincerely yours,

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Professor of Medicine

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Director
California National Primate Research Center (CNPRC)
University of California
Davis, CA 95616

Excluded by Requester

May 4, 2014

Dear

Excluded by Requester

I am delighted to provide a letter of support for the renewal of the NIH Base Grant that supports the California National Primate Research Center (CNPRC). I have had extremely productive interactions with the investigators at UC Davis Excluded by Requester and the staff at the CNPRC. I am a biochemist by training and have no prior experience of working with non-human primate models. Further, my research laboratory is at the University of California Merced, which is the newest UC campus, and our small animal facility has no plans to include primates. Since the trend at the NIH is toward translational research, I found myself unable to move from the lab to an animal model to continue my research. Therefore, I was extremely happy to begin a collaboration with Excluded by Requester in order to have access for the first time to primate models that could be used to advance our experiments. Excluded by Requester was extremely open and encouraging from our first meeting, actually suggesting a collaboration before I knew whether one might be feasible.

Working with

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and the Primate Facility staff has been an excellent experience. Everyone was very interactive, from initially working with me to set up the scientific basis of our proposed experiments, to determining the types of animals at the facility that could be used and how to do that most efficiently. The CNPRC researchers and staff were absolutely invaluable, as their extensive expertise of the in the studies of HIV prevention and pathogenesis using the SIV model of AIDS allowed us to map out our experiments. Our conversations were enlightening and thought provoking, and they continue to be so, in my continuing education regarding primate experiments. As we were preparing our recent grant proposal, the Davis group was extremely responsive, with multiple emails and phone conversations per day, allowing us to submit a strong grant proposal. **This collaborative interaction was critical for our success in obtaining this NIH grant in the first round (1R01AI112011-01 "Silk-based formulation for microbicide delivery").**

Our research is centered on developing proteins as highly potent HIV entry inhibitors. Our group has made many protein variants and studied them both structurally and functionally. The most exciting use of our recent work is in the field of "HIV microbicides" which are intended to prevent the sexual spread of HIV. The field has been moving very quickly, so while a couple years ago the common wisdom was that known inhibitors formulated into a gel would serve this purpose, very recent clinical trials have shown that more advanced formulations would be required. Properties that are now deemed necessary for clinical trials include stability at high temperatures, and time release capability, among others. This has required assembling a multi-disciplinary group of investigators from multiple institutions to form the best team for producing and testing new inhibitors and formulations.

Therefore, we are currently using our highly potent inhibitors in a silk film formulation, with the goal of determining whether this first-of-its-kind microbicide is suitable for human use. One of the first necessary steps is to examine the properties of the microbicide in non human primates, and these experiments will be carried out at UC Davis. There are very few animal models that are suitable for HIV studies, so it is critical for the experiments to have access to the UC Davis primate facility where SIV/SHIV can be used.

I support the renewal of the CNPRC in the strongest possible terms. The CNPRC offers a robust environment for a wide range of disease studies in nonhuman primate models. From a small, young university I was able to leverage their expertise and facilities to put together a multidisciplinary team that is now proceeding to carry out state of the art experiments that were otherwise simply not available to us. I very much look forward to working with CNPRC researchers and staff for future accomplishments in both basic and translational biomedical research.

Sincerely,

Excluded by Requester



University of California
San Francisco

Division of Experimental Medicine
Department of Medicine, San Francisco General Hospital

Excluded by Requester

April 28, 2014

Excluded by Requester

Director
California National Primate Research Center (CNPRC)
University of California
Davis, CA 95616

Dear

Excluded by Requester

I am very happy to provide this letter of support for the renewal of the NIH Base Grant that supports the CNPRC. For over three decades now, I've worked on various aspects of the HIV/AIDS epidemic, including the development and use of animal models of the disease. At this juncture, I'm convinced that the best model is within nonhuman primates – and it is clearly important to have centers such as yours. Indeed, the work of investigators at UC Davis (including

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and others) has advanced macaque models of SIV (and SHIV) infection for elucidating mechanisms of pathogenesis (including dysfunction of the GI tract), vaccine development (evaluation of various vaccine approaches and mucosal transmission of virus and immunity), and anti-viral therapies (including analysis of viral reservoirs). Given the relatively large size of the macaque population at the CNPRC and the fact that it is a breeding facility, this resource offers unique opportunities to conduct disease studies in a wide age-range of animals as exemplified by previous and ongoing work on AIDS pathogenesis and drug development in pediatric settings as well as juvenile and adult animals. As an example that highlights the importance of nonhuman primate models in general and of CNPRC in particular, I work on aspects of immune ontogeny and on the fetal immune response to HIV, and the only model system in which this can be done is in nonhuman primates – and the only nonhuman primate center in the world with the requisite capabilities is yours.

I wish you the best of luck in the submission of your grant. I very much look forward to future accomplishments in both basic and translational biomedical research at the CNPRC.

Sincerely yours,

Excluded by Requester

Professor of Medicine
Chief, Division of Experimental Medicine



July 3, 2014

Vaccine and Gene
Therapy Institute

Research Development and
Administration

505 N.W. 185th Avenue
Beaverton, OR 97006
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Interim Director

California National Primate Research Center, UC Davis
One Shields Avenue
Davis, CA 95616

Excluded by Requester

Dear

We are writing to offer our unequivocal endorsement for your Base Grant renewal submission to NIH. In particular, we want to emphasize the unique capabilities, expertise, and technologies the CNPRC offers to investigators using the nonhuman primate models for lifespan health. Our research at the Vaccine and Gene Therapy Institute (Oregon Health & Science University) focuses on exploiting key aspects of cytomegalovirus natural history to develop a novel vaccine platform for many of the infectious pathogens that continue to plague humanity throughout the globe, including HIV and *Mycobacterium tuberculosis*. We have been using the nonhuman primate model as a preclinical venue to evaluate whether engineered variants of rhesus cytomegalovirus (RhCMV) expressing ectopic antigens can induce protective immune responses against pathogen challenge. Our work in rhesus macaques has clearly demonstrated that RhCMV expressing antigens of SIV induce protective T effector cell-based immune responses that protect 50% of vaccinated monkeys against repeated low dose mucosal challenge.

A key step in advancing these studies to clinical trials is to evaluate RhCMV vector safety, and for this we have been using scientific expertise and research models available only through the CNPRC. In particular, we have had a long-standing and successful collaboration with

because of extensive work on RhCMV natural history and work on fetal growth and development.

Collectively, we have been able to construct modified RhCMV variants that (1) retain the potential for inducing protective immunity in juvenile and adult macaques, (2) are attenuated for growth in *in vivo*, and (3) are attenuated for pathogenesis for pathogenesis in the acutely sensitive fetal macaque model of Drs.

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The results from the fetal macaque model are critically informing our approach for developing human CMV-based vaccine vectors.

In sum, we strongly support the efforts by the CNPRC to maintain and expand the nonhuman primate resources for enabling preclinical studies in a highly relevant primate host prior to human clinical trials.

Sincerely,

Excluded by Requester

**Associate Director, Vaccine and Gene Therapy Institute
Oregon Health & Science University -- West Campus**

Excluded by Requester

**Senior Scientist, Vaccine and Gene Therapy Institute
Oregon Health & Science University -- West Campus**

SCIENTIFIC COMPONENTS: INFECTIOUS DISEASES RESEARCH UNIT

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Reproductive Sciences and Regenerative Medicine Research Unit

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No 1.a. If YES to Human Subjects Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No IRB Approval Date: Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No 2.a. If YES to Vertebrate Animals Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No IACUC Approval Date: Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No 4.b. If yes, please explain: 4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No 4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No 5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No 6.a. If yes, identify countries: 6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename RSRM_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	RSRM_BibliographyReferencesCited.pdf
10. Facilities & Other Resources	RSRM_FacilitiesOtherResources.pdf
11. Equipment	RSRM_Equipment.pdf

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT**ABSTRACT**

Core Scientists in the **Reproductive Sciences and Regenerative Medicine Research Unit** contribute to the California National Primate Research Center (CNPRC) mission through research projects supported by the NIH and other extramural sources (~\$41.5 million) and by data-sharing through peer-reviewed publications (~110); by contributing expertise to the reproductive management of the CNPRC colonies; through a range of services to the greater research community (e.g., CNPRC Cores, consultations, NIH-supported Centers and outreach programs); and by mentoring and training undergraduate and graduate students, postdoctoral/clinical fellows, and faculty at all levels. Unit Core Scientists have an outstanding track record in the formation of multidisciplinary partnerships and teams as evident by grants, publications, and integration with UC Davis NIH-supported Centers including the Clinical and Translational Science Center (CTSC), West Coast Metabolomics Center, and Comprehensive Cancer Center; the UC Davis Stem Cell Program, Institute for Regenerative Cures, and Good Manufacturing Practices (GMP) Facility; the Radiochemistry Research and Training Facility; and the Center for Health and the Environment. Unit Core Scientists are committed to conducting translational research with nonhuman primates, and mentoring the next generation of investigators with expertise in primatology and the use of the monkey as a model for human health and disease. Unit Core Scientists will continue to bring their unique expertise and strong track record to collaborative multidisciplinary partnerships and teams in gamete biology and reproductive toxicology, regenerative medicine and gene therapy, the application of *in vivo* imaging tools and technologies for translational research, and the conduct of preclinical and investigational new drug (IND)-enabling studies for clinical translation. The depth and breadth of expertise of the Unit Core Scientists contributes substantially to the CNPRC mission, enhances the resource, and ensures that investigators nationwide can conduct state-of-the-art research with nonhuman primates at the highest quality level.

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT**FACILITIES AND OTHER RESOURCES****Laboratories:**

Excluded by Requester [redacted] occupies 2,400 sq. ft. of laboratory space in the Genome and Biomedical Sciences Facility (GBSF) Upper Hall (both less than 1 mile from the Primate Center) including a biomedical instrumentation laboratory with multiple data acquisition stations, a dedicated dark room (250 sq. ft.) with optical bench, ambient light controls, plus five dedicated data acquisition stations for evaluating PET detector performance consisting of light-tight box, NIM modules, digitizers, and data acquisition software. Laboratory equipment includes sealed radioactive sources (^{68}Ge , ^{22}Na , ^{55}Fe , ^{57}Co), translation and rotation stages, scintillators (LSO, GSO, LuAP, BGO, NaI(Tl), CsI(Tl), plastic), many photodetectors (including photodiodes, APDs, PMTs), a wide array of pulse-processing NIM electronics, chilled dry air and liquid nitrogen-based detector cooling systems, ~~monochromator diamond~~ saw, polishing machine, oven, furnace, and UV curing station for optical epoxies.

Excluded by Requester [redacted] occupies laboratories at the Primate Center encompassing 500 sq. ft., and laboratory space in Upper Hall encompassing 800 sq. ft. Additional laboratory space is associated with the Immunology and Pathogen Detection Resources Core (see Core).

Excluded by Requester [redacted] occupies laboratories at the Primate Center encompassing 968 sq. ft. and four laboratories at the Center for Health and the Environment that are dedicated to endocrine methods including radioimmunoassays, HPLC, enzyme immunoassays, and tissue culture.

Excluded by Requester [redacted] occupies ~1,500 sq. ft. at the Primate Center with laboratories that are fully equipped for cell and tissue culture; processing blood, marrow, and tissues; quantitative PCR; ELISAs and other related assays; immunohistochemistry; *in situ* hybridization; and all essential methodologies under appropriate biosafety conditions (BSL2+). Four laboratories are dedicated for work with stem and progenitor cells (e.g., renal and endothelial progenitors, mesenchymal and hematopoietic stem and progenitor cells, human embryonic stem cells, induced pluripotent stem cells), and a separate laboratory is dedicated for the use of viruses and viral vectors (lentiviral and AAV vectors) and the radiolabeling of stem/progenitor cells for *in vivo* imaging. One laboratory is dedicated for the processing of specimens and two for isolation of DNA and RNA and related procedures. Imaging suites in the animal quarters for ultrasound and optical imaging also include areas for ~~other animal-related~~ procedures, including related equipment.

Excluded by Requester [redacted] occupies 968 sq. ft. laboratory space which is fully equipped for cell culture studies and cryopreservation of gametes.

Clinical: Clinical care and related procedures at the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see **Primate Services**).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and **Information Technology Services** provides desktop support and other related services. Biostatistics services and Biomedical Informatics support are also provided on campus and through the UC Davis CTSC. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are all available.

Office:

Excluded by Requester [redacted]

Excluded by Requester [redacted] all occupy an individual office at the CNPRC. Dr. [redacted] has an office at the GBSF, and Dr. Lasley has an office at the Center for Health and the Environment.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT**EQUIPMENT**Excluded by
Requester

NIM bins and electronics (including high voltage supplies, preamplifiers, shaping amplifiers, constant fraction discriminators, logic units, delays, gate and delay generators), pulse generators, data acquisition stations with light tight boxes, translation stages and automated data acquisition, fast digital oscilloscopes, photodetectors (PMTs, MCPMTs, PSPMTs, APDs, PS-APDs, SiPMs), oven, diamond saw, polishing table, and radioactive sources. The CMGI, a campus facility for *in vivo* and biospecimen imaging

Excluded by Requester has a cyclotron and a radiochemistry laboratory, led by Excluded by Requester and managed by Excluded by Requester. This laboratory contains an RDS 111 (Siemens Molecular Imaging, Knoxville, TN) 11 MeV ion biomedical cyclotron, primarily for the production of ^{18}F and ^{11}C to support PET imaging studies

(see Multimodal Imaging Core). A MicroXCT-200 scanner (Xradia, Santa Rosa, CA) for high resolution specimen CT with a resolution of 1-20 μm , a fluorescence cryomicrotome (Barlow Scientific, Olympia, WA) that supports high resolution imaging of fluorescence in large tissue samples/whole organs, and a phosphor storage autoradiography system (Amersham Storm 860). Biomedical Engineering Machine Shop: Equipped with 2 upright mills (Bridgeport Series 1) with 2 axis CNC capability, a lathe (12"x36", with direct read out), a band saw, a drill press, and a grinder/belt sander to fabricate components for mounting detectors and sources, and construct phantoms. Rapid prototyping facility: 3D printers (Objet Eden).

Excluded by Requester

Temperature controlled CO_2 incubators (4), $\leq -20^\circ\text{C}$ (2) and $\leq -80^\circ\text{C}$ (2) freezers, liquid nitrogen tanks for cellular cryopreservation (1), Zeiss inverted microscopes (2), biosafety cabinets (4), temperature-controlled table top centrifuges (2), microfuges (2), heatblocks, gel and immunoblot apparatus, Perkin-Elmer GeneAmp 9600/9700 thermal cyclers (1), Omni Bead Mill homogenizer used in preparation of tissue samples for microbiome work.

Excluded by
Requester

Beta scintillation counter, gamma counter, HPLC, robotic pipetting station (2), shaker, pH meters, scales, balances, refrigerator, freezers (2), fume hoods (3), microtiterplate readers, plate washers, table top centrifuges, absorbance monitors (2), gel electrophoresis equipment, Savant speed vac, robot liquid handler, spin plates, Centaur Assay Platform (see Endocrine Core), and other miscellaneous laboratory equipment.

Excluded by
Requester

Available equipment includes Hereus incubators (14), $\leq -20^\circ\text{C}$ (10) and $\leq -80^\circ\text{C}$ (10) freezers, liquid nitrogen tanks for cellular cryopreservation (12), Zeiss and Leica microscopes (brightfield, darkfield, inverted) (5), WILD stereomicroscopes with fiberoptic illuminators for microdissection, biosafety cabinets (8), PCR enclosures (5), table top centrifuges (4), microfuges (4), QIAcube automated sample preparation system (1), an ultracentrifuge, spectrophotometers (2), ELISA plate readers (2), rotating waterbaths (4), heatblocks, gel and immunoblot apparatus, Perkin-Elmer GeneAmp 9600/9700 thermal cyclers (4), temperature controlled centrifuges (3), and controlled rate programmable CryoMed cryopreservation units (2). Equipment dedicated for research using NIH-approved human embryonic stem cells and induced pluripotent stem cells is provided in the Translational Human Embryonic Stem Cell Shared Research Facility (TSRF) in close proximity to the Primate Center (FACS ARIALL for flow cytometry and cell sorting, QIAcube, Leica cryostat, microtome, Zeiss Axio Imager microscope with fluorescence, Eppendorf Realplex² Mastercycler). Imaging equipment includes a Phillips HDI@5000 SonoCT Ultrasound Imaging System, Xenogen IVIS@200 imaging system, and GE Discovery@ 610 PET/CT (see Multimodal Imaging Core).

Excluded by Requester

Temperature controlled CO_2 incubators (5), pH meter, refrigerator and freezer, Nikon dissection microscopes (2), Olympus CK2 inverted microscope with Hoffman optics, laminar flow hood, fume hood, centrifuge, microcentrifuge, Mettler AE240 balance, CryoMed programmable liquid N_2 freezer, liquid N_2 sample storage tank, Beckman 640 Spectrophotometer, Olympus BH-Series phase contrast/fluorescent microscope with a model WV 3300 color Panasonic video camera, and electronic field timer, a Panasonic model NV-8200 1/2 inch video cassette recorder and a TV monitor, Nikon TE300 Inverted microscope with hoffman optics, fluorescence, environmental chamber and camera and Oosight imaging system; PM1000 cell microinjector, Narishige MN-188NE micromanipulators, microforge, pipette puller and BTX 2001 Electroporation apparatus.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	36,300.00	7,913.00	44,213.00
2.					Core Scientist			0.0	0.0	18,150.00	7,239.00	25,389.00
3.					Core Scientist			0.0	0.0	7,605.00	2,544.00	10,149.00
4.					Core Scientist			0.0	0.0	15,845.00	491.00	16,336.00
5.					Core Scientist			0.0	0.0	18,150.00	6,071.00	24,221.00

Total Funds Requested for all Senior Key Persons in the attached file**Additional Senior Key Persons:**

File Name:

Total Senior/Key Person**120,308.00****B. Other Personnel**

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			27,855.00	14,735.00	42,590.00
Excluded by Requester	Technical Support				40,854.00	21,612.00	62,466.00
	Core Scientists				29,841.00	9,982.00	39,823.00
4	Total Number Other Personnel					Total Other Personnel	144,879.00
					Total Salary, Wages and Fringe Benefits (A+B)		265,187.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,000.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,000.00
2. Publication Costs	6,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	283,187.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	283,187.00	64,283.00
		Total Indirect Costs	64,283.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	347,470.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RSRM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	36,300.00	8,289.00	44,589.00
2.					Core Scientist			0.0	0.0	18,150.00	7,659.00	25,809.00
3.					Core Scientist			0.0	0.0	7,681.00	2,705.00	10,386.00
4.					Core Scientist			0.0	0.0	16,003.00	496.00	16,499.00
5.					Core Scientist			0.0	0.0	18,150.00	6,392.00	24,542.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						121,825.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			28,134.00	15,563.00	43,697.00
1	Technical Support				41,263.00	22,825.00	64,088.00
2	Core Scientists				29,957.00	10,550.00	40,507.00
4	Total Number Other Personnel					Total Other Personnel	148,292.00
Total Salary, Wages and Fringe Benefits (A+B)							270,117.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel**

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)

9,270.00

2. Foreign Travel Costs

0.00

Total Travel Cost 9,270.00**E. Participant/Trainee Support Costs**

1. Tuition/Fees/Health Insurance

0.00

2. Stipends

0.00

3. Travel

0.00

4. Subsistence

0.00

5. Other:

0 Number of Participants/Trainees**Total Participant Trainee Support Costs** 0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,090.00
2. Publication Costs	6,180.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,270.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	288,657.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	288,657.00	65,525.00
Total Indirect Costs			65,525.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	354,182.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RSRM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2017

End Date*: 04-30-2018

Budget Period: 3

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	36,300.00	8,561.00	44,861.00
2.					Core Scientist			0.0	0.0	18,150.00	7,929.00	26,079.00
3.					Core Scientist			0.0	0.0	8,018.00	2,920.00	10,938.00
4.					Core Scientist			0.0	0.0	16,760.00	534.00	17,294.00
5.					Core Scientist			0.0	0.0	18,150.00	6,610.00	24,760.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons:

File Name:

Total Senior/Key Person

123,932.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			29,521.00	16,861.00	46,382.00
1	Technical Support	Excluded by Requester			43,292.00	24,727.00	68,019.00
2	Core Scientists				30,744.00	11,196.00	41,940.00
4	Total Number Other Personnel					Total Other Personnel	156,341.00
						Total Salary, Wages and Fringe Benefits (A+B)	280,273.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,548.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,548.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,183.00
2. Publication Costs	6,365.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,548.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	299,369.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	299,369.00	67,956.00
Total Indirect Costs			67,956.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	367,325.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RSRM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	36,300.00	8,815.00	45,115.00
2.					Core Scientist			0.0	0.0	18,150.00	8,164.00	26,314.00
3.					Core Scientist			0.0	0.0	8,310.00	3,118.00	11,428.00
4.					Core Scientist			0.0	0.0	17,314.00	568.00	17,882.00
5.					Core Scientist			0.0	0.0	18,150.00	6,809.00	24,959.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						125,698.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			30,438.00	17,903.00	48,341.00
1	Technical Support	Excluded by Requester			44,642.00	26,257.00	70,899.00
2	Core Scientists				31,300.00	11,742.00	43,042.00
4	Total Number Other Personnel					Total Other Personnel	162,282.00
Total Salary, Wages and Fringe Benefits (A+B)							287,980.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,834.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,834.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,278.00
2. Publication Costs	6,556.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,834.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	307,648.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	307,648.00	69,836.00
Total Indirect Costs			69,836.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	377,484.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RSRM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*	
1.	Excluded by Requester					Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	36,300.00	9,069.00	45,369.00
2.						Core Scientist			0.0	0.0	18,150.00	8,416.00	26,566.00
3.						Core Scientist			0.0	0.0	8,560.00	3,306.00	11,866.00
4.						Core Scientist			0.0	0.0	17,834.00	603.00	18,437.00
5.						Core Scientist			0.0	0.0	18,150.00	7,009.00	25,159.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						127,397.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			31,351.00	18,999.00	50,350.00
1	Technical Support Excluded by Requester				45,982.00	27,865.00	73,847.00
2	Core Scientists				31,826.00	12,290.00	44,116.00
4	Total Number Other Personnel				Total Other Personnel		168,313.00
					Total Salary, Wages and Fringe Benefits (A+B)		295,710.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00
Additional Equipment: File Name:	

D. Travel

	Funds Requested (\$)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,129.00
2. Foreign Travel Costs	0.00
Total Travel Cost	10,129.00

E. Participant/Trainee Support Costs

	Funds Requested (\$)*
1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,376.00
2. Publication Costs	6,753.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	10,129.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	315,968.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	315,968.00	71,725.00
		Total Indirect Costs	71,725.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	387,693.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RSRM_BudgetJustification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist, Unit Leader	% Effort			
	Core Scientist				
	Core Scientist				
	Core Scientist				
	Core Scientist				
TBN	Core Scientist	10	0	90	100
TBN	Core Scientist	10	0	90	100
Excluded by Requester	Administrative Assistant	% Effort			
	Unit Safety Coordinator				

TBN=to-be-named

Excluded by Requester **PhD, Core Scientist and Unit Leader** EFFORT months % Effort Excluded by Requester is

Professor and Vice Chair for Research in the Department of Pediatrics, with a joint appointment in the Department of Cell Biology and Human Anatomy, School of Medicine. She is the Director of the Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases, Associate Director of the UC Davis Stem Cell Program, and Multimodal Imaging Core lead. Excluded by Requester translational research program has a particular focus on the fetus and infant with ongoing studies that address regenerative medicine across the age groups, tissue engineering, stem cell transplantation, gene therapy, and the application and use of state-of-the-art *in vivo* imaging modalities and tools.

Excluded by Requester **PhD, Core Scientist** EFFORT months % Effort Excluded by Requester is Professor, Department of Biomedical Engineering, College of Engineering, with a joint appointment in the Department of Radiology, School of Medicine. Excluded by Requester the Director of the UC Davis Center for Molecular and Genomic Imaging, and a member of the Multimodal Imaging Core. Excluded by Requester research interests center around biomedical imaging and in particular the development and application of *in vivo* molecular imaging systems. His major accomplishments have been in developing and applying very high resolution systems for PET, in particular the invention of the microPET technology for preclinical imaging that was subsequently widely adopted in academia and industry and used extensively for nonhuman primate intracranial imaging.

Excluded by Requester **MD, PhD, Core Scientist** EFFORT months total EFFORT months % Effort is shared with the Infectious Diseases Research Unit. Excluded by Requester is Assistant Professor, Department of Medical Microbiology and Immunology, School of Medicine, and leads the Immunology and Pathogen Detection Resources Core. Excluded by Requester is interested in microbial control over immune system development, and in immune responses to gene transfer vectors and stem/progenitor cells in organ systems including the eye. He is participating in projects related to the microbiome and developmental paradigms that include a focus on immune ontogeny, the impact of environmental exposures, and the fetal/maternal interface.

Excluded by Requester **PhD, Core Scientist** EFFORT months % Effort Excluded by Requester is Professor Emeritus, Department of Population Health and Reproduction, School of Veterinary Medicine, Associate Director, Center for Health and the Environment, and leads the Endocrine Core. Excluded by Requester research program encompasses women's healthy aging, and he brings a focus on environmental hazards to human reproductive health. His research activities have led to a novel hypothesis for the rise in adrenal steroids during the menopausal transition, and the validation of the nonhuman primate model for these and related studies.

Excluded by Requester **PhD, Core Scientist** EFFORT months % Effort Excluded by Requester is Professor-in-Residence and Director, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and

Gynecology, School of Medicine, and the Chair of the Molecular, Cellular, and Integrative Physiology Graduate Group, [Excluded by Requester] provides services in assisted reproductive technologies including semen cryopreservation and distribution through Colony Management and Research Services (see Primate Services). [Excluded by Requester] research focuses is on the use of the rhesus monkey as a model for human reproduction in the areas of sperm biology and cryopreservation, oocyte maturation and early embryo culture, and reproductive toxicology.

TBN Core Scientists (2) (1.2 calendar months – 10% each Core Scientist). The commitment of the Provost and respective Dean's of the Schools of Medicine and Veterinary Medicine, and the Colleges of Biological Sciences, Engineering, and Letters and Sciences (see **Overview**) to new faculty positions includes two Unit Core Scientist positions (see Research Strategy). One of the new faculty recruitments is proposed at the junior investigator level and one with a more established research program.

[Excluded by Requester] **Administrative Assistant** [EFFORT] months [% Effort] [Excluded by Requester] provides administrative support for Primate Center-related activities and programs.

[Excluded by Requester] **MS, Unit Safety Coordinator** [EFFORT] months [% Effort] [Excluded by Requester] serves as the Unit Safety Coordinator, provides assistance in the training of staff and students, coordinates and prepares sample shipments to investigators, and maintains the required documentation associated with these activities.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June).

EQUIPMENT

None requested

TRAVEL

\$9,000 total is requested for each Core Scientist to attend a national meeting in their respective area(s) of expertise (6 x \$1,500).

SUPPLIES

\$3,000 in supplies is requested to support activities with new investigators and sharing of resources.

OTHER EXPENSES

\$6,000 is requested for manuscript preparation and submission (6 x \$1,000).

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		619,160.00
Section B, Other Personnel		780,107.00
Total Number Other Personnel	20	
Total Salary, Wages and Fringe Benefits (A+B)		1,399,267.00
Section C, Equipment		0.00
Section D, Travel		47,781.00
1. Domestic	47,781.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		47,781.00
1. Materials and Supplies	15,927.00	
2. Publication Costs	31,854.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,494,829.00
Section H, Indirect Costs		339,325.00
Section I, Total Direct and Indirect Costs (G + H)		1,834,154.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

2. Human Subjects

Clinical Trial? ☒ No ☐ Yes

Agency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☐

No

☒

Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s):☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

0043

0062

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*:

☒

Yes

☐

No

If the answer is "Yes" then please answer the following:

Previously Reported*:

☐

Yes

☒

No

7. Change of Investigator / Change of Institution Questions☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

RSRM_SpecificAims.pdf

3. Research Strategy*

RSRM_ResearchStrategy.pdf

4. Progress Report Publication List

RSRM_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

RSRM_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

RSRM_LettersofSupport.pdf

13. Resource Sharing Plan(s)

Resource_Sharing_Plan.pdf

Appendix (if applicable)**14. Appendix**

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT

SPECIFIC AIMS

Unit Core Scientists have established extramural-funded programs; successfully developed new models, tools, and technologies that are unique to the CNPRC; and provide a range of services to the research community through established Cores and NIH-supported service programs. Unit Core Scientists fulfill the CNPRC mission by enhancing the nonhuman primate resource through new assay and model development, new *in vivo* imaging paradigms, sharing unique cells and tissues, by participating in the management of the reproductive colonies, and through the mentoring of trainees and junior faculty. The action plan for the next funding period focuses on promoting translational research opportunities with nonhuman primates, developing and validating refined primate models of human disease, recruiting new faculty to the program, and capitalizing on campus initiatives and growth areas. Core Scientists will continue to build and sustain partnerships locally, regionally, and nationally in response to NIH strategic priorities and investigator needs, and promote the recruitment of trainees at all career stages.

Specific Aim 1. Advance the CNPRC resource through scientific achievements and research excellence in reproduction and development, regenerative medicine, gene therapy, and *in vivo* imaging.

Plan. The goals for the next funding period include studies with nonhuman primate models of human reproductive health and disease and innovative regenerative strategies to support new clinical trials. Studies will contribute to the understanding of the underpinnings of lifespan health through state-of-the-art research and technology development at the maternal/fetal interface, in reproductive maturation and aging, and using new biomarkers, diagnostic tools, and stem/progenitor cell populations across the age spectrum. Monkeys share many reproductive, developmental, genetic, and immunologic features with humans and these similarities offer the opportunity for Core and Affiliate Scientists to explore susceptibility to the environment, which can have a lasting impact depending on the timing and type of exposure. Investigations will also focus on overcoming roadblocks to human clinical trials with genetic and cell-based therapies that are tailored to the age of the patient, and address long-term safety and cell fate.

Specific Aim 2. Contribute unique expertise and services to enhance the nonhuman primate resource at the local, regional, and national levels.

Plan. The extensive expertise of Core Scientists contributes to the foundation for services in established Cores (e.g., Endocrine, Immunology, Multimodal Imaging) and colony management; through extensive outreach efforts in the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases; and in grants and contracts where investigators from other institutions serve as principal investigator (PI) and Core Scientists serve as the on-site PIs. Unit Core Scientists will ensure scientific and technologic expertise is available for investigators at all career stages, and maintain unique specimen repositories with nonhuman primate cells and tissues for collaborative research opportunities, pilot projects, and NIH grant submissions.

Specific Aim 3. Mentor and train the next generation of translational nonhuman primate investigators.

Plan. Core Scientists will ensure trainees at all levels develop expertise in primatology; the design, development, and study of primate models of human disease; team science; and the conduct of multidisciplinary translational investigations. They will continue to provide mentoring to undergraduate trainees through internships and related UC Davis programs and graduate students in a range of graduate groups; participate in training programs for students, fellows, and junior faculty (e.g., Stem Cell Training Program; Building Independent Research Careers in Women's Health [BIRCWH]; CTSC T32, Mentored Clinical Research Training Program, K12); serve as Instructor-of-Record and through didactic lectures in core courses; plan and participate in seminar series, symposia, and workshops; and present at national and international meetings on the research and training opportunities at the CNPRC. The Unit will promote the recruitment of new faculty to the CNPRC program and through joint appointments in academic departments.

Specific Aim 4. Promote high standards of research and animal care.

Plan. Core Scientists will continue to contribute to high quality standards and research through service support to the colony and by meeting current and future research needs of investigators and trainees nationwide.

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT

RESEARCH STRATEGY

INTRODUCTION

Core Scientists in the Reproductive Sciences and Regenerative Medicine Research Unit (Figure 1) contribute to the CNPRC mission by their respective areas of research excellence; providing their expertise in the reproductive management of the CNPRC colonies; through a range of services to the greater research community (e.g., Cores, consultations, collaborations, NIH-supported Centers and outreach programs); and by mentoring trainees at all levels. Unit Core Scientists have an outstanding record in the formation of multidisciplinary partnerships and teams and are well-integrated in UC Davis NIH-supported Centers including the Clinical and Translational Science Center (CTSC) and West Coast Metabolomics Center; the UC Davis Stem Cell Program, Institute for Regenerative Cures, and Good Manufacturing Practices (GMP) Facility; the Radiochemistry Research and Training Facility; and the Center for Health and the Environment. Core Scientists bring their expertise and strong track records to collaborative, multidisciplinary partnerships and teams in gamete biology and reproductive toxicology, regenerative medicine and gene therapy, and the use of *in vivo* imaging modalities and tools for translational research. Extramural grants have been the primary source of support for Unit Core Scientists (see below).

Figure 1. Organizational Chart: Reproductive Sciences and Regenerative Medicine

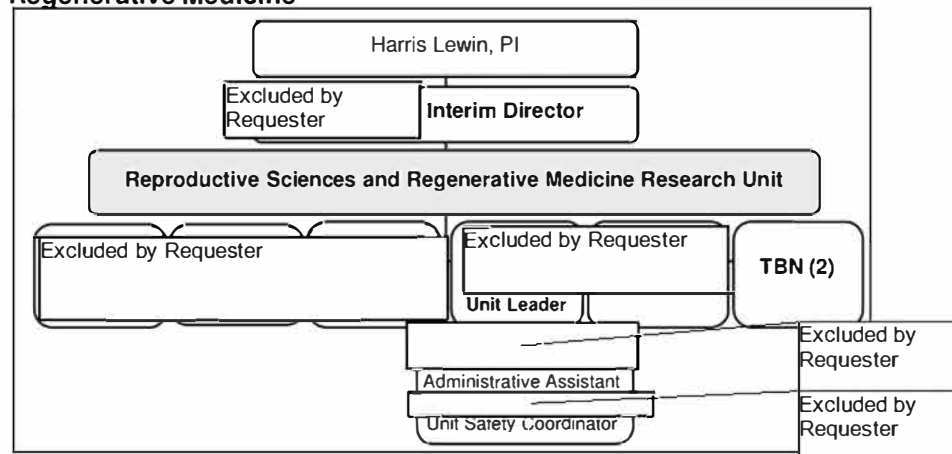


Table 1. Reproductive Sciences and Regenerative Medicine Research Unit Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Biomedical Engineering, College of Engineering	• Core Scientist • Multimodal Imaging Core
	Department of Medical Microbiology and Immunology, School of Medicine	• Core Scientist • Immunology and Pathogen Detection Resources Core
	Department of Population Health and Reproduction, School of Veterinary Medicine	• Core Scientist • Endocrine Core
	Departments of Pediatrics and Cell Biology and Human Anatomy, School of Medicine	• Core Scientist, Unit Leader • Multimodal Imaging Core • CNPRC Committees
	Department of Obstetrics and Gynecology, School of Medicine	• Core Scientist • Primate Services • Colony Management Committee
TBN (2)	Based on joint recruitments	Core Scientists
Excluded by Requester	CNPRC	Administrative Assistant
	CNPRC	Unit Safety Coordinator

*Joint appointment in Infectious Diseases Research Unit; TBN=to be named

Table 2 shows the support for the Reproductive Sciences and Regenerative Medicine Unit per the FOA. A small component of salary is supported on the P51 base grant (see budget justification), and represents the commitment to the mission, outreach, and services.

Table 2. Support for the Reproductive Sciences and Regenerative Medicine Research Unit (does not include research grants per FOA. See Unit grant funding Table 3, below)

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$262,557	\$283,187
Program Income from P51	\$0	\$0
Other Sources*	\$1,263,697	\$931,139
TOTAL	\$1,526,254	\$1,214,326

*R24 and other related resource grants

reviewers' comments

Response to Summary Statement.

reviewers' comments

SIGNIFICANCE

During the current funding period, Unit Core Scientists collaborated with 86 Affiliate Scientists and other investigators from institutions across the U.S. (60 from UC Davis), published 110 manuscripts, and mentored 92 trainees (undergraduate students to junior faculty). Extramural grants during the current funding period totaled approximately \$37 million (\$41.5 million with Excluded by Requester grants) (Table 3).

Table 3. Extramural Funding for Reproductive Sciences and Regenerative Medicine (May 1, 2010 to April 30, 2014)

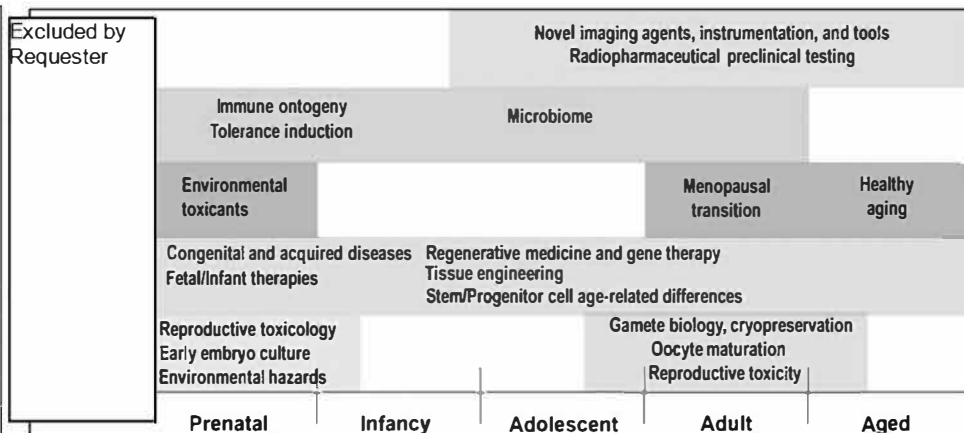
May 2010 - April 2011	May 2011 - April 2012	May 2012 - April 2013	May 2013 - April 2014	TOTAL*
\$10,817,567	\$10,334,292	\$7,200,313	\$8,614,629	\$36,966,801*

*Does not include \$4.5 million for Dr. Cherry's funded grants administered by the Department of Biomedical Engineering or currently funded grants May 1, 2014 to April 30, 2015, to date, of \$7,366,284

Progress and Major Accomplishments: Contributions to the CNPRC Mission

Focus on Lifespan Health. Monkeys and humans share many reproductive and developmental features that emphasize their importance as translational models. Rhesus monkey colonies at the CNPRC parallel the human lifespan, and Unit Core Scientists have a clear dedication to the study of lifespan health from the earliest stages of development through aging populations. The unique expertise in the Unit provides a means to address research questions associated with all developmental stages (embryo, fetus, newborn, infant), juveniles; young adults; pre-menopausal/transitional reproductive stages; and advanced geriatrics (Figure 2). Core Scientists conduct studies on gamete biology and the impact of environmental factors, reproductive and developmental toxicology, utilize unique fetal models of congenital and acquired diseases (e.g., obstructive renal disease, acquired infectious diseases with colleagues in the Infectious Diseases Research Unit), and have unique strengths in gene therapy and stem cell transplantation across the age spectrum. They have also made seminal discoveries on the menopausal transition as it relates to healthy aging that has had a major impact on the field and provided insights of direct relevance to humans.

Figure 2. Core Scientists in the Reproductive Sciences and Regenerative Medicine Research Unit address all developmental stages in their research, conduct studies through the maturation and aging process, and utilize geriatric rhesus monkey populations in their research. The fastest growing population in the U.S. consists of older adults; the Unit is in a unique position to address consequences of early life exposures on future health and aging.



1. Reproductive Biology and Toxicology. Studies focus on *in vitro* maturation and cryopreservation of oocytes and address improving cryopreservation techniques for gametes that do not survive well with current protocols, with special emphasis on methods compatible with artificial insemination. Understanding the function of granulosa and cumulus cells and their impact on the health of oocytes includes the **NIH Primate Embryo Gene Expression Resource (PREGER)** led by [Excluded by Requester] (Michigan State University), and a series of publications that assess gene expression in mural granulosa and cumulus cells as well as oocytes, to predict oocyte quality and embryo developmental outcome, which can be applied to evaluation of human

[Excluded by Requester] et al. [Excluded by Requester] 2012; [Excluded by Requester] [Excluded by Requester] 2011]. This resource also provides cells to investigators and [Excluded by Requester] serves genetic diversity.

Studies at the CNPRC include discovery and development of new methods to monitor human reproductive health using assays to identify and characterize ovarian cycles and changes that occur with reproductive maturation and aging [Excluded by Requester] 2013; [Excluded by Requester] 2001]. For example, dehydroepiandrosterone sulfate was established as a marker for female aging and found to be useful in evaluating monkeys in the aged colony. It was demonstrated that ovarian steroids change both the structure and function of the adrenal glands, which may explain differences in menopausal symptoms and health trajectories in women. Studies in

[Excluded by Requester] in collaboration with Affiliate Scientist [Excluded by Requester] (**Brain, Mind, and Behavior Research Unit**) in aged monkeys showed that hormone replacement protocols may fail to provide substantial cognitive benefit. The translational impact of these studies is evident in the Study of Women's Health Across the Nation (SWAN), which emphasizes the importance of nonhuman primates for reproductive research, and the contributions made by Unit Core Scientists.

Investigations have also shown that mature female rhesus monkeys provide an excellent model for investigating both the natural progression of aging and changes in susceptibility to the adverse effects of environmental toxicants, which can have a different impact depending on the timing of exposure. Studies by

[Excluded by Requester] have focused on models of reproductive toxicology including environmental exposure to endocrine-disrupting chemicals and effects of binge alcohol consumption [Excluded by Requester] 2014]. The gene expression patterns of oocytes were also altered, indicating a potential for transgenerational effects. In collaboration [Excluded by Requester] (Washington State University), studies by [Excluded by Requester] investigated the effects of Bisphenol A (BPA) on metabolism with a particular emphasis on the ovary [Excluded by Requester] al. 2012]. The impact on other tissues was shown [Excluded by Requester] 2014; Tharn 2012] included lung in collaboration with an Affiliate Scientist in the **Respiratory Diseases Unit** [Excluded by Requester] 2013].

2. Regenerative Medicine. Essential in the translation of cell-based therapies to the clinics is establishing safety, and nonhuman primates provide the essential bridge between mouse studies and human clinical trials. The human xenograft model developed by [Excluded by Requester] provides a way to study human cells in a primate host with an intact immune system. For example, effective methods to expand human umbilical cord blood CD34+ cells for fetal transplantation has been accomplished and new postnatal imaging paradigms developed in this model. These and related investigations have provided important insights not previously appreciated by the collection of blood or bone marrow and showed the importance of bioluminescence imaging (BLI) to longitudinally monitor cell fate *in vivo* (see **Multimodal Imaging Core** [Excluded by Requester] 2010). Based on extensive expertise in regenerative medicine research, funding from the California Institute for Regenerative Medicine (CIRM) was achieved for two Disease Team grants during the current funding period. These grants focus on the conduct of IND-enabling studies with nonhuman primates in order to

Excluded by Requester

provide FDA required data for a Phase I clinical trial. In collaboration with [Excluded by Requester] studies are advancing a cell-based therapy for Huntington's disease. The funding of this \$17.8 million grant benefited from two pilot projects conducted at the CNPRC, one using the fetal model for safety testing of the cell product (supported through philanthropic funds) and a second pilot project in juvenile monkeys which was supported by the UC Davis CTSC. Recent funding of a CIRM Disease Team award (Co-PIs [Excluded by Requester] represents an international effort with partners in the UK that is focused on tissue engineering or replacement trachea to meet FDA requirements for an IND application. Grant funding of \$4.4 million was specifically designated for studies to be conducted with nonhuman primates.

- 3. Gene Therapy.** The **NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases**, established in 2001, is a unique resource that serves a crucial role in the gene therapy field by addressing essential questions in gene delivery and providing investigators collaborative opportunities to test new vector constructs that advance the field [Excluded by Requester] 2012]. Any investigator funded by the NHLBI is eligible to submit a Letter of Intent. The call for proposals (see right) is circulated annually, posted on the NHLBI website under *Resources* and on the Center for Fetal Monkey Gene Transfer, CNPRC, CTSC, and American Society of Gene and Cell Therapy websites, presented at national meetings, and published in *Molecular Therapy* on the back cover annually. Applications are requested after review and approval of the submitted Letters of Intent. Investigators selected for funding by a standing advisory committee have the opportunity to participate in the study. This program also routinely provides cells, tissue sections (frozen, formalin-fixed), RNA, and DNA to investigators nationwide upon request throughout the calendar year. During the current funding period the program successfully achieved a second competitive 5-year renewal, continuing a highly successful outreach program that has provided access to and supported studies with nonhuman primates for over 44 NHLBI investigators nationwide (Table 4).

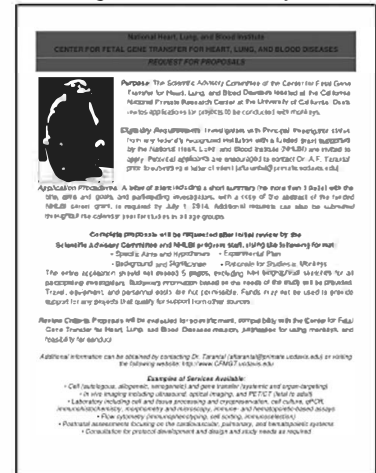


Table 4. Examples of Investigators with Pilot Projects Supported by the Center for Fetal Monkey Gene Transfer

Investigator	Institution	Grant #	Project Title
Excluded by Requester	Indiana University	HL053586	Administration of c-kit Blocking Antibody to Rhesus Monkeys and Effects on Hematopoiesis
	University of North Carolina	HL089221	Systemic and Cardiac Gene Transfer with Novel AAV Vectors
	University of Pennsylvania	HL059407	Efficiency, Stability, and Safety of AAV-Mediated Liver-Directed Gene Transfer in Neonatal Monkeys
	Baylor College of Medicine	HL087836	Evaluation of the Safety and Expression of Hexon PEGylated Adenoviral Vector Expressing Human FVIII
	UC San Francisco	HL082665	Translational Primate Studies to Assess Efficacy and Safety of Autologous Transplantation
	Childrens Hospital LA	HL060231	Developmental Modulation of Fibrosis in Fetal Lung
	University of Florida	HL059412	Studies on Repeat Administration of rAAV9 Vector for Cardiac and Respiratory Myopathies
	UCLA	HL073014	<i>In Vivo</i> Transduction of a Lentiviral Vector Expressing ADA in Infant Rhesus Monkeys
	UCLA	HL053586	Examination of the Immune Response to Transgene-Encoded Proteins in the Early Neonatal Period
	Stanford	HL099776	Co-Stimulation Blockade to Prevent Stem Cell Rejection

Studies have also addressed long-term safety (lentiviral and adeno-associated virus [AAV] vectors) in monkeys up to ~10 years of age that were transferred prenatally (e.g., intraperitoneal, intrathoracic, intramyocardial, intraportal, intrahepatic) (see **Multimodal Imaging Core**). The leap from preclinical discovery to human subjects research is challenging, and the program has proven crucial in navigating the regulatory process by supporting projects that provided data for new clinical trials. Each aspect of the clinical development plan was facilitated aiding investigators in addressing regulatory barriers. Examples include:

- Assessed the use of busulfan in young monkeys to model non-myeloablative conditioning which were critical for translating this approach into a current ongoing ADA-SCID clinical trial [Excluded by Requester] 2014 [Excluded by Requester] 2013].

- A series of studies have been instrumental in achieving the overall goal of utilizing AAV expression of human acid alpha-glucosidase in Pompe patients [Excluded by Requester University of Florida; see letter). Initial studies established the utility of AAV serotype 1 in nonhuman primate muscle, and the results of this and a related study were a component of an IND submission for the use of AAV in 3 to 14-year-old patients who had developed ventilator dependence [Excluded by Requester 2013]. Studies also identified novel properties of AAV2/9, and showed Rituximab and Sirolimus were effective in overcoming neutralizing antibodies to AAV.
- A study in young monkeys focused on identifying a safe and robust AAV delivery method for regional limb gene transfer for Duchenne muscular dystrophy patients. Outcomes were incorporated in a pre-IND submission [Excluded by Requester University of North Carolina at Chapel Hill; see letter).
- Through an NIAID supplement to the Gene Therapy Center, studies in monkeys assessed safety and gene transfer efficiency of a lentiviral vector that showed no adverse events in fetal and juvenile monkeys. These studies were critical in gaining approval for an IND application and conducting the first-in-human trial of an expressed siRNA in a lentiviral vector [Excluded by Requester City of Hope] [Excluded by Requester 2010].

4. Translational Imaging. The Unit has a long-standing commitment to providing imaging services to the research community (see **Multimodal Imaging Core**). This service function was initiated with the Ultrasound Imaging Program [Excluded by Requester 2005] and more recently, the development of BLI specific to monkeys which has transformed the ability to monitor long-term gene expression [Tarantal and Lee, 2010], and provided new ways to compare and contrast outcomes when different cell sources and routes of transplantation are used. The recent acquisition of a state-of-the-art GE Discovery®610 PET/CT scanner (NIH S10 High-End Instrumentation Grant [Excluded by Requester]) represents a major achievement. This is the first hybrid unit with a 64-slice CT installed in the U.S. and at a Primate Center (see Core). New imaging paradigms are under development including those focused on the maternal/fetal interface. Projects have also focused on the synthesis of new radioimmunoconjugates using radioactive copper (^{64}Cu) and zirconium (^{89}Zr) for cell trafficking, and radiolabeling methods to identify engrafted human cells [Excluded by Requester 2012; 2013].

Serving the Needs of Investigators Locally, Regionally, and Nationally. Unit Core Scientists play an extensive role in collaborations and providing unique and accessible opportunities for investigators and trainees that contributes substantially to the NPRC mission. Figure 3 highlights interactions in a social network analysis.

[Excluded by Requester]

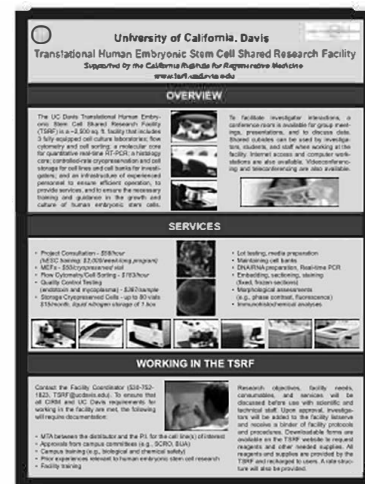
Figure 3. Collaborations represent institutions nationwide and internationally. Green shows examples of institutions in California, blue are institutions nationally, and red are international collaborations. The size of the nodes represent the number of collaborations for each Core Scientist, and the number of collaborations with other Core Scientists are evident by the width of the lines.

Mentoring: Opportunities for Trainees and Investigators. Core Scientists trained and mentored 32 undergraduate students (through 199 special study research credits, the UC Davis Internship and Career Center, and the Biology Undergraduate Scholars Program, BUSP), 23 graduate students in a variety of graduate groups (e.g., Biomedical Engineering; Biochemistry, Molecular, Cell, and Developmental Biology; Comparative Pathology; Immunology; Molecular, Cellular, and Integrative Physiology), 17 postdoctoral fellows, and 20 junior investigators and physician-scientists during the current funding period (Table 5).

Table 5. Examples of Trainees Mentored by Reproductive Sciences and Regenerative Medicine Core Scientists

Trainee	Training Experience	Outcomes
Excluded by Requester	BUSP year-long internship and Summer Honors project	Selected in 2013 to represent UC Davis at the Annual Biomedical Research Conference for Minority Students
	Tissue engineering strategies: focus on the kidney	CTSC T32 trainee and Stem Cell Training Program Scholar; current postdoctoral fellow at Stanford
	Oocyte cryopreservation	Returned to complete graduate program, University Medical Center Gottingen, Germany
	Constructed one of the first PET insert prototypes for use in a 7T MRI based on solid state photo detectors	Awarded the prestigious Bruce Hasegawa Young Medical Imaging Scientist Award from the IEEE in 2013
	Children's Miracle Network Resident Mentored Research Project	2012 Pediatric Resident Research Award from the Western Society for Pediatric Research; current fellow at UCSF
	CTSC Highly Innovative Award to study the distribution of Lp(a) in the rhesus monkey model	<ul style="list-style-type: none"> Accepted into the BIRCWH Training Program Undergraduate trainee involved in the study presented at campus forum

- The Stem Cell Training Program (co-PIs Excluded by Requester) includes a core curriculum linked with the CTSC, a Stem Cell/Regenerative Medicine Seminar Series, and weekly journal club which is led by a CNPRC Senior Scientist, Excluded by Requester who completed training in the inaugural year of the program. Affiliated with the UC Davis Stem Cell Program is the Translational Human Stem Cell Shared Research Facility, a campus-wide service facility dedicated to the study of human stem cells. The facility includes cell culture laboratories, cell sorting, a molecular and histology core, controlled-rate cryopreservation and cell storage, and an infrastructure of experienced personnel that provide services and training (see flyer, right). This centralized facility is located on-site at the CNPRC and provides training opportunities to students at UC Davis, UC Merced, and the California State Universities (e.g., Sacramento, Humboldt). The facility was established with a \$3 million CIRM investment and UC Davis matching funds.



- Core Scientists are also members of other training programs including: Interdisciplinary Training for Autism (led by Excluded by Requester); **Brain, Mind, and Behavior Research Unit**; and Comparative Lung Biology (led by Excluded by Requester). UC Davis was one of the first institutions to receive a Broadening Experiences in Scientific Training (BEST) Award that is linked with the CTSC (co-PIs Excluded by Requester).

- The NHLBI Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases is currently in the 13th year of NIH support (matching support provided by the CNPRC and CTSC). The intent of these annual interdisciplinary scientific symposia is to provide a novel and informal scientific setting for the dissemination and exchange of new ideas and research findings by bringing together students, fellows, and junior investigators who do not typically interact at other meetings. Trainees are supported through a competitive process and have the opportunity to present their research in a brief oral presentation followed by a poster session, and interact with leading scientists in the gene therapy and regenerative medicine fields.

INNOVATION

Unit Core Scientists have outstanding records of achievement that highlight innovation and support that studies that are at the forefront of nonhuman primate research. Examples include:

- Models of Reproductive Toxicology, Senescence, and Aging.** An established CNPRC strength is the depth of reproductive endocrinology research and related assays developed by Excluded by Requester [2012; 2013]. Over the past decade a great deal of information has been accumulated in monkeys regarding the interaction of hormone signals governing the ovarian cycle (see **Endocrine Core**). Urinary biomarkers are applied to characterize follicular growth with urinary estrone conjugates, the synchrony of the periovulatory hormone cascade at ovulation, the development of the corpus luteum (pregnanediol-3-glucuronide, PdG), and conception (monkey chorionic gonadotropin [mCG]). The comparison of these patterns allows the identification of differences in endocrine function in cohorts of animals classified by age. New models of reproductive toxicology have been developed reflecting environmental exposure to endocrine disrupting

chemicals, the increasing occurrence of alcohol consumption/binge drinking, and the impact of BPA exposure and potential link with future disease.

- **Fetal Proof-of-Concept Models.** The fetal proof-of-concept model has been utilized for a range of applications including to explore new strategies for treating congenital diseases by capitalizing on the functional immaturity of the fetal immune system. Prenatal transplant of human cells has established xenograft models for testing new transplant and imaging protocols (see **Multimodal Imaging Core**), as well as a rigorous model in which to evaluate safety. For example, a fetal intracranial approach was used for the transplant of human mesenchymal stem/stromal cells (MSC) in proof-of-concept studies focused on patients with Huntington's disease. The fetal rhesus cytomegalovirus (RhCMV) pathogenesis model, jointly optimized

Excluded by Requester [redacted] (Infectious Diseases Research Unit) Excluded by Requester [redacted] et al., 2006 Excluded by Requester [redacted] 2002], is a component of research efforts of Affiliate Scientist Excluded by Requester [redacted] (Oregon Health and Sciences University) to evaluate human CMV as a vaccine vector for HIV and other clinically relevant pathogens for which no vaccines exist. In an effort to translate findings in the monkey model to human clinical trials, this team is testing modified RhCMV vectors for safety, which is supported by NIH grants and a Private Source award. These studies inform Excluded by Requester [redacted] decisions on the vectors to advance to preclinical/clinical testing. In other collaborations with Affiliate Scientist Excluded by Requester [redacted] (UCSF) that builds on prior findings of fetal:maternal microchimerism Excluded by Requester [redacted] 2003; 2005], a new strategy targeting polymorphic MHC gene sequences was used to show that maternal:fetal microchimerism occurs in the monkey comparable to humans Excluded by Requester [redacted] 2014]. Other studies with Excluded by Requester [redacted] supported by NIH grants and a Private Source award Excluded by Requester [redacted] the unique aspects of the fetal model to explore innovative hypotheses on the induction of tolerance to SIV *in utero* as a means to protect against postnatal challenge.

- **Translational Imaging.** The campus Research Investments in Science and Engineering (RISE) Program was implemented to facilitate the formation and enhancement of interdisciplinary teams to carry out research in areas of strategic importance (see **Overview**). Following a rigorous review process, one of the 13 projects selected was a submission by theme leader and Core Scientist Excluded by Requester [redacted] with theme faculty Drs. Excluded by Requester [redacted] (Department of Radiology), and Excluded by Requester [redacted] PI, UC Davis CTSC). The goal is to translate novel molecular imaging agents and devices for clinical research studies, and perform first-in-human molecular imaging studies at UC Davis. Dynamic PET/CT imaging using the new imaging system is a major component of these studies (see Core). New compounds produced in the UC Davis GMP facility will ensure the necessary data is obtained to conduct FDA-approved clinical trials. These studies represent a strong example of innovation for *in vivo* imaging driven by Unit Core Scientists.

APPROACH

The goals for the next funding period build upon expertise, productivity, and innovation; strong ties with institutional and national programs; and maximize resources for research. Core Scientists will expand areas of common interest, translate research findings to clinical trials, and continue a strong track record of building partnerships nationally, and in response to NIH strategic priorities. The Unit will actively promote recruitment of investigators, and provide expertise and services to meet the growing needs of investigators and trainees.

Specific Aim 1. Advance the CNPRC resource through scientific achievements and research excellence. **Reproductive health and toxicology** are high priority research areas where nonhuman primates will continue to play an essential role, and where Core Scientists provide their expertise. Reproductive health is tightly linked with the focus on lifespan health, and the impact of early environmental exposures on the development and evolution of reproductive function particularly during lifetime transitions (e.g., puberty, menopause). Models of BPA exposure will be expanded to focus on how the effects during development may impact juvenile and adult health as a collaborative effort. The binge ethanol model has important implications for epigenetics and advising young women about alcohol consumption pre-pregnancy. These models have cultivated new local and national collaborations and the plan is to expand to interface with other disciplines such as breast cancer in later life, and the role the oocyte plays in the epigenetics of transgenerational effects.

Progress in the **regenerative medicine and gene therapy** fields will depend on predictive primate models. Ongoing investigations will build on existing strengths to explore:

- New resources and tools to provide opportunities for the *in vitro* design (cells, natural scaffolds) and *in vivo* testing (transplant, *in vivo* imaging) of regenerative strategies tailored to patient age and disease.
- The role and fate of seeded stem/progenitor cells in tissue-engineered tracheal implants, the safety of the approach, and the efficacy of these interventions. These are critical questions that necessitate thorough investigations in nonhuman primates to address central issues required by the FDA Excluded by Requester [redacted] 2013].

- Innovative chimeric AAV capsid vectors developed through library and rational design for defined disease and cell targeting. For example, giant axonal neuropathy is an early-onset fatal neurodegenerative disorder, and represents an excellent candidate for gene replacement therapy using capsid backbones that show unique neuronal tropism. These recently initiated studies will benefit from new funding opportunities in the NIH Brain Initiative and current collaborations with junior faculty in the MIND Institute (see Pilot Research Program).
- Tracking of radiolabeled stem/progenitor cells is limited by half-life thus a new approach for long-term imaging is under development that will permit repeat administration of any stem/progenitor cell population. These investigations leverage expertise, infrastructure, and tools that will ensure success in translation including human instrumentation; whole-body dynamic imaging; and a Radiochemistry Facility that provides the logistics for bench-to-bedside radiopharmaceutical conveyance.

Long-standing expertise in fetal development and fetal/maternal interactions (e.g., cell and DNA trafficking) will be critical in the study of models focused on the **developmental origins of disease**. The NICHD *Scientific Vision for the Next Decade* highlights research areas where nonhuman primates will serve a critical role such as the pathophysiology of maternal/fetal interactions, maternal/fetal immunity, and the exposome (effect of environment on the fetus). The rise in allergic and autoimmune diseases highlights the susceptibility of immune pathways, and inflammation is a common theme for many chronic diseases [Excluded by Requester 2014].

The NIA *Living Long and Well in the 21st Century: Strategic Directions for Research on Aging* includes a research goal on improving the **understanding of healthy aging and disease**. The challenges and roadblocks identified include determining how cellular changes associated with aging contribute to decreased function, and the role stem and progenitor cells and their microenvironment play. Core and Affiliate Scientists are in a unique position to adapt current insights to develop new biological resources, tools, and technologies for studies focused on aging including the role of chronic inflammation, regeneration/repair, and new *in vivo* imaging tools that breaks new ground and extends prior discoveries. **In vivo imaging** will focus on sensitive tools such as:

- Anatomical and functional data to establish normative reference values for monkeys as they age in correlation with low-level chronic inflammation.

[Excluded by Requester] is in an NIH grant with [Excluded by Requester] (Brain, Mind, and Behavior Unit) on the role of circulating maternal antibodies that have been proposed to alter key fetal events associated with autism spectrum disorder.

- Studies that address new ways to radiolabel human stem/progenitor for long-term analyses post-transplant.
- New radiopharmaceuticals and imaging agents; the unique partnership with PETNET functions as a pipeline for commercialization of the concepts and compounds developed, which will be tested in rhesus monkeys.

Specific Aim 2. Contribute unique expertise and services.

Services, Outreach, and Resources. Unit Core Scientists will continue to advance translational research by fostering an environment that encourages and supports scientific expertise critical to the mission of the CNPRC, enhances research infrastructure, and increases efficiencies in the use of CNPRC resources. Services currently provided through Cores and outreach programs such as the Gene Therapy Center will continue, and new opportunities will be expanded such as through the West Coast Metabolomics Center. The CTSC Facilities, Cores, and Resources website will be updated with new resources and services as they are developed.

Repositories. [Excluded by Requester] will continue to provide cryopreserved reproductive tissues (see Colony Management and Research Services [Excluded by Requester] maintains a biorepository of paraffin- and OCT-embedded tissues, DNA, RNA, serum and plasma, cryopreserved whole tissues, peripheral blood mononuclear cells, and stem/progenitor cells (e.g., hematopoietic, mesenchymal, endothelial; fetal to aged) to meet investigator needs. All specimens are collected, processed, and stored according to standard protocols and documented in a secure database. This database has an automatic backup function performed by CNPRC IT staff to ensure integrity, and storage systems are armed with alarms that are monitored by UC Davis facilities 24/7.

Specific Aim 3. Training and Mentoring.

Core Scientists will continue their strong track record in training and mentoring at all career stages. The commitment of the Provost and Dean's of many UC Davis Schools and Colleges to new faculty positions at the CNPRC provides unprecedented opportunities to link with campus strategic opportunities such as the School of Medicine Translational Genomics Initiative with a recruitment that emphasizes expertise in early life genomics. This will also effectively capitalize on the strengths in the Genome Center, NIH West Coast Metabolomics Center, and BGI@UCDavis; early life genomics is one of the thematic focus areas in the School of Medicine Translational Genomics Initiative. In addition, similar to the recruitment of [Excluded by Requester] regenerative expertise in the lung will address lifespan health and targeted therapies based on age. While specific areas can be identified it will be important to cast a wide net for these recruitments to attract a broad and diverse candidate pool that can bring novel research synergies and opportunities, and applicants that can meet the NIH

requirements for Core Scientists. The School of Medicine Mentoring Academy and the well-established CTSC focus on junior faculty career development provides many opportunities to support these recruitments. Other recent School of Medicine recruitments in the vision sciences/regenerative medicine field include [Excluded by Requester] who will be transitioning to UC Davis and participate as a CNPRC Affiliate Scientist. The further mentoring of other Affiliate Scientists is an ongoing priority (e.g., [Excluded by Requester] through pilot projects and submitted grants. Other PhD-level investigators in the Unit (e.g., [Excluded by Requester] have developed unique primate-related expertise in reproductive sciences and regenerative medicine, are submitting grants, and will continue to add strength to the program as the CNPRC builds for the future.

Specific Aim 4. Promote high standards of research and animal care.

Core Scientists will continue to contribute to the highest quality research standards and service support to meet current and future research needs of investigators nationwide. As a component of the mentoring and training mission, Unit Core Scientists educate investigators at all career stages on ways to appropriately balance the research needs with the highest ethical standards while meeting the regulatory requirements. Core Scientists will continue to contribute to the CNPRC through their campus service activities in the Institutional Animal Care and Use Committee (IACUC) and Animal Care Program, and participation in key CNPRC committees such as the Research Advisory Committee, Colony Management Committee, and Morbidity and Mortality Committee.

CORE SCIENTIST NARRATIVES

Core Scientist [Excluded by Requester] **PhD**, Professor, Department of Biomedical Engineering, College of Engineering, Director of the UC Davis Center for Molecular and Genomic Imaging, Multimodal Imaging Core

Research Program: [Excluded by Requester] research interests center around biomedical imaging and in particular the development and application of *in vivo* molecular imaging systems. His major accomplishments have been in developing and applying very high resolution systems for PET, in particular the invention of the microPET technology for preclinical imaging that was subsequently widely adopted in academia and industry. He has contributed to the development of very high performance detectors for PET, and to multimodality imaging systems. He developed the first hybrid PET/MRI system, and this technology is now being translated for clinical use. The technologies developed have been broadly applied in biomedical science to study disease processes and measure the effects of novel therapeutic interventions. Major projects at the present time are: (1) the development of a total-body PET scanner for human biomedical research that will allow PET studies to be performed 40-times faster, or with 40-times lower radiation dose; (2) evaluation of new ceramic scintillator materials and silicon photomultipliers for PET detectors; (3) development of next generation animal PET and PET/MRI prototype scanners; (4) compact single photon imagers for animal studies; (5) novel phosphor-coated scintillators for depth-of-interaction encoding in PET; and (6) developing the concept of Cerenkov luminescence imaging as a novel way to image beta-emitting radionuclides non-invasively. [Excluded by Requester]

Contributions to the CNPRC Mission: Multimodal Imaging Core; work with [Excluded by Requester] on long-term strategic planning for *in vivo* imaging at the CNPRC; oversee radiotracer development (with [Excluded by Requester] and quality control and quality assurance of PET scanners; *in vivo* imaging workshops (2010 to 2012); search committee for new CNPRC Director; 23 publications (May 1, 2010 to April 30, 2014).

Table 6. Examples of Affiliates and Collaborations (Selected)

Name and Institution	Project Title	Collaborative Activities
[Excluded by Requester]	Enabling technologies for Ultra-high Sensitivity PET scanners (PQ13)	R01-CA170874
[Excluded by Requester]	High Throughput Design, Synthesis, and <i>In Vivo</i> Evaluation of Targeted Molecular Imaging Agents	RC4-EB012836

Core Scientist [Excluded by Requester] **MD, PhD**, Assistant Professor, Department of Medical Microbiology and Immunology, School of Medicine, Immunology and Pathogen Detection Resources Core

Research Program: [Excluded by Requester] is interested in microbial control over immune system development, and in immune responses to gene transfer vectors and stem/progenitor cells. He is participating in projects related to the microbiome and developmental paradigms that include a focus on immune ontogeny, the impact of environmental exposures, and the fetal/maternal interface.

Contributions to the CNPRC Mission: Immunology and Pathogen Detection Resources Core; leadership on microbiome and metabolome projects; 6 peer-reviewed publications (May 1, 2010 to April 30, 2014).

Table 7. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
[Excluded by Requester]	Aberrant T Cell Function and Immunopathogenesis of CMV Immune Recovery Uveitis	R21-EY018559

Excluded by
Requester

Core Scientist: [REDACTED] **PhD**, Professor Emeritus, Department of Population Health and Reproduction, School of Veterinary Medicine. Associate Director, Center for Health and the Environment, Endocrine Core **Research Program:** [REDACTED] research program encompasses two distinct disciplines, the first directed towards women's healthy aging. He is the lead of the animal core for P42-ES04699, which is in its 8th year and employs the nonhuman primate model for studies relevant to the health assessment and management of mid-aged women. He is also involved in the population-based SWAN that has studied over 3,000 mid-aged women longitudinally for 12 years in five clinical sites. Together, these activities have led to a novel explanation for the rise in adrenal steroids during the menopausal transition and the validation of the nonhuman primate model. The second aspect of his research program focuses on environmental hazards to human reproductive health. These projects are compound-specific and range from industrial solvents (benzene) to personal care product enhancements (triclorcarban in bar soaps) as well as off-gased plasticizers (phthalates). He participates in a Superfund Program Project supported for 18 years by NIEHS/EPA in which he serves as the Project Leader.

Contributions to the CNPRC Mission: Endocrine Core; colony management, diagnostic assay development; 17 peer-reviewed publications (May 1, 2010 to April 30, 2014).

Table 8. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	<i>In Utero</i> and Neonatal Effects of Triclorcarban	R21-ES016802
	Genes and Hormonal Fetal Antecedents to Sex Difference in the Brain in Depression	P50-MH082679
	Neurological and Reproductive Effects of Hexane	R01-ES014049

Excluded by Requester

Core Scientist: [REDACTED] **PhD**, Professor and Vice Chair for Research Department of Pediatrics and Department of Cell Biology and Human Anatomy, School of Medicine, Unit Leader, Multimodal Imaging Core **Research Program:** [REDACTED] translational research program has a particular focus on the fetus and infant with ongoing studies that address regenerative medicine, tissue engineering, stem cell transplantation, gene therapy, and the application and use of *in vivo* imaging modalities. She has a long-standing and productive track record in fostering partnerships and productive collaborations. She has studied human and nonhuman primate renal, endothelial, hematopoietic, mesenchymal, epithelial, and embryonic stem and progenitor cells from a lifespan perspective and for transplant purposes, and developed novel transplant paradigms that use *in vivo* imaging to monitor cell trafficking and fate. [REDACTED] integrates with campuswide programs and presents the importance of nonhuman primates for translational research at the national level.

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Contributions to the CNPRC Mission: Unit Leader, Research Advisory Committee, Multimodal Imaging Core; Director, NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases; Colony Management Advisory Committee and Mortality Review Committee; coordinate and facilitate investigator and trainee research needs (e.g., pilot projects, NIH grants); Stem Cell Training Program; Chair/Vice Chair, UC Davis IACUC and Animal Care Program Leadership Team; member of the CTSC leadership team; 32 peer-reviewed publications (May 1, 2010 to April 30, 2014).

Table 9. Examples of Affiliates and Collaborations (Selected)

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Phase I/II Study of AAV9-GAA Gene Transfer in Pompe Disease	IND-enabling studies
	Development of Live Attenuated Vaccines against Chlamydial Genital Tract Disease	CNPRC P51 Pilot Project and Private Source
	West Coast Central Comprehensive Metabolomics Resource Core	U24-DK097154 (Promotion and Outreach Core; Pilot projects)
	Development and <i>In Vivo</i> Characterization of Safety-Enhanced RhCMV/SIV Vectors; Development of an Effector-Memory T Cell AIDS Vaccine; Development of an Attenuated CMV Vector for an HIV/AIDS Vaccine	<ul style="list-style-type: none"> • R01-AI095113 • P01-AI094417 Private Source

Excluded by Requester

Core Scientist: [REDACTED] **PhD**, Professor-in-Residence and Director, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, School of Medicine, and the Chair of the Molecular, Cellular, and Integrative Physiology Graduate Group **Research Program:** The majority of [REDACTED] research focuses on the use of the rhesus monkey as a model for human reproduction in the areas of: (1) sperm biology and cryopreservation, (2) oocyte maturation and early embryo culture, and (3) reproductive toxicology. In order to improve the outcome for all males, not a select few, her research has focused on freezing epididymal sperm and a multifactorial design to individualize

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freezing extender components. Contraception development is also a major emphasis of male reproduction studies. Investigations on oocyte maturation and embryo development have focused on growth factors and gene expression as well as mechanisms for transgenerational effects. [Excluded by Requester] has utilized all of the above systems to evaluate reproductive impact of potential toxicants. Collaborations with clinical faculty provide human samples and the basis for translational studies on oocyte health and ovarian/reproductive tract function.

Contributions to the CNPRC Mission: Banking of sperm from males at colony endpoints; development of an alternative diet for idiopathic chronic diarrhea; identify obesity in the colony and approaches for prevention; provide frozen sperm to primate researchers; Colony Management Advisory Committee; 27 peer-reviewed publications (May 1, 2010 to April 30, 2014)

Table 10. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
[Excluded by Requester], University of Maryland	Gluconeogenesis and Energy Substrates in Primate Ovary	Pending Support
Michigan State University	Effect of Follistatin on Embryo Development	Pilot studies

Table 11. Reproductive Sciences and Regenerative Medicine Research Unit Funded Grants (does not include grants administered by the Department of Biomedical Engineering)

PI (Core Scientist PI)	Institution	Type	Title	Description
[Excluded by Requester]	University of Pittsburgh	Private Source	Development of Attenuated Vaccines against Chlamydial Genital Tract Disease	Testing of novel immunization strategies to overcome chlamydia-related disease
	UC Davis	NIH R01 (HL068035)	Flow Effects on Endothelial/Trophoblast Interactions	Studies focus on how migration of placental trophoblast cells is regulated by blood flow
		NIH R01 (HD057114)	Mechanisms of Rhesus Trophoblast Stem Cell Differentiation	Characterization of a novel trophoblast stem cell system
	UCSF	NIH R01 (HL107974)	Positive/Negative Selection in Minimally Ablative Transplants	Address issues limiting allogeneic transplantation by a novel gene delivery vector to genetically engineer donor stem cells
	UC Davis	NIH P42 (ES004699)	Biomarkers of Exposure to Hazardous Substances	This is a superfund basic research and training program
	Loma Linda University	NIH R01 (AI052079)	Nonhuman Primate Models for Human Xenotransplantation	Studies to overcome gal antibodies that result in rejection in xenogeneic transplants
	UCLA	NIH R01 (AI074043)	<i>In vivo</i> ADA Gene Delivery for the Treatment of SCID	New gene transfer techniques for ADA-SCID using lentiviral vectors in infant monkeys
	Michigan State University	NIH R24 (RR015253, OD 012221)	Primate Embryo Gene Expression Resource	Online resource with a database and other useful tools including oocytes and embryos converted to cDNA libraries
	UC Davis	Private Source	Supplemental FAA on Formula Intake	Test new formulas in infant monkeys
			Metabolomics	Study metabolomics biomarkers in relation to infant nutrition
	UCSF	NIH R01 (AI090677)	The Impact of Tolerance in the Newborn on Lentiviral Infection	Oral tolerance induction tested prenatally and SIV challenge postnatally
		NIH R01 (AI084109)	Interruption of Maternal-Fetal transmission of HIV	Studies on novel prenatal transfer techniques to induce tolerance and block SIV infection postnatally
		Private Source	Design of an Effective Vaccine against HIV: An Alternative	Novel approach to vaccination in fetal and infant monkeys
	UC Davis	NIH R01 (RR016581)	Response of Rhesus Sperm to Cryopreservation	Study methods to efficiently cryopreserve sperm
	Mt. Sinai	NIH P01 (AG016765)	Estrogen and the Aging Brain	Reproductive endocrine studies in aging monkeys

Excluded by Requester	UC Davis	Private Source	Task order #19	New imaging PET radioligand
	University of North Carolina	NIH P01 (HL112761)	Neutralizing Antibody and AAV FIX Gene Therapy	New approaches for studies on AAV to overcome neutralizing antibodies for hemophilia
	UC Davis	NIH R13 (HL072168)	Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases	Support for a multi-year national gene therapy symposium
		NIH R24 (HL085794)	Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases	Gene transfer strategies with lentiviral and AAV vectors in monkey models; extensive outreach to NHLBI investigators
		NIH S10 (RR025063)	PET/CT for Nonhuman Primate Imaging	Equipment grant to purchase a GE PET/CT clinical imaging system
		NIH S10 (OD016261)	Ultrasound Imaging for Nonhuman Primate Translational Research	Equipment grant to replace an ultrasound clinical imaging system
		NIH S10 (OD018102)	Nonhuman Primate IVIS Spectrum Imaging	Equipment grant to replace an optical imaging system
		CIRM CL1-00504	Translational Human Embryonic Stem Cell Shared Research Facility	Support for campus facility and infrastructure specifically for human stem cell research
		CIRM CG-99019, 99029, 99039, 07538	Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases	Additional support for 9 th , 10 th , 11 th , 12 th Annual Gene Therapy Symposium supported by the NHLBI (new funding each year)
		CIRM DR3-07281	Tissue Engineered Recellularized Tracheal Implants	IND-enabling studies for tissue engineered trachea replacements
		CIRM RC1-00144	Preclinical Model for Labeling, Transplant, and <i>In Vivo</i> Imaging of Differentiated Human Embryonic Stem Cells	Differentiation of human ES cells towards renal lineages and transplant into the fetal monkey model of obstructive renal disease
		CIRM RT1-01019	<i>In Vivo</i> Imaging for the Detection and Quantitation of Transplanted Stem/Progenitor Cells in Nonhuman Primates	Studies focus on enhancing PET imaging technologies for stem cell research
		CIRM TR1-01269	<i>In Utero</i> Model to Assess the Fate of Transplanted Human Cells for Translational Pediatric Therapies	These studies focus on fetal hematopoietic stem cell transplantation and methods to enhance engraftment
	UC Davis	Private Source	Immunoprotective Properties of Sperm Glycocalyx	Understand reproductive fitness and diagnostics for male infertility
	UC Davis	NIH R24 (RR025880, OD 010967)	Rhesus Monkey Oocyte Resources	Provide bank of oocytes, accessory cells, ovarian tissue, and cell lysates for investigators
		NIH R01 (ES016770)	Effects of Fetal Bisphenol A Exposure on Oogenesis	With co-PI Patricia Hunt, study maternal exposure to BPA and impact on fetal oogenesis
		NIH R01 (AA019595)	Binge Ethanol and Oocyte Quality	Impact of binge ethanol consumption on oocyte quality
		Private Source	Efficacy of Ultrasound Treatment as Male Contraceptive	Effects of therapeutic ultrasound on sperm and role as potential contraceptive
	UC Davis	CIRM DT2	MSC Engineered to Produce BDNF for Huntington's disease	IND-enabling studies for the treatment of Huntington's disease
	UC Davis	NIH R01 (DK075415)	Differentiating Human ESC towards Hepatocytes	Cell differentiation and transplant into the fetal monkey model

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE UNIT

PUBLICATIONS (May 1, 2010 to April 30, 2014)

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SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, [Excluded by Requester] and the IACUC. [Excluded by Requester]

1. **Proposed Use of Animals.** The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal] of indoor animal space. The outdoor animal housing area includes [Specific Animal Location] field corrals [Specific Animal] corn cribs [Specific Animal Location]. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLTV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. **Justification of Animal Use, Species Choice, and Numbers.** The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.
3. **Veterinary Care.** The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester]. Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations. Animals in the outdoor

animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

- 4. Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
- 5. Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

SCIENTIFIC COMPONENTS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT

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SCIENTIFIC UNITS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT**LETTERS OF SUPPORT**

Letters of support from the individuals named below are provided on the pages that follow.

1. Excluded by Requester MD, PhD, Professor and Powell University Chair in Genetics; Director, Powell Center for Rare Disease Research; Associate Chair of Pediatrics, University of Florida
2. Excluded by Requester MD, Professor, Microbiology, Immunology & Molecular Genetics and Pediatrics, University of California, Los Angeles
3. Excluded by Requester MD, Associate Professor in Residence, David Geffen School of Medicine, University of California, Los Angeles
4. Excluded by Requester PhD, Assistant Professor, Department of Psychiatry and Behavioral Sciences, UC Davis ~~WIND Institute~~, University of California, Davis
5. Excluded by Requester PhD, Professor, Department of Psychology; Director, Gene Therapy Center, School of Medicine, University of North Carolina at Chapel Hill
6. Excluded by Requester MD, PhD, Professor, Department of Pathology & Laboratory Medicine; Director, Gene Therapy Program, University of Pennsylvania School of Medicine



College of Medicine
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July 10, 2014

Excluded by Requester

Professor, Departments of Pediatrics and Cell Biology and Human Anatomy,
School of Medicine Reproductive Sciences Unit Leader, California National Primate Research Center,
Center for Fetal Gene Transfer for Heart, Lung, and Blood Diseases
University Of California, Pedrick and Hutchison Roads Davis, CA 95616-8542

Dear

Excluded by
Requester

Please accept this letter as enthusiastic support of your renewal application for funding of the California National Primate Research Center. Over the previous nine years of NHLBI support through your Center for Fetal Monkey Gene Transfer for Heart Lung and Blood Diseases we have had the opportunity to conduct critical experiments with the goal of bringing gene transfer studies to pediatric populations with inherited disease. The first collaboration lead to a key understanding of the biodistribution and longevity of expression of AAV vectors in primates. Subsequently, we were able to establish a novel feature of AAV9 in its ability to transduce cardiac tissue. These studies have lead the way to a series of experiments in support a clinical program in young children with Pompe disease. Facilitated by the support of data from the Center we received approval of an Investigational New Drug Application by the FDA for a novel gene therapy study and the study has just completed enrollment. One year data from the first cohort is very promising and several key publications have resulted from this work. The long-term success of this and related clinical studies will certainly depend future collaboration with the Center.

There is also no doubt that the annual symposia on Fetal Gene Transfer provides participants with a unique opportunity to interact with colleagues in a small, topic-focused setting that encourages discussion and collaboration. The interactions at this meeting have proven to be an excellent context for collaboration with members of the gene therapy community as well as with members of the Center for Fetal Gene Transfer. As an example, from my own laboratory, several students have had the opportunity to participate in the meeting and give oral and poster presentations, which has been an invaluable experience. The participation of students and post-doctoral fellows in the symposia is especially important and allows those who are in the early stages of their career to gain experience in presentation as well as the chance to participate in discussions with established investigators. This unique training opportunity will assure that we continue to recruit talented young scientists to the field of gene therapy.

The Center for Fetal Gene Transfer is a unique resource for primate experiments that are critical in bridging the gap between rodent studies and clinical application. For myself and the students from my lab who have participated in these symposia over the past several years, the knowledge we have gained as well

as the collaborations they have fostered have greatly benefited our work and will certainly help in assuring that the gene therapy projects we have established with continue to make an impact in human studies and change future medical care in inherited disease.

Best regards,

Excluded by Requester

Professor and Powell University Chair in Genetics
Director, Powell Center for Rare Disease Research
Associate Chair of Pediatrics

UNIVERSITY OF CALIFORNIA, LOS ANGELES

UCLA

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SANTA BARBARA • SANTA CRUZ



Excluded by Requester

July 7, 2014

Excluded by Requester

Professor and Vice-Chair for Research, Department of Pediatrics, School of Medicine
Unit Leader, Reproductive Sciences and Regenerative Medicine, California National Primate
Research Center
Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases
Translational and Pilot Programs Director, UC Davis Clinical and Translational Science Center

Dear

Excluded by
Requester

I am writing to state my enthusiastic support for the renewal of the Primate Center base grant. As you know, I have been a member of the Advisory Committee for the Center for Fetal Monkey Gene Transfer for Heart, Lung and Blood Diseases since its inception and have been involved in the review of the annual Pilot Project applications and have attended each of the annual scientific symposia. I strongly believe that this is a unique and highly valuable resource for the field of gene therapy and the pilot projects supported have been instrumental in assessing the translational potential for a variety of gene therapy approaches which has led to clinical applications. The extremely high quality of the work performed in the Center with the array of technologies available for *in vivo* interventions and imaging make these studies highly reliable as pre-clinical models. My own group has directly used the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung and Blood Diseases for pilot studies of non-myeloablative pre-transplant conditioning and direct *in vivo* gene delivery using lentiviral vectors, which are underlying current and future clinical trials of gene therapy for ADA-deficient SCID and sickle cell disease. Additionally, you and I have shared RO1 and PO1 awards for other studies done at the Center. These studies have led to direct clinical applications for our trials of gene therapy for immune deficiency diseases and sickle cell disease, e.g. the use of non-myeloablative conditioning with busulfan that we modeled in rhesus infants (1,2). Other novel studies on biodistribution of *in vivo* administered lentiviral vectors will have applications to the treatment of a variety of genetic disorders (3-6)

In addition, the annual symposia have been rich sources of knowledge sharing with great combinations of speakers from diverse areas (gene therapy, imaging science, bioengineering). The small meeting setting allows direct interactions among investigators and has spawned many productive collaborations.

The Primate Center is a crucial resource that is essential for our translational studies and ongoing collaborations with you. I am highly supportive of the renewal of this vital support.

Sincerely,

Excluded by Requester

Professor, Microbiology, Immunology &
Molecular Genetics and Pediatrics
University of California, Los Angeles

Excluded by Requester

1.

Excluded by Requester

Effects of busulfan dose

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Excluded by Requester

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3.

Excluded by Requester

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4.

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5.

Excluded by Requester

Excluded by Requester

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6.

Excluded by Requester

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**DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA**

Excluded by Requester

Associate Professor
UCLA School of Medicine

Excluded by Requester

July 14, 2014

Excluded by Requester

California National Primate Research Center
University of California, Davis
Pedrick and Hutchison Roads
Davis, CA 95616-8542

Excluded by Requester

Dear

I am very pleased to write a strong letter of support for Primate Center base grant renewal. As you know I am quite happy that you encouraged me to pursue monkey studies to examine a model with an immune system closer to that of humans. As you are aware, we have demonstrated that we have operational tolerance to foreign proteins in our mouse model by administration of gene therapy vectors in utero and in neonates. It has been quite encouraging that we saw a similar finding in the limited studies that we performed in monkeys with you as part of the pilot study and animals provided by your Center for Fetal Monkey Gene Transfer For Heart, Lung, and Blood Diseases located at the California National Primate Research Center. I

Pending Support

As you are also aware, we are completing the data analysis to submit this work as a combined mouse and monkey manuscript that I think we be of significance in the field. On the horizon, I have been working with the NHLBI Gene Therapy Resource Program to obtain approval for vector aliquots so we can perform additional studies in your monkey model in utero. This will be quite interesting to determine if the fetal immune system can be altered. As you know the aim of all of these studies is to determine if we can develop new therapies for inherited protein disorders in humans. With certain secreted and intracellular protein disorders, such as Hemophilia A and Pompe Disease respectively, the ability of overcoming the established immune response to protein replacement therapy is very difficult in what are both life threatening (Hemophilia A) and fatal (Pompe Disease) disorders that lack good alternatives today in these situations. If we can establish operational tolerance, as has been suggested by our limited data to date in monkeys, this may change substantially both the treatment and out come for patients with these and other disorders and so change the paradigm of when certain disorders can begin treatment.

I look forward to our continue collaboration in these important areas of investigation.

Sincerely,

Excluded by Requester

UNIVERSITY OF CALIFORNIA, DAVIS

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July 12, 2014

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California National Primate Research Center
Professor and Vice-Chair for Research, Department of Pediatrics, and
Department of Cell Biology and Human Anatomy, UC Davis School of Medicine
Translational and Pilot Programs Director, UC Davis Clinical and Translational Science Center
Davis, CA 95616

Excluded by
Requester

Dear

I am writing to stress how crucial the facilities and researchers at the California National Primate Research Center (CNPRC) have been for my career development at UC Davis. In particular, your support and encouragement for my plans to use the primate model have greatly expanded the horizons of my research, and led directly to new discoveries on prenatal brain development in my laboratory. I am deeply indebted and grateful for the invaluable resources, including prenatal monkey brain tissue, which you have provided for my research program.

My laboratory research centers on determining how CNS development is regulated under normal and pathological conditions, as a means for identifying factors that contribute to the etiology of neurodevelopmental disorders. The developing monkey CNS closely models the complexity of human brain development, something that is not captured by rodent models. As such, the monkey model of brain development offers key advantages. For example, monkey brain development is not compressed into a short period of time, but proceeds on a pace matched by that in the human brain - allowing us to both identify and manipulate important steps in brain development. Your support, and the innovative resources at the CNPRC have made primate research in my laboratory possible.

I am very excited to continue our established collaboration to work together on development of new primate models for CNS disorders. I also look forward to completing our investigation on neural precursor cell development in the prenatal macaque brain through our CNPRC Pilot Grant Award.

Sincerely,

Excluded by Requester

Department of Psychiatry and Behavioral Sciences
UC Davis MIND Institute
Sacramento, CA 95817



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July 6, 2014

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Professor, Departments of Pediatrics and Cell Biology and Human Anatomy
Reproductive Sciences and Regenerative Medicine Unit Leader
California National Primate Research Center
Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood Diseases
University of California, Davis

Excluded by Requester

Dear

I am pleased to provide this letter of strong support for the competitive renewal of the California National Primate Research Center (CNPRC) base grant. As a recipient of support to conduct a project in the NHLBI Center for Fetal Monkey Gene Transfer for Heart, Lung and Blood Diseases, I can speak directly to the importance of this resource. First it should be noted that the services are outstanding and make available to the research community a truly unique opportunity to carry out non-human primate studies. Similar to other colleagues, we have been able to test our novel AAV vector constructs in nonhuman primates, which would not have been possible without your assistance and support. More importantly, these experiments provide critical data for feasibility studies in humans.

For these reasons, I should mention that these experiments are crucial from a scientific perspective as well as regulatory (i.e., FDA). For example, in one of our studies we are trying to evaluate the best vector for gene delivery for the heart. As a result of the non-invasive imaging we are able to carry out at your facility; we reduced the number of animals in the experiment dramatically and could obtain data in real time. This was the data presented to the FDA in the pre IND package in order to carry out "pivotal" tox bio-distribution studies. I have not been able to find this expertise of services elsewhere truly making your capabilities "one of a kind".

Because we have a specific interest in using *in vivo* imaging techniques (PET/CT, optical imaging) to monitor gene expression long-term and non-invasively we are appreciative that you have developed very unique capabilities in monkeys that further enhances our interest and provides more opportunities to explore *in vivo* imaging in nonhuman primates. This not only advances the field but allows us to develop methods for the use of similar protocols in humans. Your center and this topic are timely since we have ongoing safety trials related to non-invasive imaging for DMD clinical studies. As we discussed, we

genetherapy.unc.edu

have plans to submit an NIH application for non-human primate studies based on the results of this project. We hope that the outcome will be a continued success as we have already experienced with your unique Center.

I also wanted to mention the new AAV targeted vectors we are now studying with you for intracranial/neural applications. Again, the unique imaging capabilities you have developed (e.g., ultrasound guided procedures, bioluminescence) are crucial in the development and study of this model.

I look forward to continued studies with you on our recently funded P01, and to further use your unique resources and expertise.

Sincerely

Excluded by Requester

Professor/Director
Pharmacology/Gene Therapy Center



Penn Medicine

University of Pennsylvania School of Medicine

Gene Therapy Program

Department of Pathology and Laboratory Medicine
Division of Transfusion Medicine

July 10, 2014

Excluded by Requester

California National Primate Research Center
University of California, Davis
Pedrick and Hutchinson Roads
Davis CA 95616-8542

Excluded by Requester

Dear

I am writing to express my support for your competing renewal application for the California National Primate Research Center.

I have interacted with your Gene Therapy Center on multiple occasions and have found the resource you provide both unique and critical to the progression of gene therapy. Before I review the specifics of the interactions I want to comment on the value of having access to nonhuman primates for gene therapy research.

My experience with gene therapy research spans 20 years and involves different vector platforms (retrovirus, adenovirus and adeno-associated virus) in small and large animals and in clinical trials. These complete data sets of experiments in mice, monkeys and humans have led to several important themes including the value of nonhuman primates in simulating host vector interactions in humans. Smaller animal models are of limited value in assessing the role of natural infections on gene therapy or the potential of T cells to capsids and transgene products in extinguishing expression. The response of the nonhuman primate to vectors much better simulates what is seen in humans. This is even more complicated when evaluating younger primates such as in the setting of in utero or immediate post natal gene therapy where nonhuman primates are necessary.

I have had the privilege of participating in the Center's annual scientific conference which is extremely well organized and of value. In the day of large society meetings we miss out on the interactions that occur with smaller meetings such as that run by the Gene Therapy Center.

Another interface with the Center was in the evaluation of novel AAV vectors discovered in my laboratory for *in vivo* gene therapy. Excluded by was one of the first to call me when we published the new the AAV vectors. She was extremely effective in establishing the scientific and administrative foundation for a sharing of reagents with her group and in the evaluation in NHPs. The data that emerged were first rate and of significant value to the field.

The more recent collaboration we forged in the Gene Therapy Center related to the development of gene therapy for liver metabolic diseases. My lab is pursuing approaches for liver directed gene therapy in parallel for two disorders which are both funded by NIH in separate P01s: familial hypercholesterolemia in the treatment of adolescents and adults and ornithine transcarbamoylase deficiency (OTCD) for the treatment of children. An Ethics Advisory Board was convened to help guide the pre-clinical development of both programs, the most complicated being that involving clinical studies of AAV gene therapy for OTCD. In collaboration with the Advisory Board and our clinical collaborators, we established a working model for using gene therapy for OTCD which involves administering vector to newborns with severe OTCD after they recover from their neonatal crisis of hyperammonemia. The goal would be to achieve some metabolic stability in the newborns as they await liver

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TRL Suite 2000, 125 S. 31st Street | Philadelphia PA 19104-3403

Letters Of Support

Page 1509

Obtained by Rise for Animals.

Uploaded to Animal Research Laboratory Overview (ARLO) on 09/19/2020

transplantation which is the standard of care but not safely done until they are about 1 year of age or 10 kg in size. In summary gene therapy would provide a “bridge to transplant.” The critical question is at what age can we deliver the vector and achieve high and stable gene transfer. Studies in mice indicated that high level expression could be achieved at any age but that transgene expression was transient when vector was administered before 1 week of age. We believe the instability was due to the early proliferation of hepatocytes realized in a new born and the dilution and/or activate of vector genomes.

We contacted the Center about performing pilot studies on human rhesus macaques administered AAV8 vector expressing a reporter gene. Specifically, 1 week old male animals (OTCD is X linked recessive) are delivered AAV8 vector via a peripheral vein and sacrificed either 1 week or 4 weeks later. Our data showed incredibly high transduction of hepatocytes (almost 90% following 3×10^{12} GC/kg) in animals sacrificed 1 week after injection. However, transduction efficiency declined 10 fold over the ensuing 3 weeks consistent with what we saw in mice. We are now conducting studies in collaboration with the Center with animals slightly older to see if we can define the window of development in primates when more stable transgene expression can be achieved. These data are viewed a seminal by the scientists, clinicians and the Advisory Board in establishing the rational for a clinical trial.

In summary, the California National Primate Research Center is crucial for ensuring the ongoing needs and opportunities provided in gene therapy remain available. Excluded by Requester runs a great program and is extremely collaborative and effective in providing access to the resources of the Center.

Sincerely,

Excluded by Requester

SCIENTIFIC UNITS: REPRODUCTIVE SCIENCES AND REGENERATIVE MEDICINE RESEARCH UNIT

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.

APPLICATION FOR FEDERAL ASSISTANCE

SF 424 (R&R)**5. APPLICANT INFORMATION****Organizational DUNS*:** 0471200840000

Legal Name*: Regents of the University of California
 Department: Sponsored Programs
 Division: Office of Research
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153

Person to be contacted on matters involving this application

Prefix: First Name*: Middle Name: Last Name*: Suffix:
 Ms. Alyssa Bunn
 Position/Title: Contracts and Grants Analyst
 Street1*: 1850 Research Park Drive
 Street2: Suite 300
 City*: Davis
 County:
 State*: CA: California
 Province:
 Country*: USA: UNITED STATES
 ZIP / Postal Code*: 956186153
 Phone Number*: 530-754-7827 Fax Number: 530-754-7879 Email: aabunn@ucdavis.edu

7. TYPE OF APPLICANT*

H: Public/State Controlled Institution of Higher Education

Other (Specify):

☒ Small Business Organization Type☐ Women Owned☐ Socially and Economically Disadvantaged**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***

Respiratory Diseases Research Unit

12. PROPOSED PROJECT

Start Date* Ending Date*
 05/01/2015 04/30/2020

Project/Performance Site Location(s)**Project/Performance Site Primary Location**

☒ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: University of California Davis
Duns Number: 0471200840000
Street1*: One Shields Ave
Street2:
City*: Davis
County:
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 956165270
Project/Performance Site Congressional District*: CA-003

File Name

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
1.a. If YES to Human Subjects	
Is the Project Exempt from Federal regulations? <input type="radio"/> Yes <input type="radio"/> No	
If YES, check appropriate exemption number: <input type="text"/> 1 <input type="text"/> 2 <input type="text"/> 3 <input type="text"/> 4 <input type="text"/> 5 <input type="text"/> 6	
If NO, is the IRB review Pending? <input type="radio"/> Yes <input type="radio"/> No	
IRB Approval Date:	
Human Subject Assurance Number	
2. Are Vertebrate Animals Used?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
2.a. If YES to Vertebrate Animals	
Is the IACUC review Pending? <input type="radio"/> Yes <input type="radio"/> No	
IACUC Approval Date:	
Animal Welfare Assurance Number	
3. Is proprietary/privileged information included in the application?* <input checked="" type="radio"/> Yes <input type="radio"/> No	
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
4.b. If yes, please explain:	
4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? <input type="radio"/> Yes <input type="radio"/> No	
4.d. If yes, please explain:	
5. Is the research performance site designated, or eligible to be designated, as a historic place?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
5.a. If yes, please explain:	
6. Does this project involve activities outside the United States or partnership with international collaborators?* <input type="radio"/> Yes <input checked="" type="radio"/> No	
6.a. If yes, identify countries:	
6.b. Optional Explanation:	
7. Project Summary/Abstract*	Filename RD_Abstract.pdf
8. Project Narrative*	
9. Bibliography & References Cited	RD_Bibliography.pdf
10. Facilities & Other Resources	RD_FacilitiesOtherResources.pdf
11. Equipment	RD_Equipment.pdf

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

ABSTRACT

The mission of the **Respiratory Diseases Research Unit** is to define the cellular and molecular mechanisms for diseases of the respiratory system as a foundation to develop therapeutic strategies. Core and Affiliate Scientists within the Research Unit utilize the nonhuman primate as an important translational animal model for understanding the pathogenesis of respiratory diseases that affect humans. Research programs within the Research Unit are multidisciplinary and synergistic, integrating the fields of inhalation toxicology, mucosal immunology, and neurophysiology in a comprehensive fashion to address critical scientific problems in pulmonary medicine. Moreover, each Unit Core Scientist serves as a resource to the California National Primate Research Center (CNPRC) by contributing unique expertise towards service cores and management. Major scientific focus areas within the Unit are to characterize the development of the respiratory system during early life, to understand the pathways by which lung development is regulated, and to investigate the long-term health impacts of environmental exposures. Unit Core and Affiliate Scientists have a long history of collaborative investigations on air pollution using rodent and nonhuman primate models to extrapolate the health effects of exposures on the human lung across the lifespan. A significant accomplishment during this funding period has been the construction of a new Respiratory Diseases Center at the CNPRC, with dedicated laboratory space for pulmonary research and a state-of-the-art Inhalation Exposure Facility. Completion of the proposed Specific Aims in this P51 renewal will strengthen the Respiratory Diseases Unit as a CNPRC resource by expanding research in emerging areas such as infectious disease, by increasing opportunities for investigators to conduct translational studies in a comparative fashion, and by mentoring junior investigators to develop into future nonhuman primate respiratory scientists.

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

FACILITIES AND OTHER RESOURCES

Laboratories: Within the Respiratory Diseases Center at the CNPRC, [Excluded by Requester] will each occupy approximately 800 sq. ft. of laboratory space and a 222 sq. ft. tissue culture room that is fully equipped for cell [Excluded by Requester] molecular biology. [Excluded by Requester] has three 200 sq. ft. laboratories fully equipped for molecular biology, [Excluded by Requester] processing, and histomorphometry located at the Center for Health and the Environment. [Excluded by Requester] has 900 sq. ft. of laboratory space fully equipped for neurophysiology studies located in VM3B on campus.

Clinical: Clinical care and related procedures at the CNPRC are conducted in the hospital area containing pre- and post-surgery suites, outpatient, hospital and isolation wards, surgery, and pathology suites. The Clinical Pathology Laboratory includes services for hematology, clinical chemistry, bacteriology, parasitology, and serology (see **Primate Services**).

Animal: The vivarium, which is part of the UC Davis AAALAC-accredited program, includes indoor animal space including animal rooms, hospitals, surgery suites, nurseries, radioactive monitoring housing areas, and infectious animal housing. The outdoor animal housing area includes half-acre field corrals and corn-cribs as described in other sections of the application. Primate Services is centralized and provides animal care, colony management, research support, training, occupational safety, and a staff of expert animal handlers. The Clinical Pathology Laboratory in Anatomic and Clinical Pathology Services provides diagnostic support services as noted. The veterinary staff includes on-site veterinarians for clinical care (24/7), veterinary pathologists, and animal health technicians, all described in other sections of the application. See Primate Services sections for more details.

Computer: Colony demographics, breeding management, and health and pathology are all computerized, and **Information Technology Services** provides desktop support and other related services. Biostatistics services and Biomedical Informatics support are also provided on campus and through the UC Davis CTSC. Multiple Macintosh and PC computer systems and appropriate software for word processing, graphics, spreadsheets, and statistical analyses are all available.

Office: Within the Respiratory Diseases Center at the CNPRC, [Excluded by Requester] each have 100 sq. ft. offices. [Excluded by Requester] has a 120 sq. ft. office at the Center for Health and the Environment. [Excluded by Requester] has a 150 sq. ft. office in VM3B on campus.

Other: The CNPRC provides the optimal environment for studies with nonhuman primates based on the facilities and support services available. All laboratories are regularly inspected by UC Davis, Yolo County, and California agencies to assure compliance with regulations regarding the use of biohazardous agents and infectious, chemical, and radioactive waste.

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT**EQUIPMENT**

Excluded by Requester

laboratory consists of laminar flow hoods (2), CO₂ incubators (2), standard 4° refrigerators (2), ≤-20°C freezer (1), bench top centrifuges (2), PCR hood, a cytospin, and waterbaths (2).

Excluded by Requester

laboratory includes laminar flow hoods (2), fume hoods (2), CO₂ incubators (4), a microscope and inverted microscopes (2), a thermocycler, 4° refrigerators (3), ≤-20°C freezers (2), a ≤-80°C freezer (located in the laboratory), one ≤-80° freezer (located in common space), a Taylor Wharton Cryogenic Storage Unit (capacity for 24,000 samples, located in common space), microcentrifuge, bench top centrifuges (2), a PCR hood, protein and DNA electrophoresis equipment, and waterbaths (4).

Excluded by Requester

A Leica LMD6000 laser capture microscope with DIC and cutting lenses from 6.3x to 150x; laser scanning confocal microscope with long working distance water immersion lenses is located in the School of Veterinary Medicine and available on a recharge basis to image fluorescently stained whole mount tissues; ABI Step One Plus Taqman machine for RT-PCR; a Nexelom Cellometer for cell counting; a plate reading spectrophotometer with kinetic capability (SpectraMax Plus); nanodrop spectrophotometer; research quality epifluorescent microscopes with cameras and imaging software (3); embedding and sectioning systems (microtomes, embedders) for paraffin, frozen and resin sections are located at the Center for Health and the Environment; a cytospin for preparing slides for cell lavage differentials.

Excluded by Requester

There is a wide array of instruments and related equipment for the measurement of pulmonary function available in laboratory and as described in the Inhalation Exposure Core.

Excluded by Requester

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

PROFILE - Senior/Key Person

Excluded by Requester

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**A. Senior/Key Person**

Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base	Calendar	Academic	Summer	Requested	Fringe	Funds Requested (\$)*	
	Name					Salary (\$)	Months	Months	Months	Salary (\$)*	Benefits (\$)*		
1.	Excluded by Requester					Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	24,411.00	9,736.00	34,147.00
2.						Core Scientist			0.0	0.0	18,150.00	563.00	18,713.00
3.						Core Scientist			0.0	0.0	18,150.00	6,071.00	24,221.00
4.						Core Scientist			0.0	0.0	12,651.00	5,046.00	17,697.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						94,778.00	

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		21,461.00	11,353.00	32,814.00
1	Technical Support	Excluded by Requester			31,619.00	16,726.00	48,345.00
2	TBN Core Scientists		2.4		29,841.00	9,982.00	39,823.00
4	Total Number Other Personnel					Total Other Personnel	
						120,982.00	
Total Salary, Wages and Fringe Benefits (A+B)							215,760.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,000.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 1**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2015**End Date*:** 04-30-2016**Budget Period:** 1

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,000.00
2. Publication Costs	6,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,000.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	233,760.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	233,760.00	53,064.00
		Total Indirect Costs	53,064.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	286,824.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RD_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	24,656.00	10,405.00	35,061.00
2.					Core Scientist			0.0	0.0	18,150.00	563.00	18,713.00
3.					Core Scientist			0.0	0.0	18,150.00	6,392.00	24,542.00
4.					Core Scientist			0.0	0.0	12,777.00	5,392.00	18,169.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						96,485.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*	
	Post Doctoral Associates							
	Graduate Students							
	Undergraduate Students							
1	Secretarial/Clerical	EFFORT			21,676.00	11,990.00	33,666.00	
1	Technical Support	Excluded by Requester			31,935.00	17,665.00	49,600.00	
2	TBN Core Scientists	2.4			29,956.00	10,550.00	40,506.00	
4	Total Number Other Personnel					Total Other Personnel		123,772.00
					Total Salary, Wages and Fringe Benefits (A+B)		220,257.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

ORGANIZATIONAL DUNS*: 0471200840000

Budget Type*: ☒ Project ☒ Subaward/Consortium

Enter name of Organization: Regents of the University of California

Start Date*: 05-01-2016

End Date*: 04-30-2017

Budget Period: 2

C. Equipment Description

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:

D. Travel

Funds Requested (\$)*

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,270.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,270.00

E. Participant/Trainee Support Costs

Funds Requested (\$)*

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 2**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2016**End Date*:** 04-30-2017**Budget Period:** 2

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,090.00
2. Publication Costs	6,180.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,270.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	238,797.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	238,797.00	54,207.00
Total Indirect Costs			54,207.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	293,004.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RD_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	<div>Excluded by Requester</div>				Scientific Unit Leader/Core Scientist	<div>Institutional Base Salary</div>	<div>EFFORT</div>	0.0	0.0	25,898.00	11,313.00	37,211.00
2.					Core Scientist			0.0	0.0	18,150.00	578.00	18,728.00
3.					Core Scientist			0.0	0.0	18,150.00	6,610.00	24,760.00
4.					Core Scientist			0.0	0.0	13,421.00	5,863.00	19,284.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	99,983.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			22,768.00	13,004.00	35,772.00
1	Technical Support	Excluded by Requester			33,544.00	19,159.00	52,703.00
2	TBN Core Scientists	2.4			30,794.00	11,215.00	42,009.00
4	Total Number Other Personnel					Total Other Personnel	130,484.00
Total Salary, Wages and Fringe Benefits (A+B)							230,467.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,548.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,548.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 3**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☒ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2017**End Date*:** 04-30-2018**Budget Period:** 3

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,183.00
2. Publication Costs	6,365.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,548.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	249,563.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	249,563.00	56,651.00
Total Indirect Costs			56,651.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	306,214.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RD_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	26,675.00	11,999.00	38,674.00
2.					Core Scientist			0.0	0.0	18,150.00	596.00	18,746.00
3.					Core Scientist			0.0	0.0	18,150.00	6,809.00	24,959.00
4.					Core Scientist			0.0	0.0	13,824.00	6,218.00	20,042.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:								Total Senior/Key Person	102,421.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			23,451.00	13,793.00	37,244.00
1	Technical Support	Excluded by Requester			34,550.00	20,321.00	54,871.00
2	TBN Core Scientists	2.4			31,300.00	11,742.00	43,042.00
4	Total Number Other Personnel					Total Other Personnel	135,157.00
Total Salary, Wages and Fringe Benefits (A+B)							237,578.00

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,834.00
2. Foreign Travel Costs	0.00
Total Travel Cost	9,834.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 4**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2018**End Date*:** 04-30-2019**Budget Period:** 4

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,278.00
2. Publication Costs	6,556.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	9,834.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	257,246.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	257,246.00	58,395.00
		Total Indirect Costs	58,395.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	315,641.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RD_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**A. Senior/Key Person**

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary (\$)	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits (\$)*	Funds Requested (\$)*
1.	Excluded by Requester				Scientific Unit Leader/Core Scientist	Institutional Base Salary	EFFORT	0.0	0.0	27,475.00	12,739.00	40,214.00
2.					Core Scientist			0.0	0.0	18,150.00	614.00	18,764.00
3.					Core Scientist			0.0	0.0	18,150.00	7,009.00	25,159.00
4.					Core Scientist			0.0	0.0	14,239.00	6,602.00	20,841.00
Total Funds Requested for all Senior Key Persons in the attached file												
Additional Senior Key Persons:			File Name:			Total Senior/Key Person						104,978.00

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary (\$)*	Fringe Benefits*	Funds Requested (\$)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical		EFFORT		24,155.00	14,638.00	38,793.00
1	Technical Support	Excluded by Requester			35,587.00	21,566.00	57,153.00
2	TBN Core Scientists		2.4		31,826.00	12,290.00	44,116.00
4	Total Number Other Personnel					Total Other Personnel	
						140,062.00	
						Total Salary, Wages and Fringe Benefits (A+B)	
						245,040.00	

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5**C. Equipment Description**

List items and dollar amount for each item exceeding \$5,000

Equipment Item	Funds Requested (\$)*
Total funds requested for all equipment listed in the attached file	0.00
Total Equipment	0.00

Additional Equipment: File Name:**D. Travel****Funds Requested (\$)***

1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	10,129.00
2. Foreign Travel Costs	0.00
Total Travel Cost	10,129.00

E. Participant/Trainee Support Costs**Funds Requested (\$)***

1. Tuition/Fees/Health Insurance	0.00
2. Stipends	0.00
3. Travel	0.00
4. Subsistence	0.00
5. Other:	
0 Number of Participants/Trainees	Total Participant Trainee Support Costs
	0.00

RESEARCH & RELATED Budget (C-E) (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, BUDGET PERIOD 5**ORGANIZATIONAL DUNS*:** 0471200840000**Budget Type*:** ☒ Project ☐ Subaward/Consortium**Enter name of Organization:** Regents of the University of California**Start Date*:** 05-01-2019**End Date*:** 04-30-2020**Budget Period:** 5

F. Other Direct Costs	Funds Requested (\$)*
1. Materials and Supplies	3,376.00
2. Publication Costs	6,753.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	10,129.00

G. Direct Costs	Funds Requested (\$)*
Total Direct Costs (A thru F)	265,298.00

H. Indirect Costs			
Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base (\$)	Funds Requested (\$)*
1. MTDC Primate Center Rate	22.7	265,298.00	60,223.00
Total Indirect Costs			60,223.00
Cognizant Federal Agency	DHHS, ERNEST WILLARD, (415) 437-7820		
(Agency Name, POC Name, and POC Phone Number)			

I. Total Direct and Indirect Costs	Funds Requested (\$)*
Total Direct and Indirect Institutional Costs (G + H)	325,521.00

J. Fee	Funds Requested (\$)*
	0.00

K. Budget Justification*	File Name: RD_Justification.pdf
	(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT**BUDGET JUSTIFICATION****PERSONNEL**

The personnel table provides an overview of the percent full time equivalent (FTE) devoted to CNPRC base grant functions and the funding source. Totals with an asterisk (*) represent those individuals whose effort is split among more than one component of the CNPRC.

Personnel	Role	Percent (%) FTE devoted to CNPRC base functions by source			
		P51	Program Income	Other	Total
Excluded by Requester	Core Scientist, Unit Leader	% Effort			
	Core Scientist				
	Core Scientist				
	Core Scientist				
TBN	Core Scientist	10	0	90	100
TBN	Core Scientist	10	0	90	100
Excluded by Requester	Administrative Assistant	% Effort			
	Unit Safety Coordinator				

TBN=10-06-Marreau

Excluded by Requester

PhD, Core Scientist and Unit Leader

EFFORT

months -

% Effort

Excluded by Requester

is Associate

Professor in the Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine. Dr. research program is focused on investigating the impact of environmental exposures (air pollution, allergens, microbes) on pulmonary and immune system development during the first year of life. The overall goal of research is to understand the mechanisms of susceptibility in the human infant that contribute to pediatric airways dysfunction, which may ultimately lead to generation of new diagnostics and preventive therapies. serves as the CNPRC Associate Director for Research.

Excluded by Requester

Excluded by Requester

EFFORT

months -

% Effort

Excluded by Requester

PhD, Core Scientist

is Professor in the Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine and served as CNPRC Director during the current funding period. research is focused on airways epithelial, inflammatory, and immune cell interactions. His laboratory uses nonhuman primate models of asthma and chronic obstructive pulmonary disease (COPD) (emphysema) to investigate lung growth, differentiation and aging, particularly in response to inhaled allergens and pollutants. He developed an unbiased stereologic method of counting alveoli that is independent of lung inflation and is an expert in the use of stereology for quantitative measures. Dr. is also a member of the Multimodal Imaging Core.

Excluded by Requester

Excluded by Requester

PhD, Core Scientist

EFFORT

months -

% Effort

Excluded by Requester

is Professor in the

Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine, and Professor of Pediatrics, School of Medicine. research interests are focused on understanding the consequences in the lung of exposure to environmental tobacco smoke in monkeys during critical perinatal periods of development (from early gestation to 13 months postnatal age), using morphological, physiological, biochemical, and immunological and molecular approaches to measure effects. He has also studied the impact of allergens on innervation of the airways using a novel technique of lung whole mount sections. is a member of the Inhalation Exposure Core.

Excluded by Requester

Excluded by Requester

PhD, Core Scientist

EFFORT

months -

% Effort

Excluded by Requester

is Professor,

Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine. research program in nonhuman primate lung physiology has focused on the development and validation of the rhesus monkey model of allergic asthma; the application of this model to study the interaction of allergen- and ozone-induced responses in infant monkeys; and the mechanism underlying the development of airway hyper-responsiveness in atopic and non-atopic asthma. He is the lead for the Inhalation Exposure Core.

Excluded by Requester

TBN, Core Scientists (2) (1.2 calendar months – 10% each Core Scientist). The commitment of the Provost and respective Dean's of the Schools of Medicine and Veterinary Medicine, and the Colleges of Biological Sciences, Engineering, and Letters and Sciences (see **Overview**) to new faculty positions includes two Unit

Core Scientist positions (see Research Strategy). One of the new faculty recruitments is proposed at the junior investigator level and one with a more established research program.

Excluded by Requester **Administrative Assistant** EFFORT months % Effort Excluded by Requester provides administrative support for CNPRC-related activities and programs.

Excluded by Requester **PhD, Unit Safety Coordinator** EFFORT months % Effort Excluded by Requester serves as the Unit Safety Coordinator, provides assistance in the training of staff and students, coordinates and prepares sample shipments to investigators, and maintains the required documentation associated with these activities.

FRINGE BENEFITS

Fringe benefits are calculated at the UC Davis federally negotiated rates, which are applied by title code and fiscal year (July through June)

EQUIPMENT

None requested

TRAVEL

\$9,000 total is requested for each Core Scientist to attend a national meeting in their respective area(s) of expertise (6 x \$1,500).

SUPPLIES

\$3,000 in general supplies is requested to support activities with new investigators and sharing of resources.

OTHER EXPENSES

\$6,000 is requested for manuscript preparation and submission (6 x \$1,000).

SUBSEQUENT YEARS

In Years 2 through 5, all non-personnel costs are increased by 3%. Personnel costs are increased based on projected salary escalations by title code and the UC Davis federally negotiated fringe benefit rates.

FACILITIES AND ADMINISTRATIVE COSTS (INDIRECT COSTS)

Indirect Costs are budgeted in accordance with the UC Davis rate agreement dated August 19, 2013 at 22.7%, which is the negotiated rate for the CNPRC Base Grant. Per the UC Davis' rate agreement, this indirect cost rate is applied on a Modified Total Direct Cost basis, which includes all salaries and wages, fringe benefits, materials and supplies, services, travel, and the first \$25,000 of each subgrant and subcontract. Excluded from the modified total direct costs are equipment; capital expenditures; charges for tuition remission; rental costs; scholarships and fellowships; as well as the portion of each subgrant and subcontract in excess of \$25,000.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals (\$)	
Section A, Senior/Key Person		498,645.00
Section B, Other Personnel		650,457.00
Total Number Other Personnel	20	
Total Salary, Wages and Fringe Benefits (A+B)		1,149,102.00
Section C, Equipment		0.00
Section D, Travel		47,781.00
1. Domestic	47,781.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		47,781.00
1. Materials and Supplies	15,927.00	
2. Publication Costs	31,854.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	0.00	
9. Other 2	0.00	
10. Other 3	0.00	
Section G, Direct Costs (A thru F)		1,244,664.00
Section H, Indirect Costs		282,540.00
Section I, Total Direct and Indirect Costs (G + H)		1,527,204.00
Section J, Fee		0.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:

First Name*: Harris

Middle Name: A

Last Name*: Lewin

Suffix:

2. Human SubjectsClinical Trial? ☒ No ☐ YesAgency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes**3. Permission Statement***

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ☒ No**4. Program Income***Is program income anticipated during the periods for which the grant support is requested? ☐ Yes ☒ No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount (\$)*	Source(s)*
.....
.....
.....
.....
.....

PHS 398 Cover Page Supplement**5. Human Embryonic Stem Cells**

Does the proposed project involve human embryonic stem cells?*

☒ No ☐ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ☐ Yes ☒ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ☐ Yes ☐ No

7. Change of Investigator / Change of Institution Questions

☐ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

☐ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application

(for RESUBMISSION or REVISION only)

2. Specific Aims

RD_SpecificAims.pdf

3. Research Strategy*

RD_ResearchStrategy.pdf

4. Progress Report Publication List

RD_ProgressReportPubs.pdf

Human Subjects Sections**5. Protection of Human Subjects****6. Inclusion of Women and Minorities****7. Inclusion of Children****Other Research Plan Sections****8. Vertebrate Animals**

RD_VertebrateAnimals.pdf

9. Select Agent Research**10. Multiple PD/PI Leadership Plan****11. Consortium/Contractual Arrangements****12. Letters of Support**

RD_Letters.pdf

13. Resource Sharing Plan(s)

RD_ResourceSharingPlan.pdf

Appendix (if applicable)**14. Appendix**

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

SPECIFIC AIMS

The mission of the Respiratory Diseases Research Unit is to define the cellular and molecular mechanisms for of the respiratory system. The respiratory system, extending from the nares to the alveolar surfaces of the distal airways, is a highly complex cellular and architectural entity. Because the respiratory system is the largest interface between the organism and the environment, it is the primary target for all classes of airborne agents; among these agents are oxidant air pollutants, particulate products, infectious agents, and allergens. The fact that most of the respiratory system's growth and differentiation occurs over an extended period of time following birth in primate species (e.g., 8-10 years in humans) makes this organ system particularly vulnerable to environmental challenges that lead to persistent lung function deficits. Defining the development of the respiratory system during early life, understanding the pathways by which it is regulated, and investigating the long-term health impact of environmental exposures is a major research emphasis for the Respiratory Diseases Research Unit. Research by Unit Core and Affiliate Scientists utilize the nonhuman primate as a critically important translational animal model for understanding the pathogenesis of respiratory diseases that affect humans. As such, the Specific Aims for the next five-year funding period include:

Specific Aim 1. Advance the California National Primate Research Center (CNPRC) resource through state-of-the art research that contributes towards understanding and treatment of respiratory disorders across the age spectrum.

Plan. Core Scientists will conduct mechanistic and interventional studies in a multidisciplinary collaborative environment using the nonhuman primate as a translational animal model for human respiratory disease. The CNPRC resource will be utilized by investigating the impact of chronologic age on respiratory immunity, lung structure, and airway physiology in the context of lifespan health. In coordination with other CNPRC Scientific Research Units and Affiliate Scientists, the Unit will assemble investigative teams poised to respond to large-scale integrative strategic initiatives.

Specific Aim 2. Contribute unique expertise and service towards enhancement of the CNPRC resource at both a regional and national level.

Plan. Core Scientists will promote the CNPRC resource by serving as experts in the field of nonhuman primate respiratory disease and facilitating research conducted by external investigators. Recent construction of the Respiratory Diseases Center on-site will provide expanded inhalation exposure capabilities and opportunities for investigation of human respiratory disease using the nonhuman primate as a laboratory animal model. The Unit will continue to serve as a specialized biological specimen repository for catalogued nonhuman primate samples obtained through NIH funded studies in respiratory disorders such as asthma.

Specific Aim 3. Train and mentor the next generation of nonhuman primate scientists in respiratory diseases.

Plan. Core Scientists will support the development of new nonhuman primate investigators who will direct the future of the CNPRC resource. Training will emphasize nonhuman primate models of human respiratory disease and graduate/postdoctoral trainees will be recruited from ongoing campus fellowship programs and nationally. We will also use the CNPRC Pilot Research Program to encourage junior faculty to address translational research questions in respiratory disease using the nonhuman primate models developed by Core and Affiliate Scientists.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care for the CNPRC resource.

Plan. Respiratory Diseases Research Unit Core Scientists will play an active role in maintaining the health of CNPRC colony animals through key leadership positions in service cores and management. From a clinical perspective, Core Scientists will work directly with Primate Services to share specialized expertise in human lung-related procedures and respiratory conditions.

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

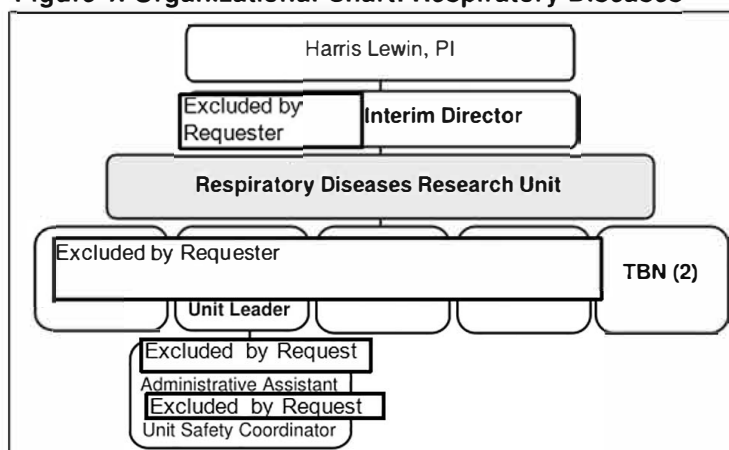
RESEARCH STRATEGY

INTRODUCTION

The Respiratory Diseases (RD) Unit is unique to the scientific unit structure of the CNPRC in that central to the research conducted by Core and Affiliate Scientists is an emphasis on a single organ system - the lung. The California National Primate Research Center (CNPRC) is also the only National Primate Research Center (NPRC) program with a scientific unit focused on pulmonary diseases (Figure 1). Because of the complexity of the respiratory system and the need to understand the basic mechanisms regulating the respiratory system's response to disease processes, the RD Unit promotes multidisciplinary integrated research programs.

As individuals, each Core Scientist within the RD Unit brings a distinct, non-overlapping area of research expertise to the CNPRC resource (Table 1). Specialized research expertise within the RD Unit includes inhalation toxicology, mucosal immunology, and neurophysiology. With Affiliate Scientists, RD Unit Core Scientists collectively have demonstrated research synergism that has resulted in support by two NIEHS P01 funding mechanisms. Construction of the Respiratory Diseases Center during the current funding period provides new centralized laboratory space to be used for recruitment of pulmonary faculty and development of junior investigators in a collabora-

Figure 1. Organizational Chart: Respiratory Diseases



ative environment. It is anticipated that expanded capacity provided by the state-of-the-art Inhalation Exposure Core will further support new research opportunities with NIH investigators and the private sector.

Table 1. Respiratory Diseases Research Unit Personnel, Affiliation, and CNPRC Role

Personnel	UC Davis Campus Affiliation	CNPRC Role
Excluded by Requester	Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine	<ul style="list-style-type: none"> • CNPRC Director (2000-2014) • Multimodal Imaging Core
	Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine	<ul style="list-style-type: none"> • Unit Leader, Research Advisory Committee • Associate Director for Research • Colony Management Committee
	Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine, and Department of Pediatrics, School of Medicine	<ul style="list-style-type: none"> • Inhalation Exposure Core
	Department of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine	<ul style="list-style-type: none"> • Lead, Inhalation Exposure Core
TBN (2)	<i>Based on joint recruitments</i>	Core Scientists
Excluded by Requester	CNPRC	Administrative Assistant
	CNPRC	Unit Safety Coordinator

TBN=to-be-named

Table 2 shows the support for the RD Unit per the FOA. A small component of salary is supported on the P51 base grant (see budget justification), and represents the commitment to the mission, outreach, and services. Extramural grant funding is shown in Table 3, below.

Table 2. Support for the Respiratory Diseases Research Unit (does not include research grants per the FOA. See Unit grant funding Table 3, below)

	May 1, 2014 to April 30, 2015	May 1, 2015 to April 30, 2016
P51 Base Grant	\$212,426	\$233,760
Program Income from P51	\$0	\$0
Other Sources	\$0	\$0
TOTAL	\$212,426	\$233,760

Response to Summary Statement

reviewers' comments

reviewers' comments

SIGNIFICANCE

Progress and Major Accomplishments: Contributions to the CNPRC Mission

During the current funding period, RD Unit Core and Affiliate Scientists generated 53 publications and \$5.1 million in extramural funding (Table 3). While NIH funding has declined due to discontinuation of P01 programs at NIEHS, we have been successful in diversifying our portfolio of extramural funding for nonhuman primate research through other granting agencies, such as the California Air Resources Board, Private Source

Private Source

Table 3. Extramural Funding for Respiratory Diseases (May 1, 2010 to April 30, 2014)

May 2010 - April 2011	May 2011 - April 2012	May 2012 - April 2013	May 2013 - April 2014	TOTAL
\$2,339,035	\$988,298	\$1,112,761	\$698,078	\$5,138,172

* Does not include currently funded grants May 1, 2014 to April 30, 2015, to date, of \$146,135

Major collaborative accomplishments by RD Unit Core Scientists using the rhesus macaque as a nonhuman primate model for respiratory disease during the current funding period include:

- Reported the detrimental effect of inhaled corticosteroid use on lung development using a rhesus model of pediatric asthma.** The risks for infants and young children receiving inhaled corticosteroid therapy are largely unknown. Clinical studies indicate that inhaled corticosteroid therapy in preschool children with symptoms of asthma result in decreased symptoms without influencing the clinical disease course, but potentially affect postnatal growth and development. Using an infant rhesus macaque model of pediatric asthma developed by RD Unit Core Scientists during the prior P51 funding period (2004-2009), this study reported that several indicators of postnatal lung growth, differentiation, and function were negatively affected by inhaled corticosteroid use, suggesting that this common pediatric treatment may pose risks for normal development of human lungs [Excluded by Requester 2012].
- Provided microarray evidence showing comparable molecular profiles between the rhesus model of allergic asthma and human atopic asthmatics.** In collaboration with investigators from Genentech, Inc., RD Unit Core Scientists reported microarray gene expression data obtained from the adult house dust mite-induced rhesus asthma model, comparing it with data from human Th2-high asthma [Excluded by Requester 2011]. A comparison of lung gene expression profiles from human Th2-high asthma, the house dust mite-induced rhesus asthma model, and a common mouse asthma model indicated that genes associated with Th2 inflammation are shared by all three species. However, pathophysiologic aspects of human asthma (e.g., subepithelial fibrosis, angiogenesis, neural biology, immune host defense biology) were best represented in the gene expression profile of the rhesus monkey model. This study has confirmed that the CNPRC rhesus model of allergic asthma most closely recapitulates the human disease phenotype.
- Developed the first nonhuman primate model of pediatric H1N1 influenza infection.** Influenza is the cause of significant morbidity and mortality in pediatric populations. In collaboration with [Excluded by Requester] from Lovelace Respiratory Research Institute in New Mexico, this study reported the outcome of H1N1 infection in infant rhesus macaque monkeys that resulted in significant pulmonary pathology that persisted long after virus infection [Excluded by Requester 2014]. Intrinsic developmental differences in infant airway epithelial cells that contributed to increased susceptibility to influenza infection were also observed. Because current pediatric influenza vaccine formulations cannot be used in children under 6 months of age, the CNPRC rhesus model of pediatric H1N1 infection will be particularly relevant for testing new immunotherapeutic approaches to prevent the respiratory complications of infection.
- Demonstrated deficiencies of innate immune function in a nonhuman primate model of pediatric airway epithelium.** The immune mechanisms for neonatal susceptibility to respiratory pathogens are poorly understood. In collaboration with [Excluded by Requester] from the University of Alabama, our published study provided the first direct evidence that Toll-like receptor responses to lipopolysaccharide

exposure in airway epithelia from infants and children are functionally distinct from adult epithelia. From a translational perspective, these findings are important as they suggest that respiratory pathogen susceptibility in infants may be partly explained by a hyporesponsive innate immune phenotype in airway epithelium [Excluded by Requester] 2011; 2013].

The **Respiratory Diseases Resource Program** currently maintains a biorepository of specimens collected from over 400 nonhuman primates utilized in multiple NIEHS and NHLBI-funded studies. Archived specimens that are banked on the CNPRC premises include fixed tissues, frozen tissues, RNA/DNA, serum, lavage fluid, and cryopreserved leukocytes. Requests for biospecimens by investigators are submitted electronically and processed by [Excluded by Requester] (RD Unit). It should be emphasized that a significant amount of biospecimen banking is routinely done as a part of individual investigator-generated grants due to the high monetary and translational value of nonhuman primate studies; no P51 resources are utilized for the collection process. Biospecimens that are not immediately used for investigator-generated grants can be made available to external investigators through the Respiratory Diseases Resource Program. P51 resources are minimally used for documentation of specimen transfers and preparation of shipments by [Excluded by Requester]. There is no charge for biospecimens but requestors must pay for shipping and acknowledge NIH support from the RD Unit investigator-generated grants and the CNPRC P51 base grant should any data result in publications. From 2010-2014, four investigators have formally requested nonhuman primate biospecimens from the Respiratory Diseases Resource Program (Table 4). In 2014 [Excluded by Requester] utilized the nonhuman primate biospecimens for generation of preliminary data [Pending Support].

Table 4. Biospecimen Distribution to Investigators Outside UC Davis

Name	Institutional Affiliation	Requested Biospecimens
[Excluded by Requester]	Boston University	Paraffin embedded lung sections, lavage fluid, serum
	Washington University	Paraffin embedded lung sections (42)
	UCSF	Paraffin embedded lung sections (27)
	National Jewish Hospital	Paraffin embedded lung sections (25)

RD Unit Core Scientists play an active role in supporting investigators new to nonhuman primate research. Since 2010, RD Unit Core Scientists have served as collaborating scientists on four CNPRC pilot projects. A 2010 CNPRC pilot project involving a collaboration between the RD Unit, the Reproductive Sciences and Regenerative Medicine Research Unit, and [Excluded by Requester] (Cincinnati Children's Hospital and Medical Center) has been particularly successful, culminating in a publication and multiple successful grant applications. A 2013 CNPRC pilot project led by [Excluded by Requester] (UCSF) and RD Unit Core Scientists as collaborators has already resulted in a June 2014 R01 grant submission with a subcontract to the CNPRC. RD Unit Core Scientists are also highly committed to training postdoctoral fellows to become the next generation of nonhuman primate investigators. For example, [Excluded by Requester] (mentored by [Excluded by Requester]) received a K08 award during the current funding period and is now an Affiliate Scientist within the RD Unit as well as a member of the **Inhalation Exposure Core** [Excluded by Requester] (mentored by [Excluded by Requester]) was an awardee of a CNPRC P51 supplemental ARRA-supported Postdoctoral Pilot Program project. [Excluded by Requester] has been highly productive during her tenure at the CNPRC, generating multiple publications and receiving competitive postdoctoral fellowship awards through the Tobacco Related Disease Research Program as well as the Hartwell Foundation. [Excluded by Requester] is actively mentored within the RD Unit as she develops an independent research program with an emphasis on nonhuman primate models.

Contribution to the CNPRC Resource

The scientific focus of the RD Unit is to enhance the use of the nonhuman primate as a translational model of respiratory disease, with the ultimate goal of developing new interventional targets and predictive biomarkers for human patients. Specific areas of research excellence within the RD Unit include inhalation toxicology, mucosal immunity, neurophysiology, and airways remodeling. RD Unit Core and Affiliate Scientists have contributed to the understanding of respiratory disease pathogenesis with the following significant research outcomes:

- **Developed the first model of adult house dust mite-induced asthma in the rhesus macaque.** The rhesus model of allergic asthma reported by CNPRC RD Unit Core and Affiliate Scientists in 2000 [Excluded by Requester] 2000] was the first nonhuman primate model to utilize the common human allergen, house dust mite. The CNPRC rhesus model of allergic asthma exhibits all parameters of human asthma, including airways hyperresponsiveness, eosinophilia, and airways remodeling.

- **Developed the first model of pediatric allergic asthma in the rhesus macaque.** In 2003, CNPRC RD Unit Core and Affiliate Scientists reported that cyclic ozone exposures enhance allergic airways disease and airways reactivity, if exposure takes place in early life [Excluded by Requester 2003]. This study provided direct experimental support for numerous human epidemiologic studies that have implicated the first year of life as a window of susceptibility for development of asthma.
- **Developed the first model of perinatal and pediatric environmental tobacco smoke exposures in the rhesus macaque** [Excluded by Requester] is a leading expert in the area of environmental tobacco smoke and has investigated the airway/immune effects of tobacco smoke during early life. Multiple studies reported by Dr. [Excluded by Requester] using the rhesus monkey as a model confirm that environmental tobacco smoke exposure both in utero and during postnatal development can have significant detrimental effects on lung function and immune profiles [Excluded by Requester 2010].

RD Unit Core Scientists are well integrated into the thematic research area of lifespan health, and have actively engaged in projects that explore the full spectrum of respiratory disorders from the perinatal period through the post-menopausal period of maturity (Figure 3).

For example, [Excluded by Requester] developed advanced stereologic techniques to accurately measure alveolar number in aged rhesus monkey colony animals. Alveolar number significantly declined with increasing age, with a greater decline in post-menopausal females when compared with males [Excluded by Requester et al., 2013]. These findings

correspond well with gender-dependent differences in susceptibility to chronic obstructive disease in human subjects, and are particularly notable in light of recent requirements for new NIH proposals to address sex differences in pre-clinical studies. During the perinatal period [Excluded by Requester] has investigated the long-term health outcomes of maternal environmental tobacco smoke exposure, which has resulted in publications describing deleterious effects on immunity, lung structure, cardiopulmonary physiology, and neural physiology in young rhesus monkeys [Excluded by Requester 2010].

In addition to independent research programs, RD Unit Core Scientists frequently collaborate with each other, as well as with external investigators on and off the UC Davis campus. As shown in the social network analysis (Figure 4), RD Unit Core Scientists are strongly linked with investigators on the UC Davis campus (as depicted by thick gray lines); close proximity between [Excluded by Requester] (emeritus from the 2010-2014 funding period), [Excluded by Requester] reflect the frequency of our interactions using the nonhuman primate model of allergic asthma. Outreach efforts by the Unit as a whole are substantial, with collaborations in California (green), nationally (blue), and internationally (red) shown.

As an example of collaborative efforts by RD Unit investigators [Excluded by Requester] (Merck), Core Scientists [Excluded by Requester] and Affiliate Scientist [Excluded by Requester] have developed a model of an emphysema phenotype or COPD. Rhesus monkeys were treated with a vascular endothelial growth factor receptor 2 antagonist (Sugen), intratracheal polyinosinic-polycytidylic acid (poly I:C), and cyclic exposures of environmental tobacco smoke over 6 months. The CNPRC

Figure 3. Lifespan Health Research Themes for Core Scientists in the RD Unit

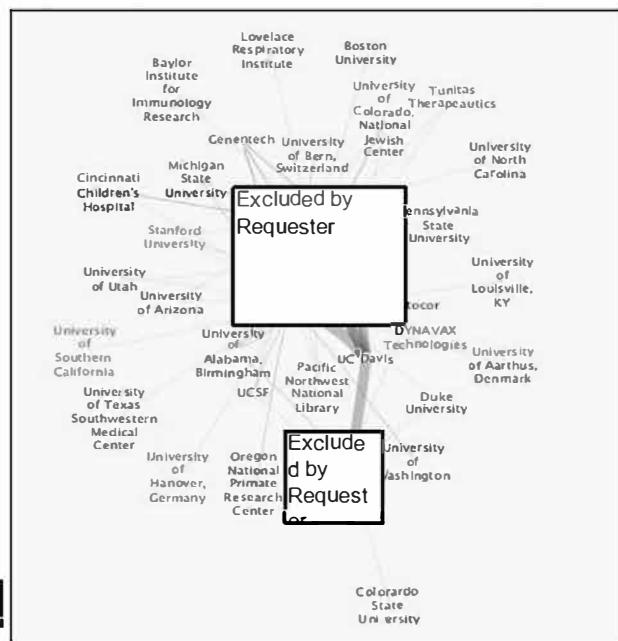
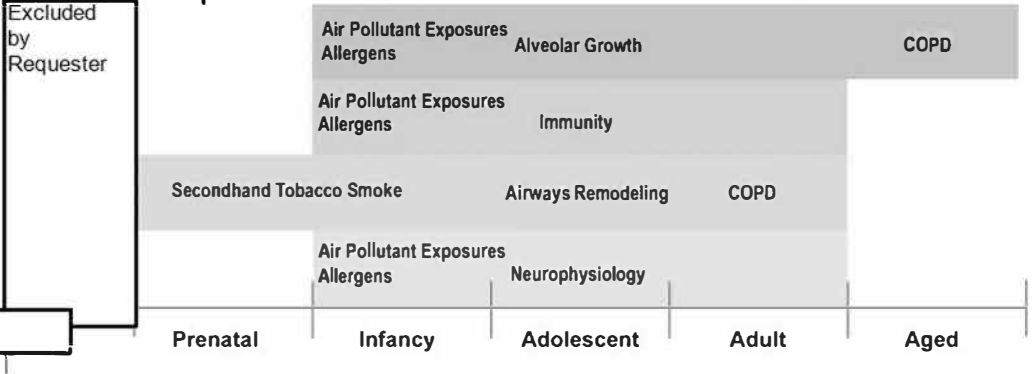


Figure 4. Network plot analysis of internal and external interactions for Core Scientists within the RD Unit.

nonhuman primate model of COPD is of particular interest to pharmaceutical companies because tobacco smoke is strongly linked to obstructive airways disease and rodent models poorly recapitulate the obstructive remodeling that is typically observed in older individuals.

INNOVATION

During the current funding period we developed a collaboration with the Reproductive Sciences and Regenerative Medicine Unit (Core Scientist [Excluded by Requester]) to establish a rhesus macaque model of chorioamnionitis in conjunction with neonatologist [Excluded by Requester] PhD, both investigators from Cincinnati Children's Hospital and Medical Center. Through the CNPRC Pilot Research Program mechanism, [Excluded by Requester] initiated studies to investigate the immune mechanisms of chorioamnionitis, which has since set forth a series of subcontracts supported by Cincinnati Children's Hospital internal funds. [Excluded by Requester] is a human immunologist who is a recognized expert in T regulatory cell biology; she was recently awarded a [Private Source] grant to continue the study of fetal immunity in the nonhuman primate model of chorioamnionitis. Further building upon her CNPRC pilot study, [Excluded by Requester] received new NIH funding with [Excluded by Requester] (see **Brain Mind, and Behavior Research Unit**) to examine the effects of perinatal stress on preterm birth and immunity. Finally, through our external collaborations, we were also awarded a subcontract through the [Private Source] to support a candidiasis mucosal immunology model to study preterm birth with [Excluded by Requester] who was recently appointed Chief Medical Officer for Cincinnati Children's Hospital.

The CNPRC is the only center within the NPRC program to have collective expertise in nonhuman primate respiratory biology organized as a scientific research unit. The research impact of our unique group of faculty was recognized as a major consideration for award of an ARRA-funded C06 building grant to construct the Respiratory Diseases Center. As fully described in the **Inhalation Exposure Core**, completion of the new Respiratory Diseases Center will significantly increase our capacity for conducting inhalation toxicology studies. The new building (certification by Fall 2014) (Figure 5) will enhance our ability to efficiently conduct large-scale exposure studies using environmental tobacco smoke and other pollutants, while providing new open bay laboratory/office space for faculty, fellows, staff, and students. The increase in laboratory space will have an additional positive effect on our program by facilitating recruitment of new UC Davis faculty with research programs in respiratory disease.



Figure 5. The CNPRC Respiratory Diseases Center.

APPROACH

Specific Aim 1. Advance the CNPRC resource through state-of-the art research that contributes towards understanding and treatment of respiratory disorders across the age spectrum.

The overarching research vision of the RD Unit is to advance the CNPRC resource by conducting innovative scientific investigations in respiratory disease pathogenesis using state-of-the art technology. Based upon our established strengths in pediatric lung disease models and long-standing expertise in inhalation biology, key thematic areas for RD Unit Core and Affiliate Scientist research for the CNPRC P51 renewal will be as follows:

- **Normal Airway Development.** RD Unit Core and Affiliate Scientists study multiple aspects of nonhuman primate airway development [Excluded by Requester] 2011 [Excluded by Requester] 2014. [Excluded by Requester] 014 [Excluded by Requester] 2014]. As individual scientists, we target different cellular populations within the airways or investigate physiological responses throughout the age spectrum. Our goal is to understand the normal development of airways from the prenatal period through adulthood, such that the detrimental health impact of environmental challenges throughout the lifespan can be accurately assessed.
- **Age-Related Impact of Environmental Exposure on the Lung.** RD Unit Core and Affiliate Scientists investigate the pulmonary effects of allergens such as house dust mite, as well as exposure to ozone, particulate matter, and secondhand tobacco smoke. The CNPRC **Inhalation Exposure Core** will serve as a critical resource for Core and Affiliate Scientists interested in highly characterized environmental exposures using nonhuman primates.
- **Age-Related Impact of Immunity on the Lung.** Immune responses within the lung mucosa are not well understood, particularly in the very young. RD Unit Core and Affiliate Scientists study the role of airway

mediators in immunity, trafficking of leukocytes, physiologic responses to inflammation, and the impact of environment on immunity within the lung.

- **Development of Therapeutics for Treatment of Chronic Lung Disease.** RD Unit Core and Affiliate Scientists have worked closely with industry collaborators to test drug targets using the CNPRC rhesus model of allergic asthma. The majority of targets have focused on the immune response in asthma [Excluded by Requester] 2007]. Central to the applicability of the nonhuman primate as a model of respiratory disease is the expertise available in the **Inhalation Exposure Core** for measures of lung function, which is frequently the standard by which treatment efficacy is determined.

Each RD Unit Core Scientist contributes a unique area of expertise to the research program, from airways remodeling [Excluded by Requester] immunology [Excluded by Requester] and toxicology [Excluded by Requester] to neurophysiology [Excluded by Requester]. Along with RD Unit Affiliate Scientists, coordinated integration of our respective research programs facilitates the Unit ability to investigate lung disease throughout all stages of life (prenatal to aging populations), in multiple animal models. The progression from rodent to nonhuman primate models promotes new discoveries and rapid translation to preclinical studies.

To diversify our research portfolio and continue to support the mission of the CNPRC, we have identified several scientific themes as emerging areas for the RD Unit, including respiratory pathogens, influence of the microbiome on lung disease, impact of stress on lung function, and systemic biomarkers of air pollutant exposures. Emerging research areas have been generated by novel and highly productive interactions between RD Unit Core Scientists and other Scientific Research Units. For example, Core Scientists in the RD Unit have collaborated with [Excluded by Requester] in the Brain, Mind, and Behavior Research Unit on an R21 to investigate infant behavioral profiles that are dramatically predictive of non-atopic asthma later in life; RD Unit Core Scientists have provided expertise in the evaluation of immunity and airways physiology. In a similar manner, RD Unit Core Scientists have collaborated with [Excluded by Requester] from the Infectious Diseases Research Unit on a R56 award to generate a larger study to investigate the early life impact of *Helicobacter pylori* infection on the development of allergic asthma. We expect that continued collaborations with the Infectious Diseases Research Unit will determine if microbial exposure, particularly in early life, has an impact on lung function and mucosal immunity.

Another emerging area of interest by [Excluded by Requester] is cardiopulmonary physiology, particularly with respect to environmental particulate matter exposures. [Excluded by Requester] is a nationally recognized expert in the area of climate change and is actively involved in NIH-supported consortium activities related to pollutant exposures. While ongoing studies and funding have emphasized rodent models, we anticipate that future proposals will incorporate nonhuman primate studies.

Contributions to Lifespan Health Research. A focus of the current funding period is to develop new pediatric models of respiratory infection, leading to increased use of the nonhuman primate to study intervention strategies. As evidenced by recent outbreaks of *Bordetella pertussis* throughout the United States, efficacy of childhood vaccines for respiratory pathogens continues to be problematic, and RD Unit pediatric models provide the opportunity to comparatively assess host-pathogen immune responses. With the completion of the new Respiratory Diseases Center, we expect that the availability of environmental tobacco smoke exposure housing for large groups of rhesus monkeys will further provide new funding opportunities for Core and Affiliate Scientists. There has been significant interest by the pharmaceutical industry to develop a nonhuman primate model of COPD that is mediated by chronic tobacco smoke exposure; it is anticipated that our new facilities will significantly enhance our capabilities. Along with experimental models, we have also taken advantage of the CNPRC colony as a valuable resource for understanding the effect of environment on lung function and mucosal immunity, investigating the impact of ambient air pollutant exposures on susceptibility to disease. The area of mucosal immunity offers outstanding opportunities for inter-unit collaborations in view of the recently funded RISE award in this area to [Excluded by Requester] a Core Scientist in the **Infectious Disease Research Unit**. Based upon recent success in identifying cellular immune phenotypes in association with an acute air pollutant exposure event in the outdoor field corrals, the aged population of rhesus monkeys within the CNPRC colony may be assessed for adverse health outcomes.

Positioning for the Future. The RD Unit will capitalize on strong host-pathogen research programs on the UC Davis campus and continue to invest our resources in the area of respiratory infectious disease. Another example of inter-unit collaboration between the RD Unit and the Infectious Diseases Unit has resulted in an investigation of *H. pylori* effects on development of lung mucosal immunity. We expect that the outgrowth of

our studies will yield valuable information on the microbiome of the infant distal lung that has not yet been reported for a primate species. In conjunction with our recent success in development of a pediatric influenza model, RD Unit Core Scientists along with influenza and vaccine investigators in the Infectious Diseases Unit are uniquely well positioned for large program funding initiatives that target respiratory infections in susceptible age groups. It should be emphasized that the ability for Core Scientists to conduct lines of investigation focused on both pediatric and geriatric age groups is a unique distinction of the CNPRC resource, capitalizing on the rich opportunities to study monkeys over the full lifespan. Further, this approach is in alignment with NIH primary prevention research proposals in which predictive biomarkers leading to early diagnosis of disease and treatment are emphasized.

Specific Aim 2. Contribute unique expertise and service towards enhancement of the CNPRC resource at both a regional and national level.

RD Unit Core Scientists enhance the CNPRC resource by way of outreach programs to support Affiliate Scientists and other investigators interested in utilizing the nonhuman primate as a model of respiratory disease. Establishment of collaborations via sharing of lung biospecimens from the Respiratory Diseases Resource Program is one approach to engaging new investigators to use the CNPRC. Information regarding specific exposure regimens and age of animals are available to outside investigators through the password-protected Unit website after application for use to Unit Core and Affiliate Scientists; this approach allows a wide use of available tissue specimens. This resource is currently available through a link on the NIH Nonhuman Primate Reagent Resource Site, available to investigators that utilize antibodies in their work. To further publicize this resource, we plan to approach the NIH Office of the Director/Office of Research Infrastructure Programs/Division of Comparative Medicine and NHLBI program officers to create a web link based on other resource databases.

Another strategy for increasing visibility of the RD Unit is to incorporate the Respiratory Diseases Center as the new location for the UC Davis Lung Research Day. The UC Davis Lung Research Day is a widely attended scientific retreat supported by the UC Davis Schools of Medicine and Veterinary Medicine and the College of Engineering; it has been held consecutively for five years and was initiated as a mechanism to increase interactions between respiratory disease investigators, students, fellows, investigators new to the area, and pharmaceutical companies (150+ in attendance, 2014) (Figure 6). Presentations and poster sessions at the retreat are thematic, with topics changing annually. Excluded by serves on the planning committee for the annual event and promotes the CNPRC resource in the context of respiratory diseases. We are preparing for the 2015 UC Davis Lung Research Day to be held at the CNPRC which offers excellent opportunities for outreach. We will use the Respiratory Diseases Center for break out and poster sessions. CNPRC tours will be incorporated to allow visiting scientists an opportunity to learn about research capabilities throughout the center.

Figure 6. Lung Research Day 2014.



In addition to our role as CNPRC investigators, RD Unit Core Scientists are actively engaged in pulmonary research across the UC Davis campus. There are over 30 faculty from 12 different departments on the campus whose research focuses on respiratory disease. The UC Davis group of pulmonary scientists has been recognized by an NHLBI-supported T32 training grant that has been continuously funded for over 35 years (Excluded by PI). As a component of the T32 training grant, a Friday morning series is offered that attracts 40-60 individuals per week and serves as a forum for multidisciplinary presentations; RD Unit Core Scientists and postdoctoral fellows present annually in this seminar series.

Specific Aim 3. Train and mentor the next generation of nonhuman primate scientists in respiratory diseases.

To ensure that the RD Unit sustains a dynamic and productive research program, it is essential that new Core and Affiliate Scientists be added to the Unit during the next funding period. Because the CNPRC is the only NPRC with a Scientific Research Unit that emphasizes lung research, NIH-funded investigators with pulmonary and nonhuman primate expertise may be a small pool to draw from for potential new hires. We are cognizant of this limitation and have established a two-tier strategy for development of new nonhuman primate scientists in respiratory diseases for the immediate and distant future of the CNPRC.

The first step towards increasing RD Unit Core and Affiliate Scientists is to identify existing UC Davis investigators with strong potential as future scientists focusing on nonhuman primates. As described in the Progress and Major Accomplishments section, we have fostered talented junior investigators such as Drs. [Excluded by Requester] to support their development of independent NIH-funded nonhuman primate research programs; both of these investigators will be provided shared laboratory/office space within the Respiratory Diseases Center where they will continue to receive career mentoring by RD Unit Core Scientists. The UC Davis School of Medicine has recently recruited [Excluded by Requester] from the University of Pennsylvania to join our pulmonary faculty in the Respiratory Diseases Center. [Excluded by Requester] is a mid-career hire and a nationally recognized expert in asthma; she is an NIH-funded investigator with a research program that primarily utilizes rodent models. [Excluded by Requester] has submitted an NIH R21 grant application to investigate the mechanisms of stress on asthma in nonhuman primates in collaboration with the RD Unit [Excluded by Requester] and the Brain, Mind, and Behavior Unit (Capitanio); her grant application is currently under review. RD Unit Core Scientists are very enthusiastic about the potential for [Excluded by Requester] to become a CNPRC Affiliate Scientist.

Other Affiliate Scientists on the UC Davis campus who utilize the CNPRC resource through the **Inhalation Exposure Core** are [Excluded by Requester] (College of Engineering) and [Excluded by Requester] (School of Veterinary Medicine). While both [Excluded by Requester] maintain research programs that emphasize rodent models of air pollution exposure, their long-term goal is to utilize nonhuman primate models in translational studies. Indeed, [Excluded by Requester] has served as a co-investigator on grant funding with RD Unit Core Scientists and has recently co a ora e with [Excluded by Requester] (Reproductive Sciences and Regenerative Medicine Unit). RD Unit Core Scientists can serve as critical nonhuman primate study liaisons for investigators with research programs that are heavily invested in rodent models. Consistent with the "One Health" concept that is emphasized on the UC Davis campus through interactions between the Schools of Medicine and Veterinary Medicine, the RD Unit comparative medicine approach is a translational pipeline, utilizing multiple animal models to conduct early discovery of novel mechanisms leading to essential safety and efficacy data for clinical trials in humans.

In addition to increased efforts to facilitate development of Affiliate and Core Scientists within the RD Unit, we seek to identify junior faculty at the Assistant/Associate Professor level who will compliment ongoing translational studies, with the ultimate goal of appointment as new RD Core Scientists. The recruitment of a new director and commitment of the UC Davis leadership to new faculty positions (see **Overview** and letter from the Provost) will provide the necessary opportunities to recruit new RD Unit Core Scientists. We will work directly with the Deans of the Schools of Veterinary Medicine and Medicine and Colleges of Biological Sciences and Engineering to establish academic positions within appropriate departments for recruited individuals; it should be emphasized that all RD Unit Core Scientists maintain academic positions within UC Davis departments. To build upon our strengths, we are particularly interested in identifying new faculty from the following scientific areas:

- **Pulmonary Infectious Disease.** In line with our recent success with a pediatric model of influenza and supported by interactions with the CNPRC Infectious Diseases Unit, a faculty member with a focus on host-pathogen and mucosal immune responses during respiratory infections will enhance our ability to conduct studies in this area. This faculty position has the potential for partnering with the Center for Comparative Medicine (CCM), further leveraging campus investments (see letter from the CCM Associate Director).
- **Respiratory Toxicology.** A faculty member who is focused on upper (nasal) airways or lower (alveolar) airways disease mechanisms will compliment ongoing expertise in tracheobronchial airways, particularly in relation to environmental exposures, asthma, and COPD.

In looking towards the future of the RD Unit, in order to position ourselves for continued success, RD Core and Affiliate Scientists will continue our efforts to mentor UC Davis undergraduate students, graduate students, professional degree (MD, DVM), and postdoctoral fellows. In the current funding period, RD Unit Core Scientists supported the completion of 5 PhD students with an emphasis on nonhuman primate research. RD Unit Core Scientists serve as faculty advisors in multiple graduate groups on campus, including Comparative Pathology, Immunology, Pharmacology and Toxicology, and Molecular, Cellular and Integrative Physiology. RD Unit Core Scientists also participate as training faculty for students receiving NIH T32 training grant support (e.g., Comparative Lung Biology, Advanced Training in Environmental Sciences, additional grants listed on biosketches). Undergraduate students from other institutions receive training in respiratory diseases at the CNPRC through summer internship programs. For example, [Excluded by Requester] a graduate of UC Berkeley, received a National Science Foundation fellowship to obtain research training at the CNPRC with [Excluded by Requester]

Excluded by
Requester

in the summer of 2013. Excluded by Requester continued to work as a 50% laboratory assistant on an NIH supported project with Excluded by Requester (Infectious Diseases Unit) and was the first to receive a diversity supplement to the CNPRC P51 base grant (Year 53, begins 07/01/14). The supplemental NIH funding will provide support for Excluded by Requester to continue conducting research and receive training at the CNPRC while she applies to the DVM/PhD program at UC Davis in Fall 2014.

Specific Aim 4. Ensure the highest standards of responsible conduct of research and animal care for the CNPRC resource.

RD Unit Core Scientists will play an active role in maintaining the health and social well-being of CNPRC colony animals through key leadership positions in Service Cores and the Colony Management Committee. From a clinical perspective, we will work directly with Primate Services to share specialized knowledge in human lung related procedures and respiratory conditions. One key example of how RD Unit Core Scientists have contributed to the health and well-being of CNPRC colony animals is illustrated in recent publications with Excluded by Requester (Brain, Mind, and Behavior Unit), in which lung function decrements and immune parameters are linked with an inhibited temperament Excluded by Requester et al., 2011 Excluded by Requester 2013]. While this study has important translational implications as noted above, it also demonstrates how behavioral phenotypes in the colony may self-identify for ongoing respiratory decline. An additional example of how RD Unit Affiliate Scientists have contributed to colony health was illustrated in 2009, when an outbreak of a novel adenovirus in the CNPRC titi monkey colony resulted in fulminant pneumonia, hepatitis, and morbidity Excluded by Requester 2011]. Prior to identification of the cause of the outbreak, Excluded by Requester shared his expertise in pulmonary and critical care medicine with the CNPRC veterinary staff, which ultimately led to a diagnosis of viral pneumonia.

CORE SCIENTIST NARRATIVES

Core Scientist: Excluded by Requester PhD, Professor of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine

Research Program: Excluded by Requester research is focused on airways epithelial, inflammatory, and immune cell interactions. His laboratory uses nonhuman primate models of asthma and COPD (emphysema) to investigate lung growth, differentiation, and aging, particularly in response to inhaled allergens and pollutants Excluded by Requester developed an unbiased stereologic method of counting alveoli that is independent of lung inflation. Using this approach, he has recently investigated the postnatal alveolar growth of the rhesus macaque and human lung to show that they are almost identical in a two-phase growth model with exponential growth in the first two years followed by sustained growth that continues to full somatic growth.

Contributions to the CNPRC Mission: CNPRC Director (2000-2014), Multimodal Imaging Core, Colony Management Advisory Committee, 25 primate publications (May 1, 2010 to April 30, 2014).

Table 5. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Satratoxin-G from the Black Mold <i>Stachybotrys chartarum</i> Induces Rhinitis and Apoptosis of Olfactory Sensory Neurons in the Nasal Airways of Rhesus	Showed that Satratoxin-G caused significant apoptosis of olfactory sensory neurons
	Cellular, Molecular, Histopathologic, and Physiologic Characterization of a Rhesus Macaque Model of Chronic Obstructive Pulmonary Disease (COPD)	Developed a rhesus monkey COPD (chronic bronchitis; emphysema) model of human disease
	Postnatal Alveolarization in Rhesus Macaques Following Treatment Ozone/House Dust Mite and Inhaled Steroids	Defined abnormal accelerated alveolar growth following treatment with inhaled steroids

Core Scientist: Excluded by Requester PhD, Professor of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine

Research Program: Excluded by Requester research program is focused on investigating the impact of environmental exposures (air pollution, allergens, microbes) on pulmonary and immune system development during the first year of life. The overall goal of Excluded by Requester research is to understand the mechanisms of susceptibility in the human infant that contribute to pediatric airways dysfunction, which may ultimately lead to generation of new diagnostics and preventative therapies. Her research projects primarily emphasize the use of an infant rhesus macaque monkey model of childhood asthma and mucosal immune system development.

Contributions to the CNPRC Mission: RD Immunology Core Lead (2010-2014); Unit Leader; Associate Director for Research; Colony Management Committee; 15 primate publications (May 1, 2010 to April 30, 2014).

Table 6. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Host-Microbe Cross-Talk and Pregnancy Outcomes	Determining the fetal immune outcome of chorioamnionitis
	Controlling Allergen-Specific Th2-Type Responses by Targeting DC Surface Lectins	Testing the efficacy of anti-Dectin treatment on parameters of allergic sensitization
	Mechanisms of Species Dependent Environmental Lung Injury	Investigated the impact of early life ozone on innate immune functions
	Immune Effects of Episodic Ozone and PM Exposure During Childhood Development	Investigating persistent immune effects of early life ambient wildfire smoke on colony monkeys

Excluded by Requester

Core Scientist: [Excluded by Requester] **PhD**, Professor of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine and Professor of Pediatrics, School of Medicine

Research Program: [Excluded by Requester] research interests are focused on understanding the consequences in the lung of exposure to environmental tobacco smoke in monkeys during critical perinatal periods of development (early gestation to 13 months postnatal), using morphological, physiological, biochemical, immunological, and molecular approaches to measure effects. He has also studied the impact of allergens on innervation of the airways using a novel technique of lung whole mount slices.

Contributions to the CNPRC Mission: Inhalation Exposure Core, 12 primate publications (May 1, 2010 to April 30, 2014)

Table 7. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Environmental Influences on Perinatal Lung Development	Impact of environmental tobacco smoke on mitochondrial damage
	Environmental Influences on Perinatal Lung Development	CNS effects of perinatal environmental tobacco smoke
	Environmental Influences on Perinatal Lung Development	Inflammatory response to environmental tobacco smoke in neonatal arteries

Excluded by Requester

Core Scientist: [Excluded by Requester] **PhD**, Professor of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine

Research Program: [Excluded by Requester] research program in nonhuman primate lung physiology has focused on: (1) the development and validation of the rhesus monkey model of allergic asthma; (2) the application of this model to study the interaction of allergen- and ozone-induced responses in infant monkeys; and (3) the mechanism underlying the development of airway hyper-responsiveness in atopic and non-atopic asthma. Dr.

[Excluded by Requester] research is focused on understanding how episodic exposure to allergens and oxidant air pollutants influences the development of airway innervation, and how altered neural development influence airway reactivity and neuro-immune function. [Excluded by Requester] continues to explore the role that components of airway serotonergic pathways play in temperament associated airway hyper-responsiveness and the role these components and airway hyper-responsiveness plays in accelerated lung aging in rhesus monkeys.

Contributions to the CNPRC Mission: Lead, Inhalation Exposure Core; 15 primate publications (May 1, 2010 to April 30, 2014)

Table 8. Examples of Affiliates and Collaborations

Name and Institution	Project Title	Collaborative Activities
Excluded by Requester	Characterization of a Rhesus Macaque Model of Chronic Obstructive Pulmonary Disease	Developed a rhesus monkey COPD (chronic bronchitis; emphysema) model of human disease.
	Development of a multichannel gas analyzer for the evaluation of lung function	Determine lung diffusing capacity, pulmonary blood flow, pulmonary capillary volume, and residual and/or functional residual volume in rhesus monkey using a rebreathing technique
	Lung Gene Expression in Rhesus Macaque Allergic Asthma	Determined molecular pathways present in a house dust mite-induced rhesus asthma model by analyzing genomewide lung gene expression

Table 9. Respiratory Diseases Research Unit Funded Grants

PI (Core Scientist)	Institution	Type	Title	Description
Excluded by Requester	UC Davis	NIH K08 (HL090913)	Airway Epithelium is Major Source of VEGF in Chronic Asthma	Investigated the role of VEGF in the nonhuman primate model of asthma
	UC Davis	Private Source	Comparative Kinetics of Metabolism of Napthalene in Nasal Epithelial Microsomes	Investigated the effect of napthalene exposure on nonhuman primate nasal passages
	Private Source		Host-Microbe Cross-Talk and Pregnancy Outcomes	This study will investigate the fetal immune effects of Ureaplasma infection during pregnancy in a nonhuman primate model of chorioamnionitis
	UC Davis		Epigenetic Effects of Cigarette Smoke on the Infant Airway	The study will investigate the mechanisms of persistence following tobacco smoke exposure in nonhuman primate airway epithelium
	Private Source		Balance of Th17 Cells and T regs in <i>Candida Albicans</i> Vaginal Colonization in Pregnant Macaques and Humans	This study will investigate the contribution of Candida infection on vaginal mucosal immunity in pregnant nonhuman primates
	UC Davis	NIH P01 (ES000628)	Pulmonary Effects of Environmental Oxidant Pollutants	Investigated the impact of ozone on the development of asthma in a nonhuman primate model
		Private Source	Cellular, Molecular, Histopathologic, and Physiologic Characterization of a Rhesus Macaque Model of Chronic Obstructive Pulmonary Disease	Developed a rhesus monkey COPD (chronic bronchitis; emphysema) model of human disease
	UC Davis	NIH R01 (HL097087)	Role of Epithelium in Airway Immunity	This study will investigate the developmental mechanisms of innate immune function in nonhuman primate airway epithelium
		California Air Resources Board	Persistent Immune Effects of Wildfire PM Exposure During Childhood Development	This study will investigate the effect of ambient wildfire smoke exposure on innate immune function and airways physiology in nonhuman primate
	UC Davis	NIH R56 (AI091893)	Role of <i>Helicobacter Pylori</i> in the Pathogenesis of Childhood Asthma	This study will investigate the contribution of Helicobacter pylori on the development of asthma using a nonhuman primate model
	Private Source	NIH R21 (AI101810)	Controlling Allergen-Specific Th2-Type Responses by Targeting DC Surface Lectins	This study will determine whether inhibition of Dectin-1 can inhibit allergic symptoms in a nonhuman primate model
	University of Alabama, Birmingham	NIH P01 (ES011617)	Mechanisms of Species Dependent Environmental Lung Injury	Investigated the contribution of infant ozone exposure on persistent lung pathology in an nonhuman primate model
	UC Davis	Private Source	Immune Effects of Episodic Ozone and PM Exposure During Postnatal Development	This study will investigate the effect of ambient wildfire smoke exposure on platelet activation in nonhuman primates

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

PUBLICATIONS (May 1, 2010 to April 30, 2014)

Excluded by Requester	
Excluded by Requester	
	Lung gene expression in a rhesus allergic asthma model correlates with physiologic parameters of disease and exhibits common and distinct pathways with human asthma and a mouse asthma model. Am J Pathol 179:1667-1680, 2011. PMID: PMC3181391
Excluded by Requester	
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SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

VERTEBRATE ANIMALS

The California National Primate Research Center (CNPRC) vivarium is a component of the UC Davis Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)-accredited program. The most recent AAALAC review of the UC Davis Animal Care Program resulted in **Full Accreditation** with no recommendations for improvements, attesting to the high quality standards at UC Davis and the CNPRC. At UC Davis, a single Institutional Animal Care and Use Committee (IACUC) oversees all animal use in research and teaching in order to ensure that the highest ethical and animal welfare standards are met. UC Davis animal facilities are routinely inspected by the UC Davis Attending Veterinarian, and the IACUC.

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1. Proposed Use of Animals. The CNPRC maintains approximately 5,000 animals for investigators locally, regionally, and nationally. The current CNPRC vivarium consists of [Specific Animal] of indoor animal space. The outdoor animal housing area includes [Specific Animal] field corrals [Specific] corn cribs [Specific Animal]. The outdoor space is used primarily to support the long-term breeding program. The rhesus production colony provides research subjects (males and females) that span the entire lifespan ranging from newborns to juveniles, prime reproductive age adults, to geriatric stages of life. Approximately 1,700 of the 5,000 rhesus monkeys at the CNPRC are housed indoors. Animal rooms are maintained within the recommended guidelines established by the current edition of the *Guide for the Care and Use of Laboratory Animals* and the Animal Welfare Act. The CNPRC maintains two SPF rhesus colonies totaling 1,730 animals. SPF Level 1 rhesus monkeys are free of *Cercopithecine herpesvirus-1* (Herpes B-virus), SRV, SIV, and STLV. The SPF Level 1 colony of ~1,500 animals range in age from newborns to mature adults. These animals are housed in designated field corrals, corn cribs, and indoor animal rooms. SPF Level 2 includes pure Indian origin rhesus that are free of seven persistent viruses including the four Level 1 viruses plus simian foamy virus, rhesus rhadinovirus, and rhesus cytomegalovirus. The CNPRC also supports 12 long-tailed macaques for long-term projects funded by other sources. All are housed indoors and according to the CNPRC Primate Well-Being Plan comparable to rhesus monkeys. A small colony of titi monkeys (~86) are socially housed generally in family groups.

CNPRC policies provide maximum occupational health and safety including mandatory guidelines for safely working with nonhuman primates and their fluids, cells, and tissues. Included are the following requirements when entering animal areas: uniforms, scrubs, or buttoned laboratory coats; designated work shoes or shoe covers; a facemask; full coverage eye goggles or face shields; and gloves. All work conducted in the laboratories is under the required BSL2+ conditions and according to the CNPRC training documents and standard operating procedures (SOPs) for the colony and experimental procedures. All work conducted in the laboratories are under the required BSL2+ conditions and according to the CNPRC employee handbook, standard operating procedures (SOPs) for the colony and for defined procedures and in the PI Biological Use Authorization (BUA), and related facility and laboratory training documents required for employment.

2. Justification of Animal Use, Species Choice, and Numbers. The CNPRC provides the optimal environment in which to conduct studies with monkeys because of the unique facilities and expertise of the personnel. The use of nonhuman primates is crucial for the study of human health and disease. Nonhuman primates provide important translational and preclinical models because of reproductive, developmental, physiologic, and immunologic similarities. The major colony at the CNPRC consists of rhesus macaques as the species most frequently used in biomedical research and requested by the majority of investigators. The colony is housed under three different conditions: indoor housing, outdoor group housing in corn cribs, and half-acre outdoor field corrals. Animal numbers selected for projects are typically determined by a power analysis as described in individual IACUC-approved protocols.

3. Veterinary Care. The CNPRC vivarium is under the direction of the Associate Director for Primate Services (Chief Veterinarian) [Excluded by Requester]. Veterinary support is provided by Veterinarians and Animal Health Technicians (AHTs) (see Primate Medicine Services). Staff clinicians provide routine surveillance of overall colony health and management practices as part of routine physical examinations.

Animals in the outdoor animal colony are weighed, tuberculin tested, immunized for measles and tetanus as needed, serum banked as required, and examined routinely by a veterinarian twice annually. Animals housed outdoors are brought indoors to the hospital for treatment until resolution of the clinical problem and then returned to the social group as quickly as possible to maintain social stability. The hospital has an approximate average daily census of 100 animals (maximum 200). Animals in the indoor colony are weighed bi-monthly, tuberculin tested twice annually, vaccinated for measles as needed, serum banked as required, and examined by a Veterinarian generally before assignment to research projects and/or during annual evaluations. Indoor-housed animals on morning health report are assessed by a clinician and typically treated in their home cages as needed. Approximately 160 animals are on health report daily with a daily average of 45 animals requiring follow-up care. In addition to clinical care, the veterinary staff members also perform research and veterinary care surgeries (~300 major surgical procedures annually). Clinical veterinary staff members also conduct colony-based projects on new anesthetic agents, improved vaccines for animal health, and new surgical techniques. Surveillance for tuberculosis is essential for the continued health status of the CNPRC colonies.

4. **Provisions to Minimize Discomfort, Pain, and Injury.** Discomfort is minimized with appropriate sedation, analgesics, and handling techniques. All possible anesthetics and analgesics are included and administered under the direction of a CNPRC veterinarian. Animals are sedated with ketamine hydrochloride (5-30 mg/kg intramuscular [IM]), telazol (5-8 mg/kg IM), or ketamine with dexmedetomidine (0.015-0.075 mg/kg IM; with reversal atipamezole at a comparable dose) routinely to minimize discomfort during experimental procedures. For surgical procedures, animals are intubated and maintained under isoflurane (to effect), with post-operative monitoring for 2-3 days and administration of oxymorphone (0.15 mg/kg) or buprenorphine (0.01-0.03 mg/kg) for 3 days per veterinary discretion. Animals are monitored by the veterinary staff for alertness and activity post-anesthesia, including daily assessment for appetite, hydration, and stool quality. Sutures and condition (e.g., appetite, hydration) are assessed daily for 7 days post-operatively, discomfort is assessed and scored 3 days post-operatively. Antibiotics and other related pharmacologic agents are administered under the supervision of a CNPRC veterinarian according to the CNPRC formulary. The CNPRC maintains a full veterinary staff (Senior Veterinarians, Veterinary Residents, Animal Health Technicians, Veterinary Pathologists, Pathology Technicians) (see all sections of Primate Services). Veterinarians are on call 24 hours a day, seven days a week. The CNPRC maintains an animal hospital, surgery and radiology suites, infectious and noninfectious nonhuman primate nurseries, an infectious isolation unit, and anatomic and clinical pathology services. UC Davis complies with NIH policy on animal welfare, the Animal Welfare Act, and all other applicable federal, state, and local laws.
5. **Methods of Euthanasia.** Animals are euthanized by an overdose of pentobarbital (≥ 120 mg/kg intravenously) consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. All methods include well-established CNPRC SOPs as noted above, which are approved by the UC Davis IACUC.

SCIENTIFIC COMPONENTS: RESPIRATORY DISEASES RESEARCH UNIT

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Submitted

SCIENTIFIC UNITS: RESPIRATORY DISEASES RESEARCH UNIT

LETTERS OF SUPPORT

Letters of support from the individuals named below are provided on the pages that follow.

1.

Excluded by Requester

 PhD, Associate Professor and Chair, Department of Environmental Health Sciences, School of Public Health, The University of Alabama at Birmingham
2.

Excluded by Requester

 MD, Professor of Pediatrics, Division of Neonatology and Pulmonary Biology, the Perinatal Institute Cincinnati Children's Hospital Medical Center



SCHOOL OF
PUBLIC HEALTH

Department of Environmental Health Sciences

June 20, 2014

Excluded by Requester

California National Primate Research Center
UC Davis
Davis, CA 95616

RE: CNPRC Respiratory Diseases Unit

Dear

Excluded by
Requester

It is with my highest enthusiasm that I write this letter of support for the renewal of the CNPRC P51 grant and, in particular, the Respiratory Diseases Unit. As you know, I am an Associate Professor and Department Chair of the Department of Environmental Health Sciences in the School of Public Health at the University of Alabama at Birmingham. I have many years of training in pulmonary toxicology and have served as Project Leader for an NIEHS supported P01 grant in which the CNPRC Respiratory Diseases Unit has played a critical role. In light of my previous experience and collaborations with CNPRC Respiratory Diseases Unit Core Scientists, it is very appropriate for me to offer feedback on the significance of this group of investigators.

The Core Scientists within the Respiratory Diseases Unit have a long history of collaborations with external investigators. For the studies conducted through my NIEHS P01 grant, I have worked primarily with Excluded by Requester to investigate the health impact of early life ozone exposure using the nonhuman primate as a model of infant development. While rodent models have provided information on toxicologic effects induced by air pollutants, understanding the long-term effects of early life exposures requires the use of a laboratory animal model that closely mimics normal growth of human children. I should emphasize that the studies conducted as a part of my P01 grant could not have been completed in any other facility within the United States, or internationally, for that matter. The CNPRC Respiratory Diseases group is optimally located in within a center that specializes in having an active breeding colony, as well as a state of the art inhalation exposure facility, providing unique expertise and resources for investigators such as myself.

Based upon my background and positive experience working with the CNPRC Respiratory Diseases Unit, I completely and unreservedly support the renewal of the CNPRC P51 grant such that translational studies in pulmonary biology will continue for investigators in the future.

Sincerely,

Excluded by Requester

Associate Professor and Chair

Excluded by Requester



June 18, 2014

change the outcome®

Excluded by Requester

California National Primate Research Center
UC Davis
Davis, CA 95616

RE: CNPRC Respiratory Diseases Unit

Dear

Excluded by Requester

I am delighted to write this letter of support for the CNPRC Respiratory Diseases Unit P51 renewal, and I do so without hesitation. I am a neonatologist by training and Professor at the University of Cincinnati Department of Pediatrics. I direct a NIH funded laboratory. My research program is focused on understanding the mechanisms of fetal lung inflammatory responses during chorioamnionitis. These earlier studies have primarily used the sheep model of pregnancy. Despite the many advantages of the sheep model, there are serious limitations. These include lack of quality reagents for high-resolution immunology. As you know, Rhesus macaques and humans have very similar immune development particularly in intrauterine life. This aspect is critical to the success of our program. I therefore actively sought your collaboration. I am particularly interested in the fetal-maternal interface at the placenta and in collaboration with my colleagues Excluded by Requester from Cincinnati Children's Hospital, I have worked on multiple models of prenatal infection in the nonhuman primate at the CNPRC. Our interactions with your respiratory research group at the CNPRC has been a very positive experience as we all share the same passion for understanding perinatal immune mechanisms and developmental origins of pulmonary disease.

With the assistance of your research group, our recent studies in the nonhuman primate have already yielded one paper and another manuscript is currently in review. We are also applying for Pending Support Excluded by Requester The CNPRC is one of the few facilities in the country that has an extensive breeding program that will allow studies during fetal development and investigators further support this program with unique expertise in mucosal immunology and lung biology. The support and help I received at the CNPRC has been uniformly outstanding. To the best of my knowledge, I would not be able to find this resource in any other institution. Therefore, I am very happy to endorse continued NIH support of the CNPRC Respiratory Diseases Unit for the next renewal period. I look forward to our continued collaborative work in Perinatal research.

Sincerely,

Excluded by Requester

Cincinnati Children's Hospital Medical Center

SCIENTIFIC COMPONENTS: BRAIN, MIND, AND BEHAVIOR RESEARCH UNIT

RESOURCE SHARING PLAN

A detailed Resource Sharing Plan is included in the Overall component of this application.