Notice of Award

PRIMATE RESEARCH CENTER GRANT
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 06/30/2017

OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P51OD011092-58
FAIN: P51OD011092

Principal Investigator(s):
JOSEPH E ROBERTSON, MD

Project Title: SUPPORT FOR NATIONAL PRIMATE RESEARCH CENTER

JASON JAWORSKI
GRANTS & CONTRACTS ADMIN
3181 SW SAM JACKSON PK RD
L106RGC
PORTLAND, OR 972393098

Award e-mailed to: orserv@ohsu.edu

Period Of Performance:
Budget Period: 05/01/2017 – 04/30/2018
Project Period: 05/01/1997 – 04/30/2019

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $12,677,878 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to OREGON HEALTH & SCIENCE UNIVERSITY 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 P51OD011092. 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,

JENELLE D. WIGGINS
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 5P51OD011092-58

Award Calculation (U.S. Dollars)

Salaries and Wages	$4,639,520
Fringe Benefits	$1,468,664
Personnel Costs (Subtotal)	$6,108,184
Materials & Supplies	$821,288
Travel	$53,657
Other	$3,122,658
Federal Direct Costs	$10,105,787
Federal F&A Costs	$2,572,091
Approved Budget	$12,677,878
Total Amount of Federal Funds Obligated (Federal Share)	$12,677,878
TOTAL FEDERAL AWARD AMOUNT	$12,677,878
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$12,677,878

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
58	$12,677,878	$12,677,878
59	$12,976,996	$12,976,996

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:	1931176109A1
Document Number:	POD011092J
PMS Account Type:	P (Subaccount)
Fiscal Year:	2017

IC	CAN	2017	2018
OD	8014499	$12,328,146	$12,627,264
AG	8470701	$349,732	$349,732

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

NIH Administrative Data:
PCC: CMP01 / **OC**: 414E / **Released**: eRA Commons User Name 06/28/2017
Award Processed: 06/30/2017 12:41:39 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD011092-58

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 – 5P51OD011092-58

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) P51OD011092. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

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)

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal

Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 5P51OD011092-58

SUBJECT FOA
This award is subject to the conditions set forth in PA-11-136, "Limited Competition: National Primate Research Centers (P51)," 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-11-136.html.
****

INTERIM FUNDING PLAN
This award is being issued at 95% of the amount committed for FY2017 in the previous Notice of Award. Once NIH funding plans are published, this award may be revised accordingly.
****

CO-FUNDING
This award reflects support from the NIA in the amount of $349,732 total costs and from the ORIP in the amount of $12,328,146 total costs.
****

DIRECT CHARGES OF F&A-TYPE COSTS
Funds requested for office and administrative supplies, administrative coordinators/assistants, custodians, computers, laptops, maintenance & repairs, telecommunications are included in the awarded budget. The allowability of charges to this project for this purpose is predicated on the grantee's compliance with the applicable cost principles.
****

MEALS
The charging of meal costs directly to a grant is an exceptional activity and contingent upon the following: the grantee institution having a written policy in place ensuring consistent treatment of charging meal costs. This policy must define what constitutes a meeting for the dissemination of technical information when meals are allowable for such meetings, and must define the limitations and other controls on these recurring costs. This policy must be consistently applied regardless of whether the meeting is related to or funded by the Federal government or another source. These costs must also be reasonable.
****

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 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.
****

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, carryover requests) 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/index.htm.
****

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: Artisha Eatmon
Email: artisha.eatmon@nih.gov **Phone**: 301-435-0845

Program Official: Sheri Ann Hild
Email: hildsa@mail.nih.gov **Phone**: 301-435-8382 **Fax**: 301-402-4104

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011092-58

INSTITUTION: OREGON HEALTH & SCIENCE UNIVERSITY

Budget	Year 58	Year 59
Salaries and Wages	$4,639,520	$5,215,962
Fringe Benefits	$1,468,664	$1,690,486
Personnel Costs (Subtotal)	$6,108,184	$6,906,448
Consultant Services		$33,708
Equipment		$304,279
Materials & Supplies	$821,288	$1,307,865
Travel	$53,657	$62,768
Alterations and Renovations		$202,009
Other	$3,122,658	$1,435,105
TOTAL FEDERAL DC	$10,105,787	$10,252,182
TOTAL FEDERAL F&A	$2,572,091	$2,724,814
TOTAL COST	$12,677,878	$12,976,996

Facilities and Administrative Costs	Year 58	Year 59
F&A Cost Rate 1	28%	28%
F&A Cost Base 1	$9,186,040	$9,731,477
F&A Costs 1	$2,572,091	$2,724,814

PRIMATE RESEARCH CENTER GRANT **Federal Award Date:** 07/17/2017
Department of Health and Human Services
National Institutes of Health

OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P51OD011092-58 REVISED
FAIN: P51OD011092

Principal Investigator(s):
JOSEPH E ROBERTSON, MD

Project Title: SUPPORT FOR NATIONAL PRIMATE RESEARCH CENTER

JASON JAWORSKI
GRANTS & CONTRACTS ADMIN
3181 SW SAM JACKSON PK RD
L106RGC
PORTLAND, OR 972393098

Award e-mailed to: orserv@ohsu.edu

Period Of Performance:
Budget Period: 05/01/2017 – 04/30/2018
Project Period: 05/01/1997 – 04/30/2019

Dear Business Official:

The National Institutes of Health hereby revises this award to reflect a decrease in the amount of $332,245 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to OREGON HEALTH & SCIENCE UNIVERSITY 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 P51OD011092. 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,

JENELLE D. WIGGINS
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 5P51OD011092-58 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$4,648,308
Fringe Benefits	$1,471,450
Personnel Costs (Subtotal)	$6,119,758
Materials & Supplies	$822,843
Travel	$53,759
Other	$2,778,180
Federal Direct Costs	$9,774,540
Federal F&A Costs	$2,571,093
Approved Budget	$12,345,633
Total Amount of Federal Funds Obligated (Federal Share)	$12,345,633
TOTAL FEDERAL AWARD AMOUNT	$12,345,633
AMOUNT OF THIS ACTION (FEDERAL SHARE)	($-332,245)

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
58	$12,345,633	$12,345,633
59	$12,976,996	$12,976,996

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:	1931176109A1
Document Number:	POD011092J
PMS Account Type:	P (Subaccount)
Fiscal Year:	2017

IC	CAN	2017	2018
OD	8014499	$11,995,901	$12,627,264
AG	8470701	$349,732	$349,732

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

NIH Administrative Data:
PCC: CMP01 / **OC**: 414E / **Released**: eRA Commons User Name 7/14/2017
Award Processed: 07/17/2017 12:12:34 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD011092-58 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 – 5P51OD011092-58 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) P51OD011092. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

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)

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal

Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 5P51OD011092-58 REVISED

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

This award is revised to adjust the calculation of total cost due to the revision of the NPRC Funding Plan.

ORIP FUNDING PLAN FOR FY2017
This revised award reflects the NIH Fiscal Policy for Grant Awards for FY2017 (see NIH Guide Notice NOT-17-086) and the implementation of the ORIP FY2017 grants funding policy (see "Grants Policies and Guidance"): https://orip.nih.gov/funding/awards-funding-policy

All previous terms and conditions remain in effect.
****

SUBJECT FOA
This award is subject to the conditions set forth in PA-11-136, "Limited Competition: National Primate Research Centers (P51)," 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-11-136.html.
****

CO-FUNDING
This award reflects support from the NIA in the amount of $349,732 total costs.
****

DIRECT CHARGES OF F&A-TYPE COSTS
Funds requested for office and administrative supplies, administrative coordinators/assistants, custodians, computers, laptops, maintenance & repairs, telecommunications are included in the awarded budget. The allowability of charges to this project for this purpose is predicated on the grantee's compliance with the applicable cost principles.
****

MEALS
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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

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****

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****

COMMUNICATIONS/PRESS RELEASE
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The ORIP WWW home page is at http://dpcpsi.nih.gov/orip/

STAFF CONTACTS

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Grants Management Specialist: Artisha Eatmon
Email: artisha.eatmon@nih.gov **Phone**: 301-435-0845

Program Official: Sheri Ann Hild
Email: hildsa@mail.nih.gov **Phone**: 301-435-8382 **Fax**: 301-402-4104

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011092-58 REVISED

INSTITUTION: OREGON HEALTH & SCIENCE UNIVERSITY

Budget	Year 58	Year 59
Salaries and Wages	$4,648,308	$5,215,962
Fringe Benefits	$1,471,450	$1,690,486
Personnel Costs (Subtotal)	$6,119,758	$6,906,448
Consultant Services		$33,708
Equipment		$304,279
Materials & Supplies	$822,843	$1,307,865
Travel	$53,759	$62,768
Alterations and Renovations		$202,009
Other	$2,778,180	$1,435,105
TOTAL FEDERAL DC	$9,774,540	$10,252,182
TOTAL FEDERAL F&A	$2,571,093	$2,724,814
TOTAL COST	$12,345,633	$12,976,996

Facilities and Administrative Costs	Year 58	Year 59
F&A Cost Rate 1	28%	28%
F&A Cost Base 1	$9,182,474	$9,731,477
F&A Costs 1	$2,571,093	$2,724,814

PRIMATE RESEARCH CENTER GRANT
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 11/27/2017

OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P51OD011092-58 REVISED
FAIN: P51OD011092

Principal Investigator(s):
Peter G Barr-Gillespie, PHD

Project Title: SUPPORT FOR NATIONAL PRIMATE RESEARCH CENTER

JASON JAWORSKI
GRANTS & CONTRACTS ADMIN
3181 SW SAM JACKSON PK RD
L106RGC
PORTLAND, OR 972393098

Award e-mailed to: orserv@ohsu.edu

Period Of Performance:
Budget Period: 05/01/2017 – 04/30/2018
Project Period: 05/01/1997 – 04/30/2019

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 OREGON HEALTH & SCIENCE UNIVERSITY 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.

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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 P51OD011092. 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,

JENELLE D. WIGGINS
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 5P51OD011092-58 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$4,648,308
Fringe Benefits	$1,471,450
Personnel Costs (Subtotal)	$6,119,758
Materials & Supplies	$822,843
Travel	$53,759
Other	$2,778,180
Federal Direct Costs	$9,774,540
Federal F&A Costs	$2,571,093
Approved Budget	$12,345,633
Total Amount of Federal Funds Obligated (Federal Share)	$12,345,633
TOTAL FEDERAL AWARD AMOUNT	$12,345,633
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (58)	
GRANT NUMBER	**TOTAL FEDERAL AWARD AMOUNT**
5P51OD011092-58	$12,345,633
3P51OD011092-58S1	$83,199
TOTAL	**$12,428,832**

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
58	$12,345,633	$12,428,832
59	$12,976,996	$12,976,996

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:	1931176109A1
Document Number:	POD011092J
PMS Account Type:	P (Subaccount)
Fiscal Year:	2017

IC	CAN	2017	2018
OD	8014499	$11,995,901	$12,627,264
AG	8470701	$349,732	$349,732

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

NIH Administrative Data:
PCC: CMP01 / **OC**: 414E / **Released**: eRA Commons User Name 11/24/2017
Award Processed: 11/27/2017 12:03:57 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD011092-58 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 – 5P51OD011092-58 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) P51OD011092. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

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)

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 5P51OD011092-58 REVISED

REVISION #2 : This award is revised to address the following issue:

CHANGE IN PI

This revision reflects ORIP approval of the change of principal investigator from Joseph Robertson to Peter Barr-Gillespie, in accordance with the grantee's request dated November 14, 2017.

All previous terms and conditions remain in effect.
****

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

This award is revised to adjust the calculation of total cost due to the revision of the NPRC Funding Plan.

ORIP FUNDING PLAN FOR FY2017
This revised award reflects the NIH Fiscal Policy for Grant Awards for FY2017 (see NIH Guide Notice NOT-17-086) and the implementation of the ORIP FY2017 grants funding policy (see "Grants Policies and Guidance"): https://orip.nih.gov/funding/awards-funding-policy

All previous terms and conditions remain in effect.
****

SUBJECT FOA
This award is subject to the conditions set forth in PA-11-136, "Limited Competition: National Primate Research Centers (P51)," 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-11-136.html.
****

CO-FUNDING
This award reflects support from the NIA in the amount of $349,732 total costs.
****

DIRECT CHARGES OF F&A-TYPE COSTS
Funds requested for office and administrative supplies, administrative coordinators/assistants, custodians, computers, laptops, maintenance & repairs, telecommunications are included in the awarded budget. The allowability of charges to this project for this purpose is predicated on the grantee's compliance with the applicable cost principles.
****

MEALS
The charging of meal costs directly to a grant is an exceptional activity and contingent upon the following: the grantee institution having a written policy in place ensuring consistent treatment of charging meal costs. This policy must define what constitutes a meeting for the dissemination of

technical information when meals are allowable for such meetings, and must define the limitations and other controls on these recurring costs. This policy must be consistently applied regardless of whether the meeting is related to or funded by the Federal government or another source. These costs must also be reasonable.
****

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 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.
****

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, carryover requests) 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/index.htm.
****

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: Artisha Eatmon
Email: artisha.eatmon@nih.gov **Phone**: 301-435-0845

Program Official: Sheri Ann Hild
Email: hildsa@mail.nih.gov **Phone**: 301-435-8382 **Fax**: 301-402-4104

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011092-58 REVISED

INSTITUTION: OREGON HEALTH & SCIENCE UNIVERSITY

Budget	Year 58	Year 59

Salaries and Wages	$4,648,308	$5,215,962
Fringe Benefits	$1,471,450	$1,690,486
Personnel Costs (Subtotal)	$6,119,758	$6,906,448
Consultant Services		$33,708
Equipment		$304,279
Materials & Supplies	$822,843	$1,307,865
Travel	$53,759	$62,768
Alterations and Renovations		$202,009
Other	$2,778,180	$1,435,105
TOTAL FEDERAL DC	$9,774,540	$10,252,182
TOTAL FEDERAL F&A	$2,571,093	$2,724,814
TOTAL COST	$12,345,633	$12,976,996

Facilities and Administrative Costs	Year 58	Year 59
F&A Cost Rate 1	28%	28%
F&A Cost Base 1	$9,182,474	$9,731,477
F&A Costs 1	$2,571,093	$2,724,814

A. OVERALL COVER PAGE

Project Title: SUPPORT FOR NATIONAL PRIMATE RESEARCH CENTER	
Grant Number: 5P51OD011092-58	**Project/Grant Period:** 05/01/1997 - 04/30/2019
Reporting Period: 05/01/2016 - 04/30/2017	**Requested Budget Period:** 05/01/2017 - 04/30/2018
Report Term Frequency: Annual	**Date Submitted:** 02/24/2017
Program Director/Principal Investigator Information: JOSEPH E ROBERTSON , MD PHD **Phone number:** 503 494-1085 **Email:** robertjo@ohsu.edu	**Recipient Organization:** OREGON HEALTH & SCIENCE UNIVERSITY OREGON HEALTH & SCIENCE UNIVERSITY 3181 SW Sam Jackson Pk Rd PORTLAND, OR 972393098 **DUNS:** 096997515 **EIN:** 1931176109A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: JASON N JAWORSKI 3181 S.W. Sam Jackson Park Rd L106RGC Portland, OR 972393098 **Phone number:** 503-494-7784 **Email:** jaworski@ohsu.edu	**Signing Official:** JASON N JAWORSKI 3181 S.W. Sam Jackson Park Rd L106RGC Portland, OR 972393098 **Phone number:** 503-494-7784 **Email:** jaworski@ohsu.edu
Human Subjects: No	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mission of the Oregon National Primate Research Center (ONPRC) is to promote scientific discovery, particularly in nonhuman primate (NHP) models, to accelerate progress in understanding human diseases, leading to better health. The availability of information about human genetics, coupled with the similarity of the NHP genome to that of humans, provides the opportunity for NHP models to make significant contributions to the discoveries of new cures and therapies. The NIH Office of Research Infrastructure Programs (ORIP) re-emphasized its mandate to foster collaborative and translational research, and has formed a consortium of the National Primate Research Centers (NPRC Consortium). Furthermore, all of the research programs have leveraged P51 funding by successfully bringing in external funding for scientific studies and training opportunities for fellows, students, interns, and visiting and collaborating scientists. After a formal strategic planning process in 2009, we defined six goals that were described in our renewal:
1. Provide leadership and infrastructure effective in setting and achieving scientific and strategic priorities.
2. Foster innovative, effective scientific divisions, interdisciplinary programs, and support cores.
3. Integrate scientific priorities with Division of Comparative Medicine.
4. Foster and enhance interactions within our campus, community, host institution, and other NPRCs.
5. Enhance the Center's resources to assure stable, diverse funding.
6. Develop effective, community-oriented outreach programs by which to educate the public about science.
Progress toward these goals was summarized in our competing renewal. In 2014, the Center leadership team led and completed another formal strategic planning process based on the Hoshin-Kanri method that we had used previously. Based on the formal SWOT analysis, we identified seven major areas of strategic focus and objectives within these areas. The seven new objectives to accomplish in the next five years are described below and are based on this renewed strategic plan.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-OVERALL_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
3P51 OD011092-57S2	Identifying HIV-1 Env-specific B cells in immunized NHPs to clone and characterize monoclonal antibodies	Specific Aims: (1) To isolate by single cell sorting neutralizing Env-specific B cells from macaques immunized with clade B and clade C Env-based motif optimized DNA and protein expression vectors and in order to develop a panel of macaque mAbs for evaluation of epitope targeting. (2) To map the targets of NAb responses in macaques immunized with clade B and C Env immunogens.	We successfully sorted memory IgG+ Env-specific B cells from 3 immunized animals. For each animal, we have >25 matched heavy and light chains representing HIV-specific monoclonal antibodies (mAbs) induced by our vaccination protocols. From these, we have been actively sequencing and cloning the NHP mAbs into expression vectors for purification, testing in vitro, and characterization of epitope targeting.
3P51 OD011092-57SI	Sheltered Group Housing Procedure Room (AIDS-related Renovation Supplement)	To modify an existing Shelter Housing Unit for AIDS/HIV small group housing studies. One of eight group housing rooms of one Shelter House Unit will be converted into a procedure & short-term (less than 12 hours) caging area. Additionally, we are proposing to modify the east/west guillotine gates to be remotely operated to allow remote shifting of groups from east to west units (and vice versa). Currently, the shelter house units only allow for remote shifting of animals from north to south, limiting group housing	We have completed the initial design and first round of cost estimating and are working on finalizing both. The final design package will be submitted to NIH by February 28th.

		options and cleaning efficacy. The conversion of the group housing room will allow for six or seven small AIDS/HIV research groups to be housed in one shelter house complex.	
1G20OD020286-01		Specific Aim 1: Add sound-dampening building materials to walls and insulation to ceilings in individual testing rooms; Specific Aim 2: Enhance ambiance by removing reflective surfaces and changing lighting to variable, non- fluorescent lights that include dimming devices; Specific Aim 3: Provide electrical signal disruption between observation rooms to assist in telemetry; and Specific Aim 4: Enhance the ability to perform and monitor remote data acquisition in the behavioral suites.	Project design was completed and approved by the NIH Technical Review Team in May 2016. The renovations were completed and the space occupied by ONPRC researchers in December 2016. Renovations also included: modifying the animal slide gates to reduce noise, addition of networking infrastructure for use of individual IPads by the monkeys, and addition of a remote computer control room with a large television for collecting data and monitoring the behavioral studies in the eight animal rooms. The suites were completely re-wired with new IT infrastructure so the electrical signal disruption was not needed. The renovated suites are now in full operation and studies are being performed.

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-OVERALL_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Scientific studies are submitted for peer review and published in appropriate scientific journals. The ONPRC works with the OHSU Office of Strategic Communications to provide press releases on scientific progress of interest to the general public. The Director's Office provides regular updates and electronic newsletters to ORIP and to OHSU Strategic Communications group to keep ONPRC current and former staff members, as well as other NPRCs and collaborators at other institutions. OHSU publishes weekly and monthly newsletters to all staff members that describe awards, grants, and key scientific breakthroughs. The ONPRC website is also updated regularly to highlight key scientific findings.

Progress on our strategic objectives is provided to the Senior Vice President for Research at OHSU, Dr. Daniel Dorsa, on a monthly basis. A summary of progress is provided to ORIP on a weekly basis via teleconference with the other NPRC Directors, and with these Directors and their senior staff at our fall and spring NPRC Directors' Meetings. We provide twice-yearly summaries to the External Scientific Advisory Board (ESAB), including one in-person meeting per year.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will be starting some new avenues of communication this year through the work of our Communications Task Force to align the overall OHSU and ONPRC communication streams. We plan to hold a Scientific Retreat at Salishan Lodge in June 2017 for the ONPRC, VGTI, and collaborating scientists and clinicians and leaders at OHSU. We will continue the work of the Task Forces and participation in the NPRC Consortium activities, including updating the websites and disseminating important scientific discoveries via the media.

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

OVERALL: ACCOMPLISHMENTS

We continued to focus efforts on our seven refined strategic objectives to assure the success of the Center as a world-class research and training institution within the OHSU research sphere that serves the mission of ORIP and NIH and results in biomedical breakthroughs to improve human health. These are noted below:

1. WORLD-RENOWNED CENTER. The ONPRC will be a world-renowned center that integrates emerging technologies and translational research in NHP models of human disease.
2. WORLD-CLASS LEADERSHIP. ONPRC has visionary leaders and world-class faculty performing integrated team science.
3. COLLABORATIVE, INTERDISCIPLINARY ENVIRONMENT. The ONPRC will provide an environment dedicated to collaborative and interdisciplinary application of the NHP model to multiple research areas.
4. TECHNOLOGY. The ONPRC will be the nationally recognized leader in the use of NHP models to elucidate the models of human disease.
5. SUSTAINABLE FUNDING. Achieve stabilized funding that is both diversified and matched to programmatic goals.
6. ONPRC INFRASTRUCTURE. The ONPRC infrastructure will be state-of-the-art with respect to animal housing, research space and support facilities, and which incorporate optimal operating and regulatory practices.
7. NHP RESOURCES "RIGHT-SIZED" AND EFFECTIVELY MANAGED. NHP Resources will be appropriately sized, effectively managed, and exceptionally maintained to provide programmatic needs.

In the second year of our strategic plan (July 1, 2015-June 30, 2016). We convened six Task Forces and leaders of these Task Forces then appointed appropriate members to develop strategies to make progress toward and to accomplish these goals. Briefly, progress to date is summarized below. The overall strategic plan breakthrough objective that fall under is noted in parentheses after the name of the Task Force, and the leader responsible for each group.

1. Faculty Retention and Collaborative Research (**COLLABORATIVE, INTERDISCIPLINARY ENVIRONMENT**; Excluded by Requester). This group developed promotion guidelines and policies that are in alignment with the OHSU School of Medicine in order to streamline and better coordinate promotions of faculty members. They also led a Center-wide scientific retreat at Skamania Lodge on March 3-4, 2016. The Center invited all core faculty, DCM unit heads, and leaders of the Research Support Cores and NHP Resources, as well as key collaborating faculty and leaders at OHSU, VGTI faculty, and Senior VP for Research Excluded by Requester and Provost Excluded by Requester. The keynote speaker was Dr. Excluded by Requester from OHSU. This Task Force continues in 2016-17.

2. Laboratory Research Space (**INFRASTRUCTURE**; Excluded by Requester). This group mapped out current space utilization and assignments on campus, and characterized space by use, funding, and personnel for each scientific division. This information proved vital to the Infrastructure Plan TF (#3). They developed recommendations for research assignment policy. The EELC has adopted their recommendations and is developing a campus-wide space policy direction and policies for the ONPRC that are consistent with OHSU Space Assignment. This Task Force completed its efforts in July of 2016.

3. Infrastructure Plan Task Force (**INFRASTRUCTURE**; Excluded by Requester). This group has taken a comprehensive and in-depth examination of needs for laboratory, NHP breeding, NHP research, and administrative space, based on various growth models for the next five years for faculty and NHP growth. The plan is based on the scientific strategic needs and takes into consideration the needs of the other groups co-located on the OHSU West Campus, particularly the Vaccine & Gene Therapy Institute. Dr. Excluded by Requester and several key research and administrative leaders participated in a yearlong effort with campus planning and architectural and engineering consultants to develop a 20-year Master Plan for the West Campus. This plan outlines the future growth and investments for the West Campus and the ONPRC. This Task Force completed its efforts in July 2016.

4. NHP Resources (**NHP RESOURCES EFFECTIVELY MANAGED**; Excluded by Requester). There are four NHP Resources that were developed at various times over the last 10-15 years to provide specific types of models for investigators: Japanese macaques, Aging, Infectious Disease, and Obese. This group inventoried the current Resources and developed a plan for review and oversight to these on a regular basis to understand return on investment for P51 resources to enhance research. We have implemented this plan and currently use our quarterly management meetings to review annual reports from each of these resources. This Task Force completed its efforts in July 2016.

5. NHP Utilization (**NHP RESOURCES EFFECTIVELY MANAGED**; Excluded by Requester) In conjunction with the Business Office, this group developed a projection tool to track grant funding, pending and planned. The colony planning group in DCM worked with the Animal Utilization Committee to develop streamlined methods for understanding the demands of pending and planned grants and how these would impact the breeding colony (availability). The then developed with Excluded by Requester a model of colony growth as a predictive model. This TF also provided critical information for TF #3. This Task Force is continuing its work in 2016-17.

6. Research Informatics Task Force (**TECHNOLOGY**; Excluded by Requester). This initiative sprang from the earlier IT Infrastructure and it spent the year inventorying current tools and developing recommendations for optimal research informatics computational and data management systems to support research in all divisions. This Task Force completed its work in July 2016.

In July 2016, we reported on the work of the six 2015-16 active Strategic Task Forces. Progress toward these breakthrough objectives was reviewed by an expanded leadership group of approximately 30 leaders, and five Task Forces were appointed for the 2016-17 year to advance the next most critical priorities within the Strategic Plan. We also convened the External Scientific Advisory Board on September 10, 2016 to vet the progress and plans. The new Task Forces are listed below, with leaders.

1. Faculty Retention and Collaborative Research Task Force (**COLLABORATIVE, INTERDISCIPLINARY ENVIRONMENT**; Excluded by Requester) This group also continued from last year and has a focus on mentoring and faculty retention. Faculty titles for Core Scientists will be changed to Professor or Research Professor (Core or non-Core). This policy as being adopted university-wide as of July 2016, to harmonize with those at other academic medical centers. The group will focus on developing a mentoring program tailored to ONPRC and complementary to OHSU faculty resources.

2. NHP Utilization Task Force (**NHP RESOURCES "RIGHT-SIZED" AND EFFECTIVELY MANAGED**; Excluded by Requester Excluded by Requester). This group continues to refine methods for colony management to meet the increasing needs of research for experimental space as well as "staging" space for animals going onto or coming off of studies. They will continue to provide new methods and refinements to support the Animal Utilization Committee, colony projections, and to assist in planning for future infrastructure investments.

3. Communications Task Force (**WORLD RENOWNED CENTER**; Excluded by Requester). This group has developed an inventory of all communication activities and is working on enhancements to all aspects of communication, both internal and external. The focus of much of this year has been internal and working to align OHSU and ONPRC activities. In the coming year, as plans for external Public Relations are developed, there will be more focus on external messaging.

4. Integrated Pathology Task Force (**WORLD RENOWNED CENTER, SUPPORTIVE INFRASTRUCTURE**; Excluded by Requester This task force is the continuation of a working group exploring the concept of an Integrated Pathology and Histopathology resource, including faculty, staff, and equipment needs. This group is analyzing information collected through an internal user survey, correspondence with internal and external colleagues, and current and future operations, to draft a model of what an ideal ONPRC Integrated Pathology "Resource" might look like for future planning, recruitment, and infrastructure improvements.

5. Scientific Symposia Task Force (**COLLABORATIVE, INTERDISCIPLINARY ENVIRONMENT**; Excluded by Requester) This group developed and is implementing a process for hosting an annual scientific symposium

representative of the ONPRC research divisions in an effort to network with the greater OHSU community and non-OHSU researchers. The goal is to share the science and services taking place at ONPRC and learn about new state of the art research and tools to enhance ONPRC NHP research while developing a stronger network. The next symposium will focus on early embryonic and fetal development with three topics: Assessment of early cognitive function in infants (Neuroscience), Assessment of oocyte quality focus involving NCTRI and CRISPR (Reproductive & Developmental Sciences), and Zika (Pathobiology & Immunology, integrated with all divisions). DCM will be incorporated into the symposium as well as other ONPRC science and service.

INDIVIDUAL PROJECTS

a. Management/Other
b. Pilot Projects
c. Research – Division of Comparative Medicine
d. Research – Comparative Research Unit
e. Research – Division of Diabetes, Obesity, and Metabolism (now Cardiometabolic Health)
f. Research – Division of Neuroscience
g. Research – Division of Pathobiology & Immunology
h. Research – Division of Reproductive & Developmental Sciences

Project Title: Summer Internship Program: Primate Center
SPID: 0034
Unit/Division: Management/Other
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
None

Project Description: ONPRC's Summer Internship program is a core component of the Center's multi-faceted education outreach program. In addition to conducting authentic research under the direction of a Primate Center scientist for 8 weeks (high school students) or 10 weeks (undergraduates), interns are intentionally immersed in the culture of science. They attend lab meetings and journal clubs, and are required to attend weekly seminars presented by Center scientists. They interact with graduate students and postdoctoral fellows on our campus and have the opportunity to meet with graduate program admissions personnel at OHSU. At the close of summer, they are required to make a presentation of their research at the Summer Science Symposium.

Progress during the reporting period (a few sentences):
During the summer of 2016, 11 undergraduate students and 5 high school students were supported in 10-week and 8-week apprenticeships, respectively. We continue to seek funding to enable the support an equal or greater number of apprentices during the summer of 2017.

Publications resulting from the project:
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: Establishment of Specific Free Rhesus and Pigtail Macques Colonies –U24
SPID: 0850
Unit/Division: Division of Comparative Medicine
Type of Project: Management/Other
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with Project:
Excluded by Requester
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description: The Indian rhesus macaque develops a disease that closely mimics human acquired immunodeficiency syndrome (AIDS) when infected by simian Immunodeficiency virus (SIV) or chimeric simian-human immunodeficiency viruses (SHIV), and represents the best animal model for HIV Infection. Preclinical vaccine development is heavily dependent on the SIV and SHIV rhesus macaque models. The value and utility of the model are markedly enhanced by improving the level of microbial and genetic characterization. Macaques free of ubiquitous viruses that are homologues of human viruses responsible for opportunistic infections are essential for a growing number of AIDS-related opportunistic infection models and for viral vaccine vector development based on these agents. The utility of macaque models for immunological research has been hindered by the unprecedented complexity of their major histocompatibility complexes. Comprehensive MHC genotyping has the potential to revolutionize the use of macaques in infectious disease research and to guide functional immunology studies. MHC-restricted cellular immune responses are key in protective immunity and resistance to infectious diseases. The comprehensive objective of this application is to increase the capacity of the ONPRC AIDS Research Expanded SPF Breeding Colony to provide genetically characterized Indian-origln rhesus macaques free of a broad number of enzootic and zoonotic agents to enhance the usefulness of the resource for cutting edge opportunistic agent and vaccine research.

Project Progress: The colony census at the close of 2015 was 198 and comprised of 101 adult breeding animals, 56 juveniles and 21 infants. Thirty-five animals were assigned to research projects. Serologic screening of the colony was completed using a multiplex protein assay, Proprietary Info that we have been beta testing for the past two years. The colony remains free of the nine expanded SPF definition agents with the exception of lymphocryptovirus (LCV). Lymphocryptovirus-positive animals have been isolated from the colony and enhanced LCV serologic testing implemented in negative animals to facilitate early detection and removal of any further LCV seroconverting animals. Several of the established expanded SPF breeding groups are scheduled to move to group housed outdoor sheltered enclosures in the spring of 2016.

Publication:
Excluded by Requester

Funding Source:
Michael K. Axthelm, D.V.M., Ph.D. NIH Office of the Director 5U24OD010850

Project Title: Technological and Physical Enhancements for Primate Behavioral Testing Suites
SPID: 0286
Unit/Division: Management/Other
Type of Project: Management/Other
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description (one paragraph):
The Oregon National Primate Research Center (ONPRC) is one of eight National Primate Research Centers whose focus is to develop and to provide models for human disease for investigators who are exploring ways to improve human health. The ONPRC has over 40 faculty principal investigators who are involved in research using nonhuman primate (NHP) models in four scientific divisions: 1) Neuroscience; 2) Reproductive & Developmental Sciences; 3) Pathobiology & Immunology; and 4) Diabetes, Obesity & Metabolism. An increasing number of these studies involve the assessment of behaviors, and for this reason the Center constructed a cluster of eight behavioral testing suites intended for shared use and located within the Specific Animal Location. These suites provide individual enclosed spaces as operant chambers for NHP behavioral observations and anterooms for observers/computers to record responses to testing. NHPs are not housed in these rooms and there is no permanent equipment in the spaces. The number of studies that include assessment of various aspects of primate behaviors relevant to our animal models of disease has increased significantly since the current behavioral testing suites were constructed. In addition to adding new technologies for assessing behavior, we have also expanded the number of animal models under study, driven in part by our success in funding this type of research. However, as more projects are funded, both technological and physical enhancements are needed to enhance the research and improve NHP well being. In this application, we are proposing to upgrade facilities that were designed and built a decade ago for this purpose, but that were built according to a different set of standards because much or all of the experimental data were acquired using anesthetized monkeys. Presently, sound travels readily between rooms, and vocalization of primates that are awake in one room disrupts the focus of the test subjects in all other rooms. Our goal is to better accommodate non-anesthetized (awake) animals in cognitive testing, which is the type of assessment needed for our currently funded grants. We propose to modernize the procedures that use computer-based data acquisition systems by providing touch screens for chambers in every room, and through the addition of a computer server with software for data acquisition, data output, and initial analyses of the various cognitive tasks. We also plan to install a monitor in the external hallway at the suite entrance for the capture of all suite activities into a single split screen, to both enhance safety and limit interruptions. Our specific aims are to: (1) Add sound-dampening building materials to walls and insulation to ceilings in individual testing rooms; (2) Enhance ambiance by removing reflective surfaces and changing lighting to variable, non-fluorescent lights that include dimming devices; (3) Provide electrical signal disruption between observation rooms to assist in telemetry; and (4) Enhance the ability to perform and monitor remote data acquisition in the behavioral suites.

Progress during the reporting period (one paragraph):
The project design was completed and approved by the NIH Technical Review Team in May, 2016 and all of the building renovations were completed and the space turned over to the ONPRC researchers in December 2016. Included in the renovations were the addition of sound dampening material in all of the walls and ceilings of the observation rooms, the removal of reflective surfaces, the replacement of existing lighting with new fixtures and dimming switches, the re-surfacing of the epoxy flooring cove base, modifications to the animal slide gates to reduce noise, the addition of extensive networking infrastructure to allow the use of individual IPads by the monkeys, and the addition of a remote computer control room with a large screen

television for collecting experimental data and for monitoring the behavioral studies being performed in each of the eight animal rooms. Because the suites were completely re-wired with new IT infrastructure the electrical signal disruption portion of the project was not needed to be performed. The renovated suites are now in full operation and studies are being performed.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):
Nancy Haigwood, Ph.D. NIH Office of the Director 1G20OD020286-01

Project Title: Establishment of Specific Pathogen-Free Rhesus Macaque Colonies – U42
SPID: 0426
Unit/Division: Division of Comparative Medicine
Type of Project: Management/Other
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester	Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester	Oregon Health & Science University, ONPRC

Project Description:
The projected need for Indian rhesus macaques for AIDS-related research exceeds availability from current domestic breeding programs and there continues to be an urgent need for breeding programs for future AIDS vaccine and pathogenesis studies. Rhesus macaques with defined major histocompatability complex (MHC) genotypes and known pedigree are becoming increasingly important for research to understand biologic variation in host immune responses and its effects on vaccine strategies and the pathogenesis of AIDS. The objective of this project is to expand the Oregon National Primate Research Center's specific pathogen-free (SPF) Indian rhesus macaque resource and sufficiently characterize their MHC haplotype to permit selected pedigree breeding for MHC class I alleles useful in AIDS research. Specific aims for accomplishing this objective include intensively managing a subpopulation of the Center's SPF Indian rhesus macaque breeding colony to maximize production of genetically diverse females to expand the breeding capacity of the colony. The breeding colony is typed for ten MHC alleles and managed for the production of MHC-defined offspring of known parentage. Selective breeding and careful monitoring of use of MHC-typed animals is used to provide a population of animals with MHC alleles important for assessing virus-specific cell-mediated immune function in simian immunodeficiency virus vaccine models for preventing AIDS virus infection.

Progress during the reporting period (a few sentences):
One hundred and forty four U42 animals were assigned to HIV/AIDS projects since the last SPID report was compiled (including animals assigned from January 2016-January 2017. Access to animal pedigree information and parentage assignment is fully implemented in the PRIMe electronic health records database. Transition of the Illumina 96-SNP array to the Fluidigm 96-SNP array for parentage analysis was completed during 2016. During this year, we performed parentage analysis and confirmed parentage for 111 SPF4/U42 macaques. We additionally genotyped 322 SPF4/U42 macaques for MHC Class I alleles. All parentage assignments and genotype data were uploaded to PRIMe. Comprehensive surveillance testing of the U42 colony by PCR and serology found no animals positive for SPF4 viruses (SIV, SRV, STLV1 or herpes B).

Animals assigned to HIV/AIDS research from the U42 to projects:

Excluded by Requester	"Development of an Effector memory T cell AIDS vaccine"; 18 NHPs
	"Consortium for AIDS Vaccine Res in NHPs"; 21 NHPs
	"Targeting the PD –1 Pathway to Eradicate SIV/HIV – "U19 AI96109"; 12 NHPs
	"Enhancing immunity with TLR4 and TLR7 agonists to achieve a functional HIV cure"; 3 NHPs
	"Elimination of long –lived latently infected T –cells in SIV –infected rhesus macaques (RM) on suppressive antiretroviral therapy (ART) with alemtuzumab –induced T –cell depletion"; 1 NHPs
Excluded by Requester	"Impact of Alemtuzumab on SIV Persistence in Antiretroviral –Treated SIV –Infected Macaques"; 1 NHP
Excluded by Requester	Outcome 8_(Activity 2.3)Development of Attenuated CMV Vectors for an HIV/AIDS Vaccine"; 4 NHPs

Excluded by Requester "Outcome 9_(Activity 2.4)Development of Attenuated CMV Vectors for an HIV/AIDS Vaccine"; 1 NHP

Excluded by Requester "Impact of Sirolimus (Rapamycin) on HIV –1 Persistence and Immune Function"; 5 NHPs

– "Core B NHP Programming HIV Immune Response for Broadly Neutralizing Antibodies by Vaccination"; 3 NHPs

Excluded by Requester "HIV B –Cell Lineage Vaccine Design Based on Replicating Ad and Env Protein in NHP"; 9 NHPs

"Reducing Latent Viral Reservoirs in Infant Macaques"; 5 NHPs

"Epitope –targeted Vaccines for HIV –1 Prevention"; 21 NHPs

"Passive transfer in macaques to investigate protection efficacy of HIV anti –V2 mAbs"; 2 NHPs

"Protective Role of V2 antibodies induced in mucosal tissues in macaques"; 8 NHPs

Excluded by Requester "Immunogenicity of RhCMV Vectored Conserved SIV Vaccine"; 2 NHPs

"CHAVI ID: Efficacy and Immunogenicity of 68 –1 RhCMV Vectors Expressing Conserved SIV Antigens "; 3 NHPs

Excluded by Requester – "Efficacy of Strain 68 –1 RhCMV Vectors Expressing 5' Leader Polypeptides "; 9 NHPs

"A Novel APOBEC –based Vaccine Approach for HIV"; 2 NHPs

"A Universal MHC –E Vaccine for HIV"; 3 NHPs

"Investigating the development of AIDS and non –AIDS defining cancers in aged SIV –infected rhesus macaques"; 3 NHPs

HIV/AIDS Publications resulting from the project.

Excluded by Requester

Excluded by Requester

Funding Sources:
Gregory Timmel, M.S., D.V.M., D.A.C.L.A.M. National Institutes for Health Office of Director 4U42OD010426

Project Title: Effects of chronic alcohol use on the sperm epigenome and ncRNA expression in rhesus macaques
SPID:
Unit/Division: Neuroscience
Type of Project: Pilot
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description (one paragraph):
Alcohol use disorders (AUDs) are highly prevalent with an estimated annual global burden of nearly 2.5 million deaths and a cost of approximately $200 billion a year. Although it is widely known that alcoholism 'runs in families,' decades of research have failed to tease apart the genetic and environmental factors that contribute to the increased familial risk. Recent studies have shown that paternal chronic stress or high-fat diet reprograms the sperm epigenome, suggesting a role in establishing the same stress and metabolic dysregulation phenotype in offspring as seen in the fathers. Despite these important findings, the effects of paternal chronic alcohol use on the sperm epigenome and sRNA expression remain unknown. We will test the hypothesis that DNA methylation and sRNA composition of sperm are significantly modified by chronic alcohol consumption using the macaque alcohol self-administration model.

Progress during the reporting period (one paragraph):
Pre-alcohol sperm samples have been collected from 12 male macaques. These subjects are currently under the alcohol self-administration protocol, and after 6 months we will collect sperm samples to evaluate the longitudinal effects of chronic alcohol use on the sperm epigenome.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Joseph Robertson, M.D., Ph.D. NIH Office of Research Infrastructure Program

Project Title: Characterization of primate germline differentiation using the rhesus macaque
SPID: 0056
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Pilot
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — UCLA, Molecular Cell and Developmental Biology

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description (one paragraph):
Generating germline cells *in vitro* from pluripotent stem cells (PSCs) is an exciting new approach to understand the molecular regulation of human germ cell development, causes of human infertility, origins of germ cell tumors, germline mutation susceptibility, and a regenerative tool that can be used to restore fertility after cancer treatment. Recent studies using PSCs, including human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hIPSCs), have strongly suggested that the molecular events governing human germline specification are different from the mouse. However, a major question is whether these differences are due to the evolution of unique differentiation strategies in the primate embryo, or an artifact of in vitro culture and differentiation. Understanding the events that govern germline specification are critical to fertility and disease because germline specification regulates the overall number and quality of germline cells used for reproductive purposes in adults. However, addressing this question with human samples is not possible because germline specification occurs around the third week of prenatal life. Thus, the use of a nonhuman primate (NHP) model known to recapitulate human development is critical for moving the field forward. Thus, the objectives of this project include isolating embryos (n = 3) at day 15-20 post-fertilization to identify the location of the germline cells in the NHP embryo and yolk sac (Aim 1), and performing single cell RNA-Seq of NHP germline and surrounding somatic cells from 3 embryos at day 15-20 post-fertilization to develop the first ever primate transcriptome database of germ cells at this early stage of development.

Progress during the reporting period (one paragraph):
Samples have been collected for Aim 1 and are currently being processed for immunofluorescence-based assessment of germ cell localization.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Joseph Robertson, M.D., Ph.D. NIH Office of Research Infrastructure Programs

Project Title: Disruption of B cell follicles in SIV elite controllers by Rituximab to enhance clearance of persistent SIV infection in follicular helper CD4+ T cells
SPID: 0057
Unit/Division: Pathobiology & Immunology
Type of Project: Pilot
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description (one paragraph):
In this project, we utilized anti-CD20 antibody (Rituximab) to disrupt lymph node B cell follicles to determine whether destruction of this immune privilege site of HIV/SIV will facilitate the clearance of persistent virus replication by SIV-specific $CD8^+$ T cells in elite controllers (EC).

Progress during the reporting period (one paragraph):
In this year, we completed the study examining whether the disruption of B cell follicles in EC by anti-CD20 antibody (Rituximab) to enhance clearance of persistent SIV infection in the lymph nodes. Three rhesus macaques (RM) with protective MHC alleles (MamuB*08) were treated with short periods (30 days) of combination of anti-retroviral therapy, two of three RM became SIV-infected ECs. The ECs were injected with three doses of Rituximab and showed significant depletion of B cells in blood and lymph nodes. Both ECs showed reduction of plasma viral load (more than 1 log) at 14 days after the first Rituximab injection. The plasma viral reduction was temporal and associated with depletion level of B cells in blood and lymph nodes.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Joseph Robertson, M.D., Ph.D. — NIH Office of Research Infrastructure Programs

Project Title: Development of Controlled Release Mitochondrial Protonophore (CRMP) as a novel treatment for Type 2 Diabetes and Non Alcoholic Steatohepatitis in diet-induced obese nonhuman primates (DIO-NHP)
SPID: 0058
Unit/Division: Cardiometabolic Health
Type of Project: Pilot
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Yale University School of Medicine

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description (one paragraph):
The overall goal of this proposal is to develop a novel treatment for nonalcoholic steatohepatitis (NASH) or the predisposing nonalcoholic fatty liver disease (NAFLD) in a clinically relevant translational model of fatty liver disease. We will achieve this goal with the following two aims:
Aim 1) Examine the pharmacokinetics and safety of once a day CRMP treatment (1-5 mg/kg) in obese non human primates. These studies will guide us in selecting the optimal dosing for CRMP efficacy studies.
Aim 2) Examine the efficacy of chronic (8 weeks) once a day oral CRMP treatment vs. placebo to reverse hypertriglyceridemia, insulin resistance and NAFLD in a diet-induced obese non human primate model of NAFLD and the metabolic syndrome. Insulin resistance will be assessed by an oral glucose tolerance test in conjunction with plasma insulin concentrations. Hepatic steatosis and rates of hepatic mitochondrial oxidation and analplerosis will be assessed by a novel state-of-the-art stable isotope NMR-LC/MS/MS method combined with a liver biopsy.

Progress during the reporting period (one paragraph):
Our studies demonstrated that CRMP is well tolerated by NHPs and can achieve the desired level in circulation with dosing the compound twice daily. During an 8-week treatment with CRMP, we observed improvements in liver triglyceride levels (~30% reduction, p=0.042), accompanied by improving trends in fasting glucose levels and hepatic glucose production. Furthermore, no adverse effects on body temperature or blood pressure were observed. This pilot data will be used to generate a R01 application which currently is in preparation.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Joseph Robertson, M.D., Ph.D. NIH Office of Research Infrastructure Programs

Project Title: Characterization of Zika Virus Infection during Pregnancy
SPID: 0059
Unit/Division: Reproductive & Developmental Sciences / Pathology & Immunology
Type of Project: Pilot
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

ONPRC, DRDS / OHSU OB/GYN
ONPRC, PATHO & IMMUNOLOGY / VGTI

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

ONPRC, NEUROSCIENCE / OHSU, AIRC
ONPRC, DRDS / OHSU, OB GYN
ONPRC, DRDS
OHSU, ARIC
ONPRC, PATHO & IMMUNOLOGY / VGTI
OHSU, PATHOLOGY
OHSU, PATHOLOGY
ONPRC, PATHOLOGY, DCM
ONPRC, PATHOLOGY, DCM
VGTI
ONPRC, DRDS

Project Description (one paragraph):
To date, the mosquito-borne Zika virus (ZIKV) has spread to more than 28 countries in the Americas. Zika viral RNA during pregnancy has been detected in both the mother and amniotic fluid, giving ZIKV direct access to infect the fetus and cause neurodevelopmental dysfunction, including microcephaly. Indeed, Brazil has seen a dramatic increase in microcephaly since Oct 2015, which has been linked to areas where the virus is known to circulate. The mechanism of causation of these pathologies, or indeed, a direct link between maternal ZIKV to adverse neonatal neurological outcomes has yet to be demonstrated. **Our central hypothesis is that maternal ZIKV infection during pregnancy initiates the fetal inflammatory response (via systemic placental transfer) and directly contributes to the development of microcephaly and other aberrations of fetal development.** Utilizing our unique non-human primate pregnancy model, our **Specific Aims** are designed to further our understanding of the pathogenesis of ZIKV infection during pregnancy and to provide proof-of-concept data for a causal role of maternal ZIKV infection with the development of microcephaly and global fetal organ injury.

Progress during the reporting period (one paragraph):
We have completed the 5 proposed animal experiments during this reporting period. Data collected throughout the study is currently being analyzed. A publication of these results is pending.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):
Joseph Robertson, M.D., Ph.D. NIH Office of Research Infrastructure Program

Project Title: The role of social learning in positive reinforcement training of monkeys
SPID: 2016
Unit/Division: Division of Comparative Medicine
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist Associated with Project:
Excluded by Requester Oregon Health & Science University

Other Core, Affiliate Scientists with Institutional Affiliation:
None

Project Description:
This grant is designed to provide high school teachers with opportunities to work in a scientific lab. The goal of this project was to examine whether rhesus macaques living in a cage could learn common husbandry tasks (e.g., presenting a body part for examination, etc.) by watching another monkey perform the task, either live or by video.

Progress during the reporting period (a few sentences):
The teacher involved in this study left the program within the first week of being at the ONPRC, and the grant was terminated. Funds were returned to the Private Source

Publications resulting from the project.
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: Self-Injurious Behavior and Primate Well Being
SPID: 8016
Unit/Division: Division of Comparative Medicine
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
University of Massachusetts Amherst

Principal NPRC Core Scientist Associated with Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate Scientists with Institutional Affiliation:
Excluded by Requester
University of Massachusetts Amherst
Washington NPRC, University of Washington
Southwest NPRC, Texas Biomedical Research Institute
National Institutes of Health

Project Description: The presence of severely abnormal behavior, such as self-injurious behavior (SIB) in laboratory housed primates, compromises the quality of the animal research resource and adversely impacts research. In rhesus monkeys, SIB consists of intense, self-directed biting that can result in serious wounds requiring veterinary treatment. Based on findings from our laboratory and others, we have developed a model proposing that SIB arises from adverse life events, is maintained by dysregulation of several neurochemical and physiological systems, and functions to reduce anxiety. Unfortunately, SIB is resistant to treatment, alleviated neither by environmental enrichment nor changes in cage size. Pharmacological treatments have shown effectiveness in reducing SIB; however, relapse is common post-treatment, and long-term maintenance on drugs is undesirable for research purposes. The long-term goal of this project is to decrease the prevalence of SIB in captive primates by (1) preventing the onset of SIB through identification of key risk factors, and (2) developing novel treatments for this disorder that are cost-effective and produce long-lasting benefit. In furtherance of this goal, the proposed project will test the hypothesis that stress exposure and anxious behavior are precipitating factors in the development of SIB. To determine the generality of this hypothesis, factors contributing to SIB onset will be studied at 4 national primate research centers. To reduce the incidence of SIB in animals that have already developed this disorder, we will test a novel pharmacotherapeutic approach involving administration of the opioid receptor antagonist naltrexone. Short- term treatment with naltrexone has been shown to yield long-term decrements in SIB in many human patients, but this compound has not yet been tested on non-human primates. Finally, hair plucking (another type of SIB) and more generally hair loss have come under increased scrutiny from federal regulators. Consequently, we have enlarged the scope of this project to include hair loss, and we will test the hypothesis that hair loss in captive primates can result from several different factors, including hair plucking, stress and anxiety, and atopic dermatitis.

Progress during the reporting period (a few sentences):
In the past year, we found that common husbandry practices, such as movements or number of sedations, has a positive correlation with alopecia at two National Primate Research Centers. In the past year, this project has resulted in three papers published in a special edition of the “American Journal of Primatology”, and one additional publication.

Publications resulting from the project
Excluded by Requester

Excluded by Requester

Funding Sources:

Melinda Ann Novak, Ph.D. University of Massachusetts Amherst/ NIH Office of Director
NIH 7R24OD011180

Project Title: CDI-Type I: Computational Models for the Automatic Recognition of Non-Human Primate Social Behaviors
SPID: 7834
Unit/Division: Division of Comparative Medicine
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester — Oregon Health & Science University
Northeastern University

Project Description: The goal of this study is to develop unobtrusive methods for observing, recording, identifying and summarizing behavior of individual rhesus macaques living in social groups. Such methodology will provide important new tools for studying the dynamic complexity of behavior, which will be invaluable not only for biomedical studies, but also for improving animal husbandry and well-being. Specifically, the aims are to: 1) Develop and evaluate a audio-visual-telemetry sensor array for unobtrusively observing and recording behavior of individuals in a social group, and 2) Develop and evaluate computational models for identifying and inferring behavior of an individual in a social group using data from this array.

Progress during the reporting period (a few sentences):
The ultimate goal of this study is to create an algorithm to automatically code the behavior of NHPs living in a social group. To date, we have successfully collected continuous audio and video recordings of five groups of 4-6 monkeys (n=24), and our colleagues from Northeastern University have recently completed evaluation of algorithms. Results from this study were presented at several conferences, and manuscripts are being prepared for submission to the American Journal of Primatology.

Publications resulting from the project.
Nothing to Report

Funding Sources:
Alexander Kain, Ph.D. — National Science Foundation BCS-1027834

Project Title: Anesthesia Toxicity in Neonatal Primate Brain
SPID: 7836
Unit/Division: Collaborative Research Unit
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Washington University

Principal NPRC Core Scientist Associated with Project:
Excluded by Requester

Other Core. Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester — Oregon Health & Science University

Project Description: A decade ago, the applicant and colleagues discovered that drugs that have either NMDA antagonist or GABAA agonist properties, a description that fits alcohol and all general anesthetics, trigger widespread death of nerve cells in the developing animal brain. We have proposed conducting NHP studies to further clarify the potential neurotoxicity of anesthetic drugs for the developing NHP brain and explore ways of modifying anesthesia protocols to enhance their safety for the developing brain. We have already developed a valuable data base, and now want to build upon that base toward the goal of achieving improved safety in the clinical application of anesthetic drugs in pediatric and obstetric medicine.

Project progress during the reporting period:
We studied the ability of LiCl to prevent the anesthesia-induced brain damage and it was found that LiCl conferred a significant and substantial degree of protection from anesthetic neurotoxity resulting from a 5 h long exposure. This finding is extremely important and suggests a clinically relevant treatment that can ameliorate the neurotoxity of anesthesia (see publication below). It is expected that there is a window of vulnerability that closes as infants age; we found that 20 and 40-day-old NHPs continue show anesthetic neurotoxity (see publication below). It is expected that shorter exposure times will be less damaging, to test this infant NHPs were exposed to 3 h isoflurane, and it was found that they still showed significant neurotoxic damage, the damage was less pronounced than that observed after 5 h but was still significant (the publication of these results is under review). We have studied in the infant NHP a clinically established sedative/analgesic agent (Dexmedetomidine) which acts through cerebral alpha-2 adrenergic receptors, and that has been shown in rodents to be less neurotoxic and potentially protective against isoflurane toxicity; the tissues from these studies are still being evaluated. We have performed experiments to study the augmentation of anesthetic neurotoxity by caffeine, and found that in fact caffeine does make the apoptosis induced by anesthesia much worse.

Publications resulting from the project.
Excluded by Requester

Funding Sources:

Kevin	Noguchi, Ph.D.	NIH Natl Inst of Child Health & Human Development NIH 5R01HD052664

Project Title: Long-term Effects of Early Post Natal Isoflurane Anesthesia on Behavior, Learning and Memory in Non-Human Primates
SPID: 0149
Unit/Division: Collaborative Research Unit
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
Excluded by Requester:Fixed Fees

Other Core, Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester
Oregon Health & Science University

Project Description: Millions of human infants and fetuses are exposed every year to anesthetic drugs, which are clearly beneficial and have traditionally been assumed to be exceedingly safe. This assumption has been called into question by mounting evidence that exposure of immature animals to general anesthetics, at clinically relevant doses, triggers widespread neuroapoptosis in the developing brain. Several independent laboratories have confirmed the neuroapoptosis reaction and have demonstrated enduring neurocognitive deficits in rodents exposed in infancy to isoflurane, ketamine, or combinations of multiple anesthetic drugs. The original evidence for this phenomenon was developed in rodent models, but susceptibility of other species, including non-human primates (NHPs), has now been demonstrated. Researchers at FDA have reported a significant neuroapoptosis response in the postnatal day 5 (P5) rhesus monkey brain following exposure to ketamine for 24 or 9 hours, and following exposure to a combination of nitrous oxide (N_2O) + isoflurane for 8 hours. They have also reported permanent long-term neurocognitive deficits following exposure of P5 rhesus monkeys to ketamine for 24 hours. The applicant and colleagues have found that exposure of the P6 rhesus macaque to isoflurane anesthesia for a duration of 5 hours is sufficient to induce widespread apoptosis of both neurons, and glia. We have determined that the vulnerable glial cell type is in the oligodendrocyte (Oligo) lineage, which raises a new question. Because Oligos are responsible for synthesis and maintenance of the myelin sheath, which is vitally important for normal neural function, could oligoapoptosis act in concert with the neuroapoptosis to increase risk of long-term neurobehavioral disturbances?

Progress during the reporting period (a few sentences):
All animal work has been completed. The behavioral analyses have been completed and a manuscript has been accepted and e-published ahead of print (see below). These results demonstrated effects of multiple anesthetic exposures on measures of motor development and behavior. The results of the functional MRI studies are being prepared for publication. Electro-physiology recordings were collected at the time of euthanasia, there were distinct differences between the isoflurane exposed and control animals; a manuscript is being prepared on these data. The results of the cognitive studies are being analyzed. Finally the tissues for histological analysis are being processed and analyzed.

Publications resulting from the project.
Excluded by Requester

Funding Sources:
Ansgar M. Brambrink, M.D., Ph.D.
Private Source
NIH 5R01HD052664

Project Title: Factor XI inhibitors
SPID: 4044
Unit/Division: Collaborative Research Unit
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
None

Other Core, Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester
Oregon Health & Science University

Project Description:
The project is intended to support Aronora's efforts to further evaluate the therapeutic potential of using inhibitors of pathological blood coagulation and platelet activation for the prevention and treatment of diseases that involve the pathological activity of the contact phase, FXI, FXII, and extrinsic factors and platelets. The effects of contact coagulation and platelet antagonists on the rate of growth and time to occlusion will be characterized in various in vitro and ex vivo models of thrombus formation in blood under flow. The effect of FXI inhibitors on platelet adhesion, fibrin formation, calcium mobilization, cellular and enzymatic responses, and/or platelet aggregation will be determined.

Progress during the reporting period (a few sentences):
We have performed experiments that compared biomarkers and pharmacological or biological responses in to standard anticoagulants and anti-thrombotic/anti-inflammatory agents to anticoagulant antibodies, oligonucleotides, or small molecule contact activation inhibitors. The research into the efficacy of coagulation inhibitors to treat cardiovascular pathologies is continuing.

Publications resulting from the project:
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: Development of Toll-Like Receptor Agonists as Neuroprotectants in Brain Ischemia
SPID: 4953
Unit/Division: Collaborative Research Unit
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists with Institutional Affiliation:
Oregon Health & Science University

Project Description: Endogenous mechanisms of ischemic preconditioning-tolerance have revealed the brain's ability to reprogram (precondition) its response to acute ischemia from that of induced cell injury signaling cascades to induction of neuroprotective pathways (tolerance). Such endogenous neuroprotection occurs through Toll Like Receptor (TLR) signaling which reprograms an inflammatory (injurious) response to stroke into an anti- inflammatory (neuroprotective) response. We offer the preferred agonists (CpG ODNs and imiquimod - IMQ) of TLR 9 and 7 respectively as lead compounds for prophylactic neuroprotection against stroke. Although robust rodent data have been produced, past and recent translational failures require additional preclinical evaluation. Accordingly, we have developed a new primate stroke model for assessment of putative pharmacotherapeutics and propose to perform rigorous trials of our recently discovered neuroprotectants to establish essential efficacy and pharmacokinetic data.

Progress during the reporting period:
We have successfully demonstrated efficacy with CpG ODN treatment in our rhesus macaque model of stroke and have initiated formal toxicology and other FDA-recommended chemical characterization, pharmacology and toxicology studies in order to develop this agent as a therapy for humans. These studies are ongoing at our contract laboratories and will continue through February 2017.

Publications resulting from the project:
None at this time

Funding Sources:
Mary P. Stenzel-Poore, Ph.D. — NIH National Institute of Child Health & Human Development 1U01NS064953

Project Title: Control of Gonadotropin Secretion During Lactation
SPID: 4643
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
Excluded by Requester

Other Core, Affiliate Scientists with Institutional Affiliation:
Excluded by Requester
Inserm, Bordeaux, France
Oregon Health & Science University
Oregon Health & Science University
University of Washington

Project Description: It is firmly established that states of energy deficiency, such as fasting, anorexia nervosa, cachexia, bulimia, lactation and exercise-induced amenorrhea, as well as states of energy overabundance, such as obesity, are both associated with disruptions in fertility. These studies focus on states of negative energy balance that are associated with a suppression of reproductive function. The identity of the specific metabolic signals or afferent neural pathways that convey information about energy balance to gonadotropin-releasing hormone (GnRH) neurons, the central hypothalamic system regulating reproduction, remains elusive. Key to elucidating this link is an understanding of the regulation of kisspeptin neurons, the primary gatekeepers in controlling GnRH neurons. Our studies use two models of negative energy balance, lactation and caloric restriction, and have shown that kisspeptin signaling is greatly suppressed during these states. A key hypothesis of this proposal is that suppression of kisspeptin signaling is the primary factor in the inhibition of GnRH during states of negative energy balance. Although it is a widely held view that hypoleptinemia is the critical factor linking energy balance and suppressed GnRH, our recent studies demonstrate that restoring leptin to normal physiological levels does not reverse the inhibition of kisspeptin or GnRH in either lactation or caloric restriction. Thus, hypoleptinemia does not appear to be the primary metabolic factor responsible for the suppression of reproductive function.

Progress during the reporting period: In the past 12 months, we have examined the metabolic hormonal profile of animals both during negative energy balance as well as upon immediate exit from negative energy balance. During calorie restriction, reproductive function is inhibited but upon refeeding animals appear to recover reproductive function quickly. We examined hormone profiles both during calorie restriction and 24 hours later to determine which hormones may be responsible for the resumption of reproductive function. These studies identified potentially inhibitory signals that were up with calorie restriction and suppressed following refeeding as well as potentially stimulatory signals that were suppressed with calorie restriction but elevated with refeeding. We have also examined the role of the intestinal hormone glucagon-like peptide and observed that this peptide is capable of stimulating kisspeptin cells, and GLP producing neurons in the brain make contact onto both GnRH and kisspeptin cells. However, restoration of GLP signaling during negative energy balance was not sufficient to restore reproductive function.

Publications resulting from the project
Excluded by Requester

Funding Source:
Kevin L. Grove Ph.D. NIH/National Institute of Child Health & Human Development R01 HD014643

Project Title: Developmental programming of leptin signaling in arcuate neuropeptide Y neurons
SPID: 1306
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate Scientists with Institutional Affiliation:
None

Project Description:
We have gained important knowledge in the development and regulation of brain neurons that drive appetite. We have established that poor nutrition in early life directly affects the development of these neurons and probably alters the development of brain regions that are involved in how much we eat. Our research has shown that these changes in how neurons control appetite might be a way that animals increase food intake for growth. However, these developmental changes most likely decrease the animal's ability to respond to metabolic challenges such as overeating in adulthood. Furthermore, we have studied differences in the number of signals to brain pathways that encourage or discourage food intake during important periods of development. Our research showed that feeding circuits in the brain may have the brakes taken off in order to stimulate crucial food intake during development. Strikingly, we found that there are more signals in the brain of adult animals that drive us to eat, than signals that make us stop eating. These findings could provide important knowledge about body weight gain in adults, which can lead to obesity and Type 2 diabetes. As we continue to study the brain circuits that regulate feeding behavior, we expect that alterations in diet during critical periods of brain development will increase the animals' susceptibility to metabolic diseases such as diabetes. These studies will provide important insights about early nutritional reprogramming, and may help to further our understanding of childhood obesity and its long-term impact on the development of diabetes.

Progress during the reporting period:
This work was completed as of June 2017. In the final report we noted the following three major findings:
Most significant findings:
1) Offspring from mothers fed a HFD overconsumed highly palatable energy-dense food.
2) Offspring from mothers fed a HFD displayed elevated body weights at 6 months; an increase in body weight was maintained at 13 months when maternal HFD was combined with postnatal HFD.
3) Offspring from mothers fed a HFD had developed abnormalities in both homeostatic (melanocortin) and hedonic (dopamine) brain circuits involved in the control of feeding behavior.

Publications resulting from the project.
Nothing to Report

Funding Sources:
Excluded by Requester
Private Source

Project Title: Evaluation of a novel analog alone and in combination with a GLP-1 agonist, on food intake and body weight in obese rhesus macaques
SPID: 7016
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description:
Peptide YY3-36 (PYY) and glucagon-like peptide 1 (GLP-1) are anorexigenic hormones that are secreted from the gut in response to a meal. Endogenous concentrations of both hormones are low in the fasting state and rise within 30 min of a meal, and it is likely that these hormones play a role in the feelings of hunger and satiety. Further, research has demonstrated that, in obesity, PYY serum levels are reduced (11) (12, 13), and both PYY and GLP-1 secretion is blunted in response to a meal. As mentioned above, gastric bypass surgery followed by significant weight loss in humans correlates with an enhanced secretion of both PYY and GLP-1, making a strong case for the potential therapeutic effectiveness of these two peptides (14) (15). Exogenous administration of either PYY or GLP-1 has been shown to reduce food intake in several species, including rats and rhesus macaques (16) (17). While both of these targets work well in rodent models to significantly reduce body weight, they have been less successful in higher species. GLP-1 analogues are currently clinically used in the treatment of diabetes, and they have been shown to cause modest reductions in body weight. PYY analogues have been used by several group and show mild to modest reductions in food intake in humans, but little effect on body weight. Unfortunately, there have been mixed results in efficacy for both peptides.
Based on these findings, we initiated a collaboration to study the effects of a novel PYY analogue and its effectiveness of food intake and body weight reduction. These studies resulted in very interesting findings that provided a novel insight into the biology of PYY analogues. These results allowed us to further refine the design of the PYY analogue, and we would now like to test the new PYY analogue in obese rhesus macaques in a dose ramp study followed by a monotherapy phase and its potential to provide synergism with GLP-1 agonists

Progress during the reporting period:
We tested a novel compound and compared this compound to the effectiveness of Liraglutide, a known compound to reduce food intake and body weight. We demonstrated changes in body weight and related measures during this reporting period.

Publications resulting from the project.
Nothing to Report

Funding Sources (PIs and sources):
Excluded by Requester
Private Source

Project Title: Immune Therapy of Insulin Resistance in Diet Induced Obese (DIO) Rhesus Macaques with Humanized Antibody in NKB2D, a Natural Killer Cell Activating Receptor
SPID: 1061
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester — Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description:
Pre-diabetic diet induced obese (DIO) Rhesus macaques have a unique metabolic profile that is very much like what is seen in humans. With over-nutrition the animals get obese, hyperinsulinaemic, insulin resistant, pre-diabetic and also have increased inflammatory and cardio-vascular markers in the circulation. Recent studies from several groups, including our own, have shown that diet induced obesity – a precondition for the development of T2DM – is associated with a progressive decline of the adaptive immune response. Our group has shown that therapies associated with improved immune function also show improvements in insulin sensitivity. The purpose of this study is to investigate whether treatment with such an immune-modulator can reverse the suppressed immune function, insulin resistance and dyslipidemia caused by chronic high fat diet (HFD) in pre-diabetic DIO Rhesus macaques.

Progress during the reporting period:
In this period the animals were recovering from previous studies. No new interventional experiments were performed at this time. We are tracking the progression of obesity and diabetes in these animals closely.

Publications resulting from the project.
Nothing to Report

Funding Sources (PIs and sources):
Excluded by Requester — Private Source

Project Title: Interrupting the vicious cycle of obesity and metabolic syndrome
SPID: 2676
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description (one paragraph):
The major focus of this grant will be on detailed longitudinal based investigations in the offspring of obese mothers focusing on juvenile physiology (including food intake and energy expenditure), functional and morphological changes in 3 key tissues: liver, pancreas, and skeletal muscle, along with genomic events across tissues and time. In Aim 1 offspring of obese or lean mothers will be weaned to healthy chow-based control diet or continued WSD, and animals followed up to 3 years of age (just prior to puberty). To interrupt this viscous cycle, obese mothers consuming a WSD diet will be supplemented with Resveratrol (Aim 2), an antioxidant with anti-inflammatory properties, or a healthy chow based diet (Aim 3) just prior to conception. The offspring of both resveratrol and diet-switched mothers will be studied up to 14 mo. of age. Such studies will provide important mechanistic insights into how maternal diet and metabolic health impact development, adaptability and postnatal function of the liver, pancreas, and skeletal muscle--tissues that are inaccessible in humans, but with direct clinical and translational implications for the development of obesity and type 2 diabetes. Our studies continue to address the need for controlled, mechanistic studies to identify the respective contributions of maternal obesity and pre- and post-weaning diet exposures on key metabolic systems in offspring of a model directly relevant to humans.

Progress during the reporting period:
We started the first of two interventions to determine what the effect of diet reversal will be on the offspring. We also increased the size of the breeding colony to increase the numbers of offspring for these studies. Tissues of animals that were collected in previous years were distributed to several of our collaboratos. Furthermore, several of the contributors were invited speakers at national meetings and several publications resulted from these studies.

Publications resulting from the project:
Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Funding Sources:

Jacob	Friedman, Ph.D.	University of Colorado R24	R24 DK090964

Project Title: Maternal High Fat Diet and Melanocortin System in Offspring
SPID: 9194
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core. Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester
Oregon Health & Science University

Project Description: The incidence of preventable metabolic diseases in children has increased markedly over the past two decades. Currently, there is little information to determine the underlying causes or whether therapeutic or dietary interventions might be successful at preventing or reducing metabolic health risks in children from obese pregnancy. These studies will use a nonhuman primate (NHP) model to investigate the impact of poor maternal metabolic health and diet on the development of metabolic systems in the developing fetus, as well as its postpartum growth, development, and susceptibility to diet induced obesity and diabetes. For these studies, breeding NHPs will be chronically maintained on a diet high in fats and calories (HFD). The NHP is a critical model as it shares developmental features similar to human fetuses, including placental function, brain, and pancreas development. This proposal will focus on the placenta, pancreas, liver and muscle as these form the core metabolic systems that are critical for normal regulation of body weight and glucose homeostasis. The hypothesis is that abnormalities beginning with placental dysfunction (i.e., blood flow, cytokine production and nutrient delivery) directly impact the development of all metabolic systems in the offspring that contribute to life-long risk for metabolic disease. Furthermore, it is hypothesized that supplementation with agents that reduce oxidative stress and inflammation will prevent or attenuate the structural, metabolic, and molecular disturbances observed during pregnancy while on a HFD, and will prevent the abnormal development of metabolic systems in primate offspring. These studies will determine if a complete dietary switch from the HFD to a low fat diet just prior to pregnancy can reduce or prevent complications in fetal development. It will also be determined if dietary supplements with either fish oil or resveratrol, to prevent inflammation, oxidative stress, will provide similar protection. These studies will identify the risks and complications in the developing fetus associated with poor maternal metabolic health and diet. Furthermore, these studies will test dietary supplements/interventions that can be quickly translated to the clinic that may help prevent or reduce metabolic diseases in children. RELEVANCE (See instructions): Poor maternal health and nutrition are associated with an increased risk of metabolic diseases in children. However, the underlying complications and mechanisms that lead to the increase in obesity and diabetes in children is poorly understood. The NHP is a critical model to identify these mechanisms because of the similarities in development, as well as structure and function of metabolic systems.

Progress during the reporting period:
In the last year, we presented results from our work at the national Obesity meeting in two posters. In addition we completed our metabolic challenge experiments and demonstrated that exposure to a HFD in the prenatal period does result in changes to metabolic rate. We are currently writing this work up in a manuscript, and we have submitted an additional manuscript. Currently we are investigating the effect of maternal obesity on the dopaminergic and orexin populations in the VTA area to determine the impact on the hedonic food drive.

Publications resulting from the project.
Two collaborative efforts were published in the last year using animals that were funded with this grant:

Excluded by Requester

Excluded by Requester

Funding Sources:

Paul Kievit, Ph.D NIH National Institute of Diabetes & Digestive & Kidney Diseases R01 DK079194

Project Title: Mouse models for Novo Nordisk collaboration
SPID: 5088
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description:
There is a significant disconnect between translating rodent results into translationally relevant findings in higher species. This collaboration uses tissue collection and electrophysiology to study the effects of novel therapeutics in both rodent and nonhuman primate cell based analyses.

Progress during the reporting period: This project is completed as off Dec 2016. We have been able to test several compounds using our mouse models, as well as perform some tissue culture. Some work is still ongoing to finalize the work. Some results of this collaboration will be presented at a national meeting in January 2016.

Publications resulting from the project.
Nothing to Report

Funding Sources (PIs and sources):
Excluded by Requester
Private Source

Project Title: Strategic Partnership for the Development of Novel Therapeutics for Diabetes and Obesity
SPID: 4059
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Other Core. Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Monash University, AUSTRALIA

Project Description:
While many new obesity and diabetes drugs are currently in development, there remains significant unmet medical need and opportunities for new medicines treating metabolic disease. We believe that the unique and highly translational models and strategies outlined in this proposal, combined with the expertise and capabilities of each of the partners, will make this an exceptionally powerful and productive target discovery program for diabetes and obesity.

Progress during the reporting period:
This project is currently undergoing. We are actively screening new compounds using in vivo and in vitro techniques.

Publications resulting from the project.
Nothing to Report

Funding Sources:

Excluded by Requester

Private Source

Project Title: Role of Fatty Acid Oxidation Defects in Insulin Sensitivity
SPID: 2813
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph):
Mitochondrial dysfunction has been implicated in the etiology and expression of insulin resistance and type 2 diabetes in animal models and humans under conditions of high fat loads either from the diet, endogenous release by adipose tissue, or both. However, controversy exists as to whether insulin resistance under these conditions results from intrinsic defects in mitochondrial energy utilization or abnormalities in free fatty aid (FFA) flux and amino acid metabolism, including the potential role of accumulated metabolic intermediates to impair insulin signaling. To address these controversies, study subjects will be recruited from a unique population of patients with inherited defects in one of three mitochondrial enzymes in the fatty acid oxidation pathway (FAO), including oxidation of long-chain fatty acids (very long-chain acylCoA dehydrogenase (VLCAD), or trifunctional protein (TFP), including long-chain 3-hydroxy acylCoA dehydrogenase (LCHAD) deficiencies), and, finally, medium-chain fatty acids (medium-chain acyl CoA dehydrogenase, or MCAD). These patients and age, sex, and BMI-matched healthy controls will undergo testing on separate visit study dates during which they receive co-infusions of either intralipid, shown to induce ectopic lipid accumulation and insulin resistance in previous studies, or a control infusion of glycerol and saline. These detailed studies in patients with FAO disorders compared to controls will give us a unique opportunity to better understand the interface between fatty acid metabolism and regulation of insulin sensitivity in humans. Not only will these studies address current controversies and gaps in our understanding in this field, but by including measurements of both cellular and systemic metabolomics, they may also help inform on-going development of potential pharmaceutical targets for the treatment of insulin resistance and type 2 diabetes.

Progress during the reporting period (one paragraph):
Major activities: Over the past year we have enrolled 6 subjects and 2 controls. Recruitment has been slower than anticipated. Specific objectives: To expand recruitment, we have modified our inclusion criteria to include subjects with carnitine palmitoyltransferase 2 (CPT2) deficiency, and posted fliers for controls around campus. We have 2 new subjects and 2 controls scheduled for the beginning of 2017. Recruitment has already increased with these recent efforts. We have also identified and addressed an issue with the bedside measure of glucose during the hyperinsulinemic-euglycemic clamp procedure by including bedside point-of-care testing with an iSTAT machine that is more accurate with turbid samples, such as blood samples obtained during an interlipid infusion. The analysis of the muscle and fat biopsy samples has been expanded to include some fiber type staining and we have established protocols for fatty acid and glucose transport in biopsy samples using fluorescent tracers.

Publications resulting from the project.
Nothing to report

Funding Sources (PIs and sources):
Jonathan Purnell, M.D. NIH National Institute of Diabetes & Digestive & Kidney Diseases R01 DK102813

Project Title: Gestational Malnutrition: A Preventable Cause of Cognitive Impairment in Children
SPID: 0865
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC core scientists associated with the project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
University of Washington

Project Description:
Gestational malnutrition, particularly protein deficiency, is a major contributor to morbidity and mortality in the developing world. In addition to acute effects of dysfunctional fetal development, nutritional deficiency can result in epigenetic changes that increase the risk for subsequent chronic diseases such as diabetes and heart disease as well as affecting brain development and cognitive ability. In order to determine the optimal nutritional supplementation that can alleviate these consequences, a suitable preclinical model is necessary. The purpose of this project is to develop a new highly relevant and translational nonhuman primate (NHP) model in which to systematically dissect the complex physiological and behavioral outcomes in offspring associated with maternal malnutrition. We believe that specifically improving gestational health and nutrition will result in significant reductions in costly health complications in infants, allowing them to grow into productive individuals that will be better able to benefit their entire community. The long-term objective of these studies is to test specific intervention strategies that effectively prevent the developmental abnormalities caused by maternal malnutrition and that are logistically viable.

Progress during the reporting period:
In the current funding period (year 2 of the project), we determined that a 33% protein restriction resulted in effects on pregnancy success and placental function were less than those observed in year 1 with a 50% protein restriction, but still significant. These findings suggest that a progressive reduction in dietary protein results in a step-wise decrease in term pregnancies associated with increased placental dysfunction.

Publications resulting from the project.
None to report at this time

Funding Sources:

Excluded by Requester

Private Source

Project Title: Targeting hypothalamic kisspeptin neurons in the brain to regulate reproductive neuroendocrine function and energy metabolism
SPID: 1024
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester	Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University

Project Description:
Infertility is associated with many metabolic disorders ranging from obesity to anorexia nervosa. Disruption of energy balance, either through over-consuming or excessive dieting, leads to a loss of menstrual cyclicity as a result of dysregulation of the hypothalamic-pituitary-gonadal axis. However, the specific pathways and nutrient systems that integrate energy homeostasis with reproductive function are poorly understood. Kisspeptin (Kiss1) expressing neurons in the arcuate nucleus of the hypothalamus (ARC) are positive regulators of gonadotropin-releasing hormone (GnRH) and downstream lutenizing hormone (LH) release and Kiss1 signaling through its receptor (Kiss1r) is essential for fertility in females. Interestingly, recent reports demonstrate that Kiss1r signaling is also essential for the maintenance of energy homeostasis as mice that lack the Kiss1r have increased body weight and adiposity. Together, these data suggest that the Kiss1 system may be a novel system that integrates energy homeostasis with reproductive function. We propose that ARC Kiss1 neurons act as an energy sensor and modulate reproductive neuroendocrine function and energy metabolism based on feedback from metabolic cues. During both negative and positive energy balance ARC Kiss1 expression is decreased, contributing to reproductive dysfunction. This decrease in ARC Kiss1 expression may be beneficial during negative energy balance as the resultant drive to eat in combination with the lowered energy metabolism will promote calorie consumption and energy storage, which is essential for survival. However, this decrease in ARC Kiss1 during positive energy balance can be detrimental because the resultant drive to eat along with the lowered energy metabolism may be exacerbating the obese phenotype. The goal of this project is to dissect out the roles of ARC Kiss1 neurons on GnRH/LH secretion and energy metabolism during calorie restriction (negative energy balance) and diet-induced obesity (positive energy balance).

Progress during the reporting period:
Final data on this project including verifying specific infection of the DREADD AAV using a fluorescent marker in kisspeptin-GFP animals. The grant was completed in March of 2016.

Publications resulting from the project.
Nothing to Report

Funding Sources:

Excluded by Requester	Private Source

Project Title: Attenuation of androgen deprivation therapy-induced metabolic syndrome by diet
SPID: 7543
Unit/Division: Cardiometabolic Health
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the Project.

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: The most common treatment for patients with early-stage prostate cancer is androgen-deprivation therapy (ADT). ADT has multiple adverse effects, including decreased quality of life, decreased lean mass and muscle strength, osteoporosis, and metabolic syndrome (MS). The later includes the early onset of sarcopenic obesity and insulin resistance, while longer duration of ADT is associated with diabetes, and dyslipidemia. Cardiovascular disease has been recognized as the competing risk and the second cause of mortality in men with prostate cancer. Moderate physical exercise can reverse muscle loss, and improve general health of patients undergoing ADT. Studies in prostate cancer patients also demonstrated that intensive lifestyle changes, including a low-fat diet (LFD), can slow the progression of prostate cancer, but the benefits of a diet restriction for reducing MS and obesity in ADT patients are unknown. Thus, the goal of the present proposal is to further our understanding of the ADT-related MS and establish the effects of dietary fats on the progression and reversal of MS in non-human primates (NHP; rhesus macaques). Similar to humans, caloric excess in rhesus monkeys brought about by a high fat diet (HFD) leads to obesity and insulin resistance, while caloric restriction results in improved insulin sensitivity, and decreased body fat.

Progress during the reporting period:
This study is complete, showing the significant diet-specific effects of androgen deprivation on muscle loss, reduced bobe density and persisting insulin resistance. Skeletal muscle biopsies were collected and subjected to gene expression analysis, using RNAseq. Adipose tissue function was examined using the ex vivo analysis of adipose explants. Activity patterns and physical activity were analyzed. The main finding of the present study is that the western-style diet and reduced physical activity exacerbate metabolic side effects of androgen deprivation therapy. The PI published three relevant research and review articles on the subject of this study. Two additional manuscript are being prepared for publication.

Publications resulting from the project

Excluded by Requester

Excluded by Requester

Funding Sources:

Oleg	Varlamov, M.D., Ph.D.	NIH National Institute on Aging	R21 AG047543

Project Title: The Landscape Of Somatic Mosaicism In Non-Human Primate Brain
SPID: 1047
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Here we propose to combine high-throughput single cell genomics, bioinformatics and the use of the non-human primate (NHP) model to start characterizing aneuploidy in the brain (neurons and glia). We will first measure the frequency of aneuploidy in brain tissues (i.e. frontal cortex) during early development (pre-natal 85 days) and in juvenile (0-2 years) monkeys to estimate occurrence and frequency of aneuploidy (Aim I). In order to determine how frequency of aneuploidy changes with age, we will analyze brains from older and elderly individuals (Aim II). Finally, we will perform expression analysis to investigate functional impact of the gain/loss of chromosomes (Aim III). The use of the NHP model (rhesus macaque) will allow us to control confounding factors that can be found in the human population, while still looking at a model genetically and anatomically similar to human. Our preliminary data show feasibility in generating high-quality sequence data from single cells together with being able to identify known aneuploidy through our established bioinformatics pipeline. Moreover, we are able to isolate nuclei stained for the presence of a neuronal marker (NeuN) from rhesus frozen brain tissues samples.

Progress during the reporting period: We have isolated and sequenced 96 single neurons from a young rhesus macaque individual to look at presence/absence of aneuploidy. Moreover, we started a collaboration with Excluded by Requester at OHSU to use a higher-throughput technology developed in his lab (SCI-seq). We obtained some preliminary data on the same individual and we are in the process of analyzing them. The data from this preliminary work was used to submit a NIH R21 proposal in June 2016 also in collaboration with Dr. Excluded by Requester and the ONPRC aging program. This proposal was scored but not funded. We are currently planning for resubmission.

Publications resulting from the project:

Excluded by Requester

Funding Sources (PIs and sources):

Excluded by Requester — Private Source

Project Title: Gaining Insight Into Brain Circuitry Using Designer Receptors Exclusively Activated by Designer Drugs in Rhesus Macaque Monkeys
SPID: 1422
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: To understand the functional role of brain micro- and macro-circuitry, it is critical to clarify the relationship between the activity of specific neuronal subtypes and behavior. The ability to manipulate brain regions/neuronal subtypes allows for assessing their contribution to behaviors and pathologies. A key step toward this goal is to use non-human primate models, both as a tool for analyzing neural function in more sophisticated models of behavior and as a potential use in clinical applications. Here we perform preliminary experiments to test the feasibility of the newest form of pharmacogenetic technology (designer receptors that are exclusively activated by designer drugs (DREADDs)) in monkeys. DREADDs are naturally mutated muscarinic receptors that have lost their sensitivity to their native ligand, acetylcholine, while gaining a greater affinity to clozapine and its metabolite clozapine-n-oxide. DREADDs allows for the reversible manipulation of brain circuitry since they are only activated in the presence of CNO/clozapine, which bypasses the pitfall of lesions. CNO and clozapine readily crosses the blood brain barrier and shown to accumulate in the brain. We focus our initial studies on the manipulation of brain circuitry within the putamen, an area implicated to play a role in habit formation and is suggested to be altered in Huntington's disease, Parkinson's disease, Tourette syndrome, obsessive-compulsive disorder, and that we have previously demonstrated to be altered in addiction and fetal alcohol syndrome.

Progress during the reporting period: We have optimized our immunohistochemistry technique to be able to use fluorescent immunohistochemistry to determine which cell types were infected by our viral constructs (AAV1-hSyn-Gq-DREADD-mCherry; AAV1-CaMKIIα-Gq-DREADD-mCherry; AAV1-hSyn-Gi-DREADD-mCherry; AAV1-CaMKIIα-Gi-DREADD-mCherry). Using mCherry as the marker for cells that were transduced we have co-labeled these neurons with a marker for a neuronal marker (NeuN) as well as a marker specific for striatal projection neurons (DARPP-32). We are currently quantifying these results. We have also conducted experiments to use fMRI techniques to visualize *in vivo* the activation of DREADDs by an intravenous administration of its ligand clozapine-n-oxide. We are currently exploring a new imaging technique of using feromoxytol to increase the signal to noise ratio in these imaging studies. We have also been in contact with Excluded by Requester that will serve as a collaborator to provide us with new ligands to use to activate DREADDs.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester Medical Research Foundation of Oregon

Project Title: Gestational Ethanol Effects on Dorsal Striatal Function and Associated Behaviors
SPID: 1760
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: The objective of the proposed research plan is to investigate the effects of gestational ethanol (EtOH) exposure on dorsal striatal circuitry that contribute to some of the behavioral abnormalities, such as impaired decision making, increased impulsivity, and motor deficits that observed in Fetal Alcohol Spectrum Disorder (FASD). Using a mouse model, we will expose individuals via a vapor chamber to ethanol throughout the embryonic and early postnatal period in order to mimic the three trimesters of human development (gestational EtOH) and examine the disposition of dorsal striatal circuitry and associated behaviors during adulthood. The completion of this project will lay the groundwork for assessing how disruptions of the GABAergic microcircuitry of the striatum underlie many of the behavioral abnormalities seen in FASD and suggest approaches to compensate for these effects.

Progress during the reporting period: Endocannabinoids have been shown to be released from medium spiny projection neurons upon depolarization of their membrane and to interact with its receptors located on parvalbumin interneurons. Our data has shown that gestational ethanol exposure increases the level of endocannabinoids while decreasing GABAergic transmission in adult mice. We have furthered our studies by expressing channelrhodopsin within parvalbumin-expressing interneurons of the striatum of control and gestational ethanol exposed adult mice. With this technique we were able to show that the increase in endocannabinoids were localized at the parvalbumin-MSN synapse.

Publications resulting from the project:
None

Funding Sources:

Verginia	Cuzon Carlson, Ph.D.	NIH/National Institute on Alcohol Abuse & Alcoholism R00 AA021760

Project Title: Genetic and Epigenetic Analysis of Alcohol Self-Administration in Monkeys
SPID: 0928
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: Investigates the implication of genetic variation and epigenetic modification on HPA axis regulation and excessive alcohol consumption in primates. Drawing upon the rhesus macaque ethanol self-administration model, which enables a longitudinal study design examining genomic DNA methylation before/after 12 months of ethanol consumption, accurate measure of ethanol intake and endocrine levels, and access to blood and brain tissue samples for the comparison of epigenetic changes. Using whole-genome approaches to measure CpG methylation levels in the tissues before/after chronic ethanol consumption. Sequencing neurotransmitter genes from the HPA axis and monoamine signaling pathways in a large cohort of animals. Tests the association between common variants and endocrine dysfunction, and evaluates potential additive effects/interactions between "risk" alleles in multiple signaling pathways. Explores the association between specific alleles or haplotypes and changes in methylation following chronic alcohol consumption.

Progress during the reporting period: We completed and published the genome-wide analysis on the effect of chronic alcohol use on CpG methylation levels within the Nucleus accumbens in rhesus macaques. Validation studies using an expanded sample set, and gene expression analysis confirm the robust nature of the discovered DNA methylation signals. Moreover, we identified alcohol dose-dependent DNA methylation regions in genes of high relevance to alcohol use, including in synaptic genes that modulate synaptic plasticity through endocannabinoid, glutamate and GABA singling. We also expanded the genome-wide analysis of the blood methylome, before and after 12 months of chronic alcohol use, identifying differential methylation regions (DMRs) that are either predictive of alcohol use, or induced by alcohol use. These signatures may represent powerful biomarkers to evaluate risk or alcohol consumption, and consequently, we are exploring their translational value in human blood samples.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Excluded by Requester

Funding Sources:

Betsy Ferguson, Ph.D. NIH/National Institute on Alcohol Abuse & Alcoholism U01 AA020928

Project Title: Genomic Sequencing to Establish a Macaque Genotype and Phenotype Research Resource
SPID: 1324
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
University of Washington

Project Description: This R24 will develop a novel and efficient approach for the large-scale genomic characterization of this heavily studied colony. We will obtain 30X whole genome sequence data on at least 200 selected individuals to generate a dense genomic map of the colony. We will then utilize genotype-by-sequencing (GBS), an approach commonly used in genomic studies of plants but still rarely used in biomedical research, in concert with genome-wide imputation to obtain complete genomic data in an additional 1,000 subjects. By leveraging the dense pedigree structure for the accurate imputation of genome-wide genotypes, we will establish a very low- cost method for the continued characterization of future generations, ensuring a lasting resource for biomedical research. To facilitate widespread use of the data we generate, we will develop a database that enables public access in near real-time to the genotype data produced. The database will also include clinical data on the same animals, making it the first publically accessible resource to provide both NHP genotype and phenotype data. The clinical/phenotypic data can be analyzed for disease associations, for the identification of animals of interest, or to download with genomic data for comparative analyses. Finally, because the characterized subjects include living animals, researchers can also identify potential study subjects based upon the presence or absence of particular genomic variants, clinical data or both. As a result of this work, we will establish the first genomically characterized, pedigreed rhesus macaque research colony, develop a sustainable approach for the continued characterization of future generations, and establish the tools, resources and methods to support genome imputation in other rhesus macaque breeding colonies.

Progress during the reporting period: We launched the start of the R24 sequencing project in July of this year. An expanded pedigree configuration, encompassing 2,000 rhesus macaque has been established for this project, with the goal of completing at least 500 individuals each year, including 96 WGS and 404 GBS. We have established a large-scale sequencing contract to support efficient and affordable WGS. We have also scaled up GBS library construction to enable high throughput approaches for the production and sequencing of libraries. A robust SNV calling pipeline has been established to allow automated variant calling for both GBS and WGS. A database structure has been developed to enable both archive of and access to the generated SNV data, searchable by animal or by locus.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Betsy Ferguson, Ph.D. NIH/Office of the Director R24 OD021324

Project Title: Washington National Primate Research Center - Collaborative Genetics Resource Unit
SPID: 0182
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
University of Washington

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Oregon Health & Science University
University of Washington

Project Description: The OR/WA Collaborative Genetics Research Program is a joint effort by the Washington and Oregon National Primate Research Centers. The purpose of this program is to develop and support genetic research investigations at both Centers and to promote collaborative projects between the two centers. The program encompasses 1) improving genotyping methods for use in genetic studies, 2) initiating phenotypic studies to identify potential animal models and to develop new genetic research projects, 3) providing technical training and expertise for investigator initiated genetic research.

Progress during the reporting period: We used RNAseq methods to establish the MHC expressed allele composition of 150 WaNPRC pigtail macaques. In addition, we reviewed all of the MHC expression data we generated on the accumulated 450 pigtail macaques analyzed over the last 3 years, which enable more refined discernment of haplotypes across the population. Both new and all revised haplotype data were reported to the WaNPRC for upload into the ARMS database. We also supported the drafting and review of the genetics section of the WaNPRC P51 base grant, which was successfully funded this year.

Publications resulting from the project:
None

Funding Sources:
David Anderson, Ph.D. NIH/Office of the Director P51 OD010425

Project Title: GDNF Gene Therapy To Block Relapse Of Heavy Alcohol Use In Monkeys
SPID: 4757
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester — Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester — Oregon Health & Science University
University of California San Francisco
University of California San Francisco

Project Description: The purpose of this project is to establish a new paradigm for the treatment of alcoholism and alcohol use disorders; one that site- specifically targets a neuro-regenerative process, reverses dependence-associated deficits in reward pathway function, circumvents the reliance on protracted patient compliance, and exhibits a permanent effect once introduced. We believe that gene therapy that culminates in the overexpression of glial-derived neurotrophic factor (GDNF) within the ventral tegmental area (VTA), a key component of the reward neurocircuitry, is such a treatment paradigm. Preliminary work conducted in rodents indicated that elevated expression of intra-VTA GDNF blocks the escalation of alcohol drinking in naive animals and significantly attenuates excessive drinking in alcohol-experienced animals whereas suppression of endogenous GDNF in the VTA enhances the progression to heavy alcohol use. A crucial next step in advancing the translation application of this treatment paradigm to human alcoholics is to first demonstrate that a similar intervention in non-human primates (NHPs) will yield a comparable benefit in reducing relapse risk. Aim 1 of this project will establish heavy alcohol self- administration in a cohort of male cynomolgus monkeys during a 6-month open access period. These methods have been validated and replicated for over a decade, with monkeys developing binge-like drinking patterns of alcohol use that resemble those observed in human alcoholics. Aim 2 will evaluate the efficacy of GDNF gene therapy in preventing relapse and the continuation of heavy drinking. An adeno-associated virus serotype 2 (AAV2)-GDNF or control vector will be bilaterally infused into the VTA of each monkey following a 1-month period of abstinence, and alcohol will be re-introduced under open access conditions and self- administration patterns will be monitored during multiple withdrawal-relapse cycles. We hypothesize that AAV2-GDNF treatment will prevent relapse-like drinking patterns and reduce the number of heavy drinking days by attenuating the incidence of binges (large bout sizes) that produce intoxicating blood alcohol concentrations. In summary, we believe this will be a transformative approach for the treatment of alcoholism that may also be applicable for the treatment of other life-threatening addictions. If successful, then our in-life data will be included in a briefing package to the U.S. Food & Drug Administration in order to advance this candidate therapeutic through an Investigation New Drug (IND) submission for future clinical testing.

Progress during the reporting period: The first monkey cohort has been successfully trained to use operant panels for food and fluid access, and is mid-way through completion of an induction procedure to establish chronic alcohol self-administration. Two animals were infused with control vector and sufficient transduction was determined in our bilateral VTA target sites, thereby demonstrating the ability of our UCSF neurosurgical team to conduct these cutting-edge procedures at the ONPRC.

Publications resulting from the project:
None

Funding Sources:
Matthew Ford, Ph.D. — NIH/National Institute on Alcohol Abuse and Alcoholism
R01 AA024757

Project Title: Nezavist, a Novel Molecule for Treatment of Alcohol Use Disorder
SPID: 1074
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Lohocla Research Corporation

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University

Project Description: Alcohol Use Disorder affects 7.9% of the U.S. population ages 18 and older and costs society over $223 billion per year in direct medical costs, accidents and lost productivity. Current pharmacotherapy is only modestly effective and has to be used in conjunction with psychosocial treatment. Primary care physicians are ill equipped to provide the currently necessary range of therapy for treating AUD and the modest effects of therapy generate a significant number of treatment failures. We have generated a novel molecule with action directly at one of the major neurotransmitter receptors altered by chronic excessive consumption of alcohol. We have also demonstrated in two different models of relapse drinking by alcohol dependent animals that our medication can reduce or prevent such relapse. Our preliminary studies on the safety and metabolism of our compound in animals provide confidence that the compound will have a good therapeutic index in human clinical trials. Prior to embarking on the trials in humans we, however, need for our drug to be approved for an IND by the Food and Drug Administration. To be able to accomplish this milestone we are proposing a series of SBIR Phase I, IND enabling studies, which include the development of an oral formulation which will be attractive for use with humans; the use of this formulation to repeat the relapse blocking effects of our compound in rats, and to extend our studies on reducing alcohol consumption with our compound to non- human primates. In these SBIR Phase I studies we will also establish the blood and brain levels of our drug after oral administration in the newly developed formulation. In the SBIR Phase II studies we will produce our drug under cGMP conditions and scale up production to meet future clinical trials. The Phase II SBIR studies will be fully focused on completing all of the FDA required studies for the IND, including complete studies of in vitro metabolism and metabolite identification, in vivo studies of Absorption, Distribution, Metabolism, and Excretion, complete studies on safety and toxicology (including toxicokinetics) in two species (rats and monkeys). These studies will include escalating acute dose studies and sub-chronic and chronic studies of up to six months duration because we anticipate that human studies may include long term maintenance of patients on our medication. If an IND designation is obtained we anticipate launching a Phase I human safety trial with an arm of this study aimed at a clinical measure of craving in alcohol-dependent subjects. If this grant is funded and our medication reaches human trials we anticipate introducing a more efficacious and much more highly utilized medication to treat AUD.

Progress during the reporting period: Rhesus monkeys are currently being trained to use operant panels for food and fluid access. Induction of alcohol self-administration is slated to begin in January 2017.

Publications resulting from the project:
None

Funding Sources:
Boris Tabakoff, Ph.D. NIH/National Institute on Alcohol Abuse and Alcoholism U44 AA024905

Project Title: Monkey Alcohol Tissue Research Resource (MATRR)
SPID: 9431
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
Baylor University
Wake Forest University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: The MATRR is a multiple PI research resource award established to provide the alcohol research community access to tissue and data generated from cohorts of monkeys that have been subjected to the same voluntary alcohol self-administration protocol. These monkeys show a wide distribution of average daily ethanol intakes (g/kg) encompassing low, binge, heavy and very heavy chronic intake patterns. Importantly, the MATRR provides an opportunity for laboratories with specific expertise in neuroscience, organ pathology, and genetic analyses the ability to extend their research to a primate model with similar genetics, developmental processes, endocrinology, immunology, physiology and neuroanatomy to humans. The MATRR is unique to the alcohol research field in promoting a translational resource for mechanistic studies of alcohol-induced pathologies.

Progress during the reporting period: This grant in in its 7th year of funding. We continue to provide support for scientists to obtain data and tissue. We have expanded greatly the data that are made available to the alcohol research community and continue to attract new users of this tissue bank.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Funding Sources:

Kathleen	Grant, Ph.D.	NIH/National Institute on Alcohol Abuse and
Erich	Baker, Ph.D.	Alcoholism R24 AA019431
James	Daunais, Ph.D.	

Project Title: INIA: Stress and Ethanol Self-Administration in Monkeys
SPID: 3510
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: The self-administration of ethanol assessed under "open-access" conditions allows the characterization of how chronic ethanol intoxication pushes the organism beyond the normal limits of homeostasis and into chronic, variable, stress responses and disease states. A critical barrier to understanding the relationship between stress and excessive ethanol drinking is the availability of data sets on the neurogenetic, neurochemical, neurophysiological, neuroendocrine, and behavioral adaptations to chronic ethanol. The macaque monkey that self-administers high doses of ethanol for >20 months can provide these data sets. In this project we provide a nonhuman primate model to address fundamental aspects of what is known in humans with respect to stress, anxiety and excessive alcohol drinking.

Progress during the reporting period: The grant was competitively renewed this past year and will enter its 16th year in February. Rhesus male monkeys are enrolled in the ethanol self-administration protocol and have just entered their second month of a 24 month phase of having 22 hr/day access to ethanol, water and meals. New aspects of the study include the use of touch screens for testing the effect of chronic ethanol drinking on cognitive flexibility. Data acquisition and analysis are progressing on schedule.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Funding Sources:

Kathleen Grant, Ph.D. — NIH/National Institute on Alcohol Abuse and Alcoholism
U01 AA013510

Project Title: Liver Cancer Risk with rAAV Gene Therapy
SPID: 0144
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester — Oregon Health & Science University

Project Description: Gene therapy based on recombinant adeno-associated virus (rAAV) vectors is showing great clinical promise. Previously, we showed that an intravenous rAAV injection could cause hepatocellular carcinoma (HCC) in newborn mice due to vector integration into and activation of a specific locus on chromosome 12 which we call the AAV-HCC locus in this proposal. Even a single integration event was sufficient to cause HCC in mice. Given that this locus is highly conserved and overexpressed in a subclass of human HCC, these mouse studies raise significant concerns about a possible risk of HCC induction in human gene therapy trials. In order to advance the promising field of liver-directed rAAV therapy, it is important to establish whether rAAV is likely to cause HCC in humans. In this proposal we systematically explore the risk of HCC caused by vector integration at the AAV-HCC locus, using three different animal models to establish the effects of clinically relevant risk factors, as well as vector design on HC induction. In addition, we will assess the risk conferred by random integration of rAAV gene therapy vectors in the liver. Our results will have a significant impact on the clinical practice of liver-directed gene therapy, not only for rAAV vectors, but also for any integrating vector, and may lead to new experimental models of human HCC.

Progress during the reporting period: The construction of the vectors has been completed and large scale preparations are being finished. No in vivo experiments have yet started. We expect to inject animals with the AAV vectors in early 2017.

Publications resulting from the project:
None

Funding Sources (PIs and sources):
Markus Grompe, Ph.D. NIH/National Cancer Institute R01 AA0190144

Project Title: Antithrombotic Factor XII (fXII or F12) Targeting
SPID: 6112
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester Oregon Health & Science University

Project Description: The purpose of the experiments is to test the hypothesis, in definitive primate studies, that Private Source fXII siRNA treatment has antithrombotic potential as compared to a low molecular weight heparin (enoxaparin) but without a detrimental effect on primary hemostasis. Transient acute experimental vascular graft thrombosis will be induced in baboons that will be pretreated with Private Source fXII siRNA product candidate in order to induce temporal acquired fXII deficiency. The results will be used to determine if acute thrombogenesis rates are altered in any direction, and the results will be used by Private Source to determine whether the siRNA treatment approach justifies further preclinical and clinical development of the product candidate in thrombosis indications, including selection of clinical targets (use indications) for the product.

Progress during the reporting period: We have performed the acute experimental vascular graft thrombosis in a single animal. The testing is ongoing.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester Private Source

Project Title: Pathophysiologic roles of the contact phase
SPID: 5110
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Acute thrombotic diseases such as heart attack, ischemic stroke, deep vein thrombosis (DVT), and venous thromboembolism (VTE) remain leading causes of morbidity and mortality in the U.S. While conventional anticoagulants are effective at both preventing and treating thrombosis, they also produce bleeding side effects that limit their use or require sub-optimal therapeutic dosing when bleeding risks are high. Consequently, a critical unmet medical need remains for a hemostatically safe antithrombotic drug. Private Source Private Source is developing an anticoagulant drug candidate that specifically target contact phase-dependent and feedback thrombin generation, interrupting pathological thrombus formation while preserving essential hemostatic mechanisms. Private Source proprietary product candidates, neutralizing anti-factor XII (FXII) monoclonal antibodies, have the potential to addresses this unmet need.

Progress during the reporting period: A single anti-factor XII (FXII) monoclonal antibody was tested in the prevention and interruption of thrombus formation. The studies indicate that the FXII antibody is sufficient to prevent and interrupt thrombus formation.

Publications resulting from the project:
None

Funding Sources (PIs and sources):
Excluded by Requester Private Source

Project Title: Hemocompatibility testing of stent coatings
SPID: 1652
Unit/Division: Collaborative Research Unit
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist Associated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Bare metal and drug-eluting coronary stents suffer an inherent lack of vascular cell and blood compatibility resulting in adverse patient responses. Researchers at the Private Source have developed a coating for metallic coronary stents that is durable withstands crimping and expansion, has low thrombogenicity and can covalently bind proteins, linker-free. The goals of this project are to test the acute thrombogenicity of the PAC coated stents.

Progress during the reporting period: The hemocompatibility testing was completed in March of 2015. The PAC stent performed significantly better with reduced platelet deposition compared to all of the tested stents. While the PAC-TE_B stents had slightly lower platelet adhesion compared to BMS and PAC-TE_A stents. This was due to the lower platelet deposition on stent #PACTE3 and #PACTE4 from the seconded tested coating. The control bare metal stent had significant platelet deposition, which leads to occlusion in 3 of the 8 devices tested. All of these occluded devices were downstream of the test devices and therefore were unlikely to alter the test device in the proximal position. Either shorter studies or a less thrombogenic base stent may improve these outcomes and enable the full 60-minute studies for all of the devices.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester Private Source /University of Iowa

Project Title: Stent Thrombosis
SPID: 6047
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Bare metal intracranial stents suffer an inherent lack of blood compatibility resulting in adverse patient responses. Private Source has developed metallic intracranial stents that have low thrombogenicity. In vitro tests indicate a 90% reduction in thrombus formation. To complement in vitro findings and in preparation of longer term implants, we propose to perform additional hemocompatibility testing of the intracranial stents, as well as industry devices and compared to the clinical standard of bare metal control stents under single and dual platelet therapy.

Progress during the reporting period: We have completed the studies in which Private Source Shield (PED and PED+Shield) stents were compared to bare metal stents and FRED stents. The data indicated a significantly lower platelet deposition on PED compared with FRED, and significant decreases in platelet deposition when ASA, clopidogrel, or Shield Technology was used. Direct comparisons of the devices within each antiplatelet condition showed consistent significant decreases in platelet accumulation on PED+Shield relative to FRED. PED+Shield reduced platelet deposition compared with unmodified PED without antiplatelet therapy and with DAPT.

Publications resulting from the project:
Excluded by Requester

Funding Sources (PIs and sources):
Excluded by Requester
Private Source

Project Title: Surface Modification Compliant Vascular Grafts
SPID: 0274
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
Mechanobiology Institute Singapore

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University

Project Description: By modulating the mechanical properties (compliance) and surface topography and examining the graft thrombosis, endothelialization, and implant intimal hyperplasia, we will define the necessary guidelines for vascular graft biomaterials. These guidelines may be applicable to numerous blood-contacting devices, which require non-thrombogenic surfaces capable of supporting rapid endothelial cell migration in vivo. To achieve this goal, the proposed studies will employ topographical modifications to the luminal surface of PVA biomaterials with variable compliance properties. PVA is a biocompatible material, which due to the tunable material properties can attain mechanical properties equivalent to native arteries as well as a large range above and below native values. By methodically changing the compliance values and examining outcomes, we will determine the desired properties and property tolerances that can be translated to any vascular graft biomaterial. The addition of surface modifications to the PVA vascular grafts has the potential to improve in vivo endothelial cell coverage, while maintaining a non- thrombogenic surface. The proposed studies will employ luminal topographical modifications to increase endothelial cell migration and maintain cell functions, while preventing smooth muscle cell migration and proliferation, both of which will protect against thrombosis and improve vascular healing. By systematically changing and examining the mechanical and luminal surface properties of the PVA biomaterials, we will determine how the modifications affect: 1) thrombus formation in native, non-anticoagulated blood under physiologic ex vivo flow conditions; 2) endothelial cell attachment, migration, and function, specifically the reduction of endothelial cell markers of thrombosis and inflammation; and 3) vascular healing and in situ endothelialization after surgical placement in clinically relevant animal models. Our team of experts is uniquely positioned to develop and study the design criteria needed for blood-contacting biomaterials. The results of the proposed studies will define the critical tolerances for graft compliance and surface properties which can be applied to cardiovascular biomaterials and devices.

Progress during the reporting period: Our progress to date has been on the in vitro preparation of the PVA biomaterials. The hemocompatibility testing and vascular healing testing remains to be performed.

Publications resulting from the project:
None

Funding Sources (PIs and sources):

Monica	Hinds, Ph.D.	NIH/National Heart, Lung, and Blood Institute
Evelyn	Kim Fai Yim, Ph.D.	R01 HL130274

Project Title: Intrinsic Vascular Smooth Muscle Cell Stiffness (PILOT)
SPID: 8231
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Rutgers University

Project Description: Two rhesus macaque monkeys were leased from the ONPRC colony, one young and one aged adult female, to train ONPRC surgical staff on the technique of placement of transducers on the upper and lower regions of the aorta. The devices provide immediate and accurate measures of blood vessel stiffness, allowing unobtrusive, longitudinal studies in awake animals. The pilot data will form the basis for future applications. Vascular tissues were collected and shipped back to Rutgers for *in vitro* analysis.

Progress during the reporting period: The surgical procedures were successful, and the ONPRC team also has some ideas for facilitating any future surgeries. Tissue results are pending.

Publications resulting from the project:
None

Funding Sources:

Stephen	Vatner, Ph.D.	NIH/National Heart, Lung and Blood Institute R01 HL102472

Project Title: Modeling stroke in the female nonhuman primate to evaluate gender difference
SPID: 0036
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: Estrogen has been posed to be neuroprotective against cerebral ischemia and its loss with menopause, coupled with aging, can be a long-term challenge for cerebrovascular health. However, studies involving females are infrequent, in part because of the need to consider the role of ovarian steroid effects on physiology. This project examined the neuroprotective effects of estrogen-replacement in female macaques against reversible, ischemia. Middle-aged animals were utilized to mimic the menopausal age found in women. Stroke outcome was evaluated in acutely ovariectomized (ovx) females given placebo or implants containing estrogen prior to ischemia. One arm of the study also involved long-term ovx animals that received estrogen. The latter group tested to see if long-term loss of the ovaries affected subsequent responsiveness to hormone treatment.

Progress during the reporting period: Although this pilot study was under-powered to detect statistical differences, the feasibility and the trends in the outcome data were encouraging. We found a positive effect of estrogen replacement in the middle-aged females, including: 1. A reduction of ischemic damage, as assessed by MRI, with less damage in long-term ovx with estrogen (best outcome) < acute ovx plus estrogen < controls (worse outcome); 2. The neurological outcomes paralleled the MRI results, with the middle-aged, long-term ovx females with estrogen replacement retaining the most function (best outcome) > acute ovx plus estrogen > acute ovx with placebo; and 3. Survival time also reflected the MRI and neurological outcomes.

Publications resulting from the project:
None

Funding Sources:

Excluded by Requester — Circle of Giving - OHSU Women's Center for Health Research

Project Title: Characterizing the FASD Cerebral Cortex in Utero with DTI
SPID: 1981
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
University of Washington

Project Description: Fetal exposure to alcohol leads to a wide range of neurological deficits collectively termed fetal alcohol spectrum disorders (FASD). The CDC estimates that FASD currently affects as many as 4.5 out of every 1000 births in the US. Existing intervention strategies can improve the quality of life in affected individuals, provided they are initiated at the earliest age possible. Unfortunately, early FASD diagnosis is difficult, partly because behavioral manifestations of the disorder are not apparent until childhood. We propose to develop a magnetic resonance imaging (MRI)-based strategy to detect cellular-level morphological alterations in the developing cerebral cortex. Nonhuman primate research subjects will be bred after being trained to drink 1.5 g/kg/day of ethanol, or an isocaloric amount of maltose/dextrin solution. Animals will continue to drink throughout the first 60 days of pregnancy, after which access to ethanol will be terminated. Fetal brain T2-weighted and diffusion tensor imaging (DTI) data will be acquired on 3 groups of ethanol or maltose/dextrin animals: group 1 will be scanned on gestational day (G)85, group 2 on G110, and group 3 on G135. Immediately after MRI, fetuses will be delivered by caesarian section and brains will be prepared for histological processing. The first aim for this experiment is to characterize the effects of early ethanol exposure on cerebral cortical thickness, surface area, and water diffusion anisotropy over the period ranging from G85 to G135. The second aim is to validate the cortical thickness effects of ethanol exposure using unbiased stereological techniques, and to characterize the biological source of the neuroimaging observations.

Progress during the reporting period: There have been no modifications to the Specific Aims, or the timeline of the original proposal. Eighteen animals have completed the study. Preliminary indications that fetal MRI can be used to detect abnormalities in brain development and placental function have been observed.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Christopher Kroenke, Ph.D. — NIH/National Institute on Alcohol Abuse and Alcoholism
R01 AA021981

Project Title: Alcohol dependence and HCV: mechanisms of combined CNS injury
SPID: 3066
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University

Project Description: Major goals: Through human studies and the establishment of an animal model of co-morbid viral infection and alcohol dependence, our goal for this translational research project is to identify specific mechanisms by which chronic viral infection and alcohol induce abnormalities in immune cell function and contribute to persistent neuropsychiatric impairments. This information will guide future pre-clinical testing of immunotherapeutic strategies to improve psychiatric function and reduce the risk of alcohol relapse.

Progress during the reporting period Excluded by Requester has completed the *in vivo* portions of the research and has a manuscript that has been published on this work (see below).

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Excluded by Requester — US Department of Veteran Affairs

Project Title: Bev Hartig Huntington's Disease Foundation
SPID: 1027
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: This project is investigating the central and peripheral tissue biodistribution of a novel gene therapy vector entitled AAV-PHP.B in the rhesus macaque central nervous system.

Progress during the reporting period: To date 4 animals have been infused with AAV-PHP.B expressing GFP into either the carotid artery or the cisterna magna and euthanized 3 weeks post-injection. Molecular and histological analyses demonstrated that the cisterna magna infusions resulted in a significantly higher vector genome copy number in multiple brain regions, particularly in cortical and spinal cord areas, compared to the carotid artery infusions. This pilot study lead to interest from Private Source and we are currently in the process of drafting a research contract with them that will extend this pilot study into a larger study assessing higher AAV-HPP.B titers, as well as a comparison of AAV-PHP.B with the gold standard in the field, AAV9.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester
Private Source

Project Title: Biodistribution and dosing of an AAV expressing RNAi construct for Huntington's disease: a pre-clinical collaboration
SPID: 4129
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: This project investigates the safety and efficacy of using RNA interference to reduce the expression of HTT, the gene affected in Huntington's disease, in the rhesus macaque putamen.

Progress during the reporting period: All tissues have been analyzed for this study and the results are currently being written up for publication. In summary, we found a dose-dependent increase in HTT mRNA suppression in the rhesus putamen that correlates directly with the dose of AAV1-miHDS1 administered. HTT mRNA suppression was at the level we are aiming for in a future clinical study, was well tolerated and was not associated with the development of astrocytosis or microgliosis. The Clearpoint surgical system developed by MRI Interventions was fully established at the ONPRC and is useful for real-time MRI-guided delivery of biological agents into the brain.

Publications resulting from the project:
None

Funding Sources:

Excluded by Requester

Private Source

Project Title: Cortico-basal ganglia connectivity in a non-human primate model of Huntington's disease
SPID: 9136
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science university

Project Description: The goal of the proposed research in this application is to characterize alterations in cortico-basal ganglia connectivity in a novel non-human primate model of Huntington's disease (HD) recently developed in my laboratory. We will test our central hypothesis that there is a progressive decline in basal ganglia connectivity in our HD NHP brains that correlates with 1) the longitudinal development of cognitive and motor phenotypes, 2) reduced glutamate and dopamine transmission in cortico-striatal and nigro-striatal connections with medium spiny neurons in the caudate and putamen and 3) neuropathology including inclusion formation, gliosis and neuronal dysfunction.

Progress during the reporting period: This study just began 2 months ago. However, in this short amount of time we have already had a follow-up animal planning meaning to secure the 18 animals needed for the study. Additionally, we interviewed and extended an offer to the to-be-determined post-doctoral fellow that will be participating on the study. She recently accepted the position and will be joining the lab in 2017.

Publications resulting from the project:
None

Funding Sources:
Jodi McBride, Ph.D. — NIH/National Institute of Neuro Disorders & Stroke
R01 NS099136

Project Title: Global RNA Interference Therapy for Huntington's Disease
SPID: 5245
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Oregon Health & Science University

Project Description: The major goals of this proposal are 1) to prepare and characterize AAV-PHP.B-mi2.4, AAV9-mi2.4 and control vectors, 2) to perform pharmacokinetic and biodistribution superiority studies of AAV-PHP.B-mi2.4 and AAV9-mi2.4 in N171-82Q transgenic HD mice to define a dose and delivery route that leads to a significant 40% reduction of mHTT in the cortex and striatum and 3) to perform in vivo efficacy and tolerability studies in 2 different HD mouse models (N171-82Q and CACHD) to establish the minimum effective dose of our lead construct that significantly ameliorates behavioral, neurophysiological and neuropathological deficits germane to each model. These proposed experiments are both significant and innovative because they represent the first steps towards a systemic strategy to attenuate the wide array of devastating symptoms that plague Huntington's patients.

Progress during the reporting period: This study just began 2 months ago. Despite this short amount of time, we have already gotten surgically trained on both the carotid artery and cisterna magna infusions and completed several trial surgeries successfully. We ordered and received all of the necessary breeding pairs of HD mice and have had several successful litters born that will be injected with AAV9 or AAV-PHP.B in the early spring. We have successfully cloned all of the necessary plasmids for this study, and they were recently sent to Virovek for recombinant viral vector production.

Publications resulting from the project:
None

Funding Sources:
Jodi McBride, Ph.D. NIH/National Institute of Neuro Disorders & Stroke R21 NS095245

Project Title: VitC to Decrease Effects of Smoking in Pregnancy on Infant Lung Function-CCCLead
SPID: 5447
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Indiana University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Indiana University

Project Description: This is an application for a double blind, placebo-controlled study to determine if vitamin C supplementation (500 mg daily) can decrease the effect of maternal smoking in pregnancy on offspring pulmonary function (VCSIP). Smoking during pregnancy remains a major public health problem as at least 12% of pregnant women cannot quit smoking during pregnancy. This addiction is the largest preventable cause of childhood respiratory illness, including asthma, and children whose mothers smoked during pregnancy show lifetime decreases in pulmonary function. Smoking is a unique morbidity in that it is addictive, heavily advertised and recent genome studies show there are genotypes that significantly increase the likelihood of being unable to quit. Teen pregnancy, low income, low education, and living with another smoker are important factors increasing the odds of smoking during pregnancy. Pulmonary function tests done shortly after birth in babies born to mothers who smoked during pregnancy show decreased pulmonary function as measured by decreased respiratory flows and compliance and altered tidal breathing patterns. These changes can still be measured even after the infants have reached adulthood. Multiple epidemiologic studies show that these decreases in pulmonary function lead to increased respiratory disease and costs of hundreds of millions of dollars per year.

Progress during the reporting period: The randomization of pregnant smokers has been completed and the desired sample size and timeline was achieved. Primary outcome measures of pulmonary function and wheeze have now been completed and data analysis will soon commence after final supporting assays are completed.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Funding Sources:

Cynthia T. McEvoy, M.D. — NIH/National Heart, Lung & Blood Institute
R01 HL105447

Project Title: Maternal vitamin C supplementation to decrease effects of smoking during pregnancy on infant lung function and health follow-up of 2 randomized trials and association with changes in DNA methylation
SPID: 3288
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigators of the project/Institutional affiliation:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester	Indiana University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Project Description: This application has 4 specific aims: 1, to create the combined cohort of offspring from the 2 RCTs of vitamin C supplementation to pregnant smokers; 2, to determine if the protective effects of maternal vitamin C supplementation to pregnant smokers on offspring pulmonary health extend to early adolescence; 3, to begin to characterize the epigenetic mechanisms that appear to underlie the effects of smoking during pregnancy on offspring lung health and on the protective effects of vitamin C; and 4, to gather core data for and interact with the overall ECHO study. Respiratory health will be assessed by longitudinal semi-annual, validated respiratory histories and yearly PFTs beginning at 3 years of age. Buccal swabs will be collected yearly and blood at 6, 9 and 12 years to provide DNA for genetic analysis. DNA methylation changes will be measured by methylation chips and bisulfite sequencing. This study will address how smoking during pregnancy affects respiratory outcomes, provide mechanistic and therapeutic insights, and provide subjects and data to ECHO to address other key outcomes.

Progress during the reporting period: This is a new project that just started. Progress to date has involved organizational efforts within the ECHO consortium and drafting of new IRB and consent forms.

Publications resulting from the project:
None

Funding Sources:
Cynthia T. McEvoy, M.D. NIH/Office of the Director UG3 OD023288

Project Title: Micromechanical Determinants of Choriocapillaris Dysfunction in AMD Pathogenesis
SPID: 0806
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
University of California - Riverside

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Oregon Health & Science University

Project Description: Excluded by Requester will be involved in providing retinal tissues from monkeys of different ages, and from older monkeys with and without drusen. Additionally Excluded by Requester and Excluded by Requester will facilitate the isolation, purification and characterization of retinal endothelial cells from these monkeys, provide advice on retinal tissue staining and experimental design involving cultured retinal cells, and assist with data analysis and interpretation.

Progress during the reporting period: We have isolated choroidal endothelial cells from 3 animals and have provided those cells to Excluded by Requester at UC Riverside for evaluation. Our goal was to collect eyes from 6 animals per year and thus we are right on track for the timeline of this project. Excluded by Requester will analyze the cells in his lab.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester
Private Source

Project Title: AAV Capsid Functions, Immune Evasion and Neuronal Targeting in Mice and NHP
SPID: 8399
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Oregon Health & Science University
Oregon Health & Science University

Project Description: Adeno-associated virus (AAV) is the most promising in vivo viral gene delivery vector currently available. However, there still remain various issues to be resolved, including the high prevalence of pre-existing anti- AAV neutralizing antibodies (NtAbs) in humans, efficacy-limiting host immune responses against viral proteins, and promiscuous viral tropism. In addition, there are species-specific differences in AAV-mediated immune responses and tropism, which often make it difficult to predict clinical outcomes from small animal studies and underscore the importance of nonhuman primate (NHP) studies. As for gene therapy for the central nervous system (CNS) diseases, the inability of AAV to efficiently cross the blood-brain barrier (BBB) poses an additional obstacle to be overcome. Therefore, to ensure a greater success for gene therapy, there is an urgent need to thoroughly address these issues. The ultimate goal of this project is to acquire a large dataset of AAV capsid amino acid sequence-phenotype relationships in cultured cells, mice and NHPs~ utilize the data to understand how the multifaceted AAV capsid phenotypes are determined in each different context~ establish means to overcome the current limitations~ and create NtAb escape AAV vectors that specifically target CNS neurons via the intravenous (IV) route in mice and NHPs.

Progress during the reporting period: In Aim 1, we have phenotypically characterized AAV8 and AAV9 capsid double alanine mutants in vitro and in mice, and identified various amino acids of structural and functional importance. We have vectorized several AAV mutants of interest into vectors expressing a marker gene and evaluated their tropism and transduction efficiencies in various organs in mice. In Aim 2, using the IP-Seq technology we have devised, we have successfully draw a comprehensive map of epitopes for human polyclonal antibodies against AAV2 capsids using 32 anti-AAV2 capsid antibody-positive human sera. Based on this information, we are currently creating novel AAV2-derived mutants that can escape from anti-AAV2 neutralizing antibodies. In Aim 3, we have built a comprehensive dataset on the AAV capsid amino acid motifs responsible for determining vector half-lives in the blood, and have created novel AAV capsids that can transduce the brain efficiently while detargeting the liver following intravenous injection of the vector. In Aim 4, we have invented a novel AAV capsid directed evolution technology, the TSP-TRADE system, with which we can evolve AAV capsid based on tissue/cell-type specific gene expression in any animal species including nonhuman primates. We have created the first version of AAV TSP-TRADE library to evolve AAV capsids that can mediate neuron-specific gene expression. We are soon injecting the AAV TSP-TRADE library into nonhuman primates to identify novel AAV capsids that can transduce nonhuman primate neurons efficiently and specifically by intravenous injection of the vector.

Publications resulting from the project:
None

Funding Sources:
Hiroyuki Nakai, M.D., Ph.D. NIH/National Institute of Neuroscience Disorders & Stroke R01NS088399

Project Title: Cognitive Nutrients and the Brain: Production of Isotopically Labeled Nutrients and Development of Animal Models
SPID: 0200
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

University of Illinois at Urbana-Champaign

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Tufts University

Project Description: Lutein is a yellow carotenoid that is highly concentrated in the macula of the retina where it protects against oxidative damage and blue light damage. It is derived from the diet, particularly from green leafy vegetables, but levels in the American diet are generally low. Lutein has a critical role in eye health throughout the lifespan and has been shown to reduce the risk of age-related macular degeneration. Recent findings suggest that it may also play a role in brain health. Lutein is the major carotenoid in both pediatric and geriatric brain tissue, and increased lutein intake is correlated with improved cognitive function in the elderly. However, its localization in brain tissue and role in neural function is unknown. Lutein is present at similar levels in human and nonhuman primate retina and brain, but at negligible levels in most other species; furthermore, only the higher primate eye possesses a macula. Therefore, nonhuman primates are the only appropriate model for investigating the metabolism and functions of lutein. There are no data on the distribution of lutein in brain regions underlying cognitive function, or on its subcellular localization in neural tissue. The first goal of this project is to use novel approaches and an appropriate nonhuman primate model to assess the pharmacokinetics of lutein uptake and localization in key areas of the monkey brain. Furthermore, because lutein is a lipid-soluble membrane constituent, we will determine its distribution in brain membranes, including neuronal, mitochondrial, nuclear and myelin membranes. Monkeys will be fed ^{13}C-labelled lutein produced from plant cultures specifically for this project. A second goal of the project is to examine the relationship of lutein intake to brain function, connectivity and organization as measured in vivo by magnetic resonance imaging. This aspect of the project will utilize unique groups of rhesus monkeys maintained throughout life on carotenoid-free diets.

Progress during the reporting period: Brain tissue from a series of areas relevant to cognitive function was collected from 16 rhesus monkeys. From each region membrane fractions were isolated, including synaptic, mitochondrial, nuclear and myelin membranes, and assayed for carotenoid content as well as fatty acid composition and markers of lipid oxidation. Lutein was detectable in all membrane fractions of prefrontal and temporal cortices, hippocampus and striatum, whereas other carotenoids were not detectable in any membrane fraction. Methods were developed for the production of ^{13}C-labelled lutein to be used in short-term dosing studies; one monkey received a dose of the labeled compound, which was detected in hepatic samples.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Excluded by Requester

University of Illinois at Urbana-Champaign
Center for Nutrition, Learning and Memory

Project Title: Evaluation of Stem Cell-derived Retinal Pigment Epithelial Cells for Retinal Disease Therapy
SPID: 1214
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester	Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester	Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	National Eye Institute

Project Description: Degenerative diseases of the retina are cumulatively the most common causes of untreatable blindness. These conditions, which include age-related macular degeneration and retinitis pigmentosa, are characterized by progressive loss of cells in the outer retina. Stem cells hold great promise for treating these diseases by repopulating cells that have been lost. A cell type that will be central to the success of this strategy is the retinal pigment epithelium (RPE). Recent technological breakthroughs make possible for the first time the production of recipient-specific donor cells through reprogramming of pluripotency in adult cells and directed differentiation. However, it is not known how RPE cells produced by these and other methods compare with respect to key biological characteristics, including immunogenicity and mitochondrial senescence, when transplanted to the healthy or diseased retina. These issues are critical to the potential use of such cells for retinal disease therapy. The goal of this proposal is to study the functionality of RPE cells generated from different stem cell sources in vitro and after transplantation to the nonhuman primate retina, including their immunogenicity, survival and effect on retinal structure. The project will make innovative use of unique resources; including allograft and autograft stem-cell-derived rhesus monkey RPE cell lines and a naturally-occurring nonhuman primate model of macular disease. These studies will provide key information on the feasibility of transplantation of RPE stem cells from different sources and under different conditions as a treatment for age-related macular degeneration and other retinal diseases.

Progress during the reporting period: An improved method was developed to deliver stem cells to the subretinal space without leakage into the vitreous. New optimized protocols for the differentiation of RPE cells from rhesus monkey induced pluripotent stem cell lines were implemented and resulted in the successful production of viable RPE cells as verified by protein expression and functional assays. When these cells were used to test the viability of transplanted cells, allografts were rejected, resulting in local loss of native RPE.

Publications resulting from the project:

In Press

Funding Sources:

Martha	Neuringer, Ph.D.	NIH/National Eye Institute R01 EY021214

Project Title: Impact of Infant Formula on Brain and Eye Development
SPID: 7269
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

University of Illinois at Urbana-Champaign

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Abbott Nutrition

Project Description: Lutein is a yellow plant-derived carotenoid that is highly concentrated in the fovea of the retina and has a critical role in eye health throughout the lifespan. Lutein is also the major carotenoid in human brain and recent evidence indicates that its intake may be beneficial for cognitive function. The macula and fovea are the parts of the retina supporting high acuity central vision, and are found only in higher primates including macaques and humans. Lutein accumulation in both retina and brain is also specific to higher primates. Thus, nonhuman primates are the only appropriate model for investigating the potential benefits of lutein to eye and brain development. Infant formulas are not routinely supplemented with lutein, resulting in low intake in formula-fed infants compared with breast-fed infants. In addition the concentration of lutein in human milk is dependent on maternal diet, and most Western women consume a diet relatively low in lutein. However, it is not known whether lutein may influence the development of both the retina and the brain, and by what mechanisms. Our collaborative group is undertaking a study that will evaluate the importance of dietary lutein for early eye and brain development by controlled feeding of rhesus monkey infants, together with comprehensive state-of-the-art assessments of retinal and brain development. This study will provide new insights into the role of lutein for eye and brain development in an appropriate animal model with high translational relevance to human infant nutrition.

Progress during the reporting period: Multiple measures of retinal and brain development were completed in groups of rhesus infants fed formulas with and without supplemental lutein, and both groups were compared to breastfed infants. Data analysis is ongoing for data from the many study outcome measures. Several modes of retinal imaging, including color photography, ocular coherence tomography (OCT), fundus autofluorescence, fluorescein angiography and adaptive optics imaging of cone photoreceptor density, were used for the first time to quantify the normative development of the fovea, the primate-specific retinal specialization that underlies high acuity vision. These structural methods also will be correlated with measures of retinal and visual cortical function. Finally, multiple modes of magnetic resonance imaging were used to examine brain development, including patterns of functional connectivity and cortical organization.

Publications resulting from the project:
None

Funding Sources (PIs and sources):

Excluded by Requester

University of Illinois at Urbana-Champaign
Center for Nutrition, Learning and Memory

Project Title: Module II: Nonhuman Primate Models of Retinal Disease
SPID: 0535
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — University of Florida
Oregon Health & Science University
Oregon Health & Science University

Project Description: Age-related macular degeneration (AMD) is the leading cause of vision loss in adults over 60 years of age. The macula, the specialized area of the retina that underlies sharp central vision, is present only in human and nonhuman primates, so that only nonhuman primates can provide an accurate model for this complex disease. Furthermore, both rhesus and Japanese macaques develop syndromes closely resembling human AMD, and in rhesus we have confirmed two genetic risk factors that are shared with humans. Availability of these nonhuman primate models of AMD makes possible tests of several promising therapeutic approaches, including gene therapy, stem cell therapy, growth factors and nutritional interventions, as well as studies of the mechanisms underlying retinal degeneration. This project's objectives are 1) to continue to develop an optimal nonhuman primate model for translational AMD therapy development by characterizing monkeys with naturally-occurring macular disease; 2) to examine the role of dietary factors in macular disease progression; and 3) to develop and evaluate gene therapy methods, particularly those targeting cone photoreceptors and the macula.

Progress during the reporting period: We continued to screen the ONPRC colony to identify both rhesus and Japanese macaques with retinal disease and characterize their syndromes with multiple state-of-the-art modes of retinal imaging. Retinal tissue from these animals were shared with collaborators examining different aspects of the underlying pathophysiological mechanisms. We also continued to follow the retinal status of groups of rhesus monkeys fed diets lacking dietary xanthophylls and n-3 fatty acids, two nutrients thought to lower the risk of AMD. These animals have developed hallmark signs of early AMD at early ages, show increased levels of retinal lipofuscin accumulation as measured in vivo by fundus autofluorescence, and some have progressed to the more advanced form of atrophic AMD, which has not been previously reported in macaque monkeys. Ocular evaluations have also been extended to monkeys fed high fat diets leading to prediabetic and diabetic status, with the goal of establishing a nonhuman primate model of diabetic retinopathy. In addition to these models, a new syndrome of inherited retinal degenerative disease was identified in the Japanese macaques: a form of neuronal ceroid lipofuscinosis with progressive retinal degeneration which can serve as an optimal model for this devastating disease.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Funding Sources (PIs and sources):

Excluded by Requester — Private Source

Project Title: Impact of select nutrients on eye and brain health
SPID: 0044
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

University of Illinois at Urbana-Champaign

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Tufts University
Abbott Nutrition
University of Illinois at Urbana-Champaign
University of Illinois at Urbana-Champaign

Project Description: Lutein levels in the diet and brain have been associated with improved cognitive function, but the mechanisms underlying these effects are unknown. This exploratory study will examine the effects of dietary lutein on gene expression and epigenetic modifications in brain regions underlying cognition. We propose to utilize next-generation RNA-Seq to evaluate gene expression patterns in prefrontal cortex and hippocampus from monkeys fed diets with and without supplemental lutein, and genome-wide epigenetics technologies to evaluate effects on DNA methylation patterns. In addition, levels of several neurotransmitters, including dopamine, serotonin, GABA and glutamate, will be measured in key brain regions using LC-MS and MALDI-MS technologies. Together, these methods are likely to provide a wealth of novel information on biological systems that are modulated by dietary lutein.

Progress during the reporting period: Lutein supplementation of infant formula resulted in several-fold increases in brain lutein concentrations in multiple brain regions. Samples of prefrontal cortex and hippocampus are being processed for RNA-Seq and epigenomic analyses, and the Sweedler laboratory at University of Illinois has conducted pilot studies to optimize methods for measurement of neurotransmitter levels in key brain areas.

Publications resulting from the project:

In Press

Funding Sources:

Excluded by Requester

University of Illinois at Urbana-Champaign
Center for Nutrition, Learning and Memory

Project Title: Human MiniPromoters for Restricted Expression of Ocular Gene Therapy
SPID: 3808
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — University of British Columbia

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester — Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester — Oregon Health & Science University

Project Description: The purpose of this project is to move toward safer and more targeted types of gene therapy for retinal diseases. Gene therapy utilizes viral vectors to insert therapeutic genes into cells. This project will refine these viral vectors by developing "minipromoters", small pieces of DNA that serve to direct the vectors to particular cell types within the retina. The overall project will design a series of minipromoters for different retinal cell types and useful for different eye diseases. Viral vectors incorporating the new minipromoters will be tested first in mice, and those with the best results will then be evaluated in monkeys. Because the monkey and human eye are so similar in structure and function, monkey studies will provide a critical translational bridge to the use of these improved vectors in human patients with otherwise untreatable retinal degenerative diseases.

Progress during the reporting period: We tested an adeno-associated viral (AAV) vector carrying the GFP marker gene, which included a minipromoter targeting retinal glial cells (Muller cells), and compared this with a vector using a ubiquitous (nonspecific) promoter. We evaluated gene expression by retinal imaging over 12 weeks. GFP fluorescence was clearly visible and increased progressively in the eyes receiving vector with the ubiquitous promoter, and as expected was less distinct but present in the eyes receiving vector with the Muller cell minipromoter. Cellular localization of vector-transduced GFP expression, assessed by immunohistochemistry and confocal microscopy, showed little transduction beyond the outer retina. A different AAV vector with a ubiquitous promoter was then tested, and demonstrated improved ability to transduce all retinal layers and cell types, including bipolar, Muller and ganglion cells.

Publications resulting from the project:
None

Funding Sources (PIs and sources):
Excluded by Requester — Private Source

Project Title: Engineering viral vectors to target the cat hypothalamus with sterilizing molecules
SPID: 1020
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

University of Iowa
Oregon Health & Science University
Oregon Health & Science University

Project Description: The objective of this new grant is to develop a gene therapy delivery agent that reliably and efficiently targets neurons of the cat hypothalamus following a single intravenous (i.v.) administration. We propose to engineer a recombinant adeno-associated virus (rAAV) as the targeting vector, using a novel approach developed by Excluded by Requester and his colleagues, which they have termed AAV Barcode-Seq. It is our expectation that this approach will be much more effective than any of the conventional approaches currently available to identify rAAV mutants capable of reliably targeting specific neuronal populations of the brain with significantly less off-target vector dissemination.

Progress during the reporting period: We have obtained conclusive results showing that cat serum containing ELISA-positive antibodies does not have an inhibitory effect on AAV vector transduction, i.e., ELISA positive antibodies detected in cats are devoid of neutralizing activity. We have also identified a set of AAV variants whose tropism has been changed so they no longer target the liver. Instead they target the hypothalamus. Further characterization of one of these mutants, termed AAV9 LD, revealed that AAV9LD targets the hypothalamus, while displaying negligible transduction of both the liver and other brain regions. This new liver-detargeting AAV9 mutant and their derivatives were included in a random octapeptide display AAV library that we recently injected into two cats. Preliminary results suggest that the hypothalamus of these animals is enriched in AAV9 variants that use liver-detargeting AAV9 mutants such as AAV9LD as the launching platform. Accordingly, it appears that such mutants will be able to target a larger fraction of hypothalamic neurons than any of the currently available AAV strains following systemic injection, while also showing minimal liver transduction.

Publications resulting from the project:
None

Funding Sources:

Excluded by Requester

Private Source

Project Title: Metabolic Control of Puberty: Epigenetic Links
SPID: 4542
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigators of the project/ Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: It has been known for years that energy balance can be permanently affected by nutritional challenges taking place during a critical period of "developmental programming", which in humans occurs during late gestation and in rodents during early post-natal life. It is also well established that these alterations affect female neuroendocrine reproductive development; increased nutritional availability advances the timing of puberty, and nutritional deficiency delays it. We recently discovered that female puberty is regulated by an epigenetic mechanism that involves lifting of a transcriptional repressive tone exerted by the Polycomb group (PcG) of transcriptional silencers, and that this repression is imposed on downstream genes involved in the stimulatory control of GnRH secretion (epitomized by the Kiss1 gene).

Progress during the reporting period: We have completed a series of studies showing that postnatal over-nutrition (animals raised in small litters) is associated with decreased expression of Sirt1 in the hypothalamus, whereas the contrary occurs in underfed animals (raised in large litters). In overfed animals loss of Sirt1 expression is associated with an increased content of activating histone marks, normally reduced by SIRT1, and a loss of PcG-dependent repressive histone marks from the promoter region of Kiss1 and Tac3, two genes required for the initiation of puberty. The opposite changes are seen in underfed animals. These results are consistent with our hypothesis that SIRT1 functions as a fuel-sensing molecule that respond to early nutritional unbalance by modifying the activity of genes involved in the stimulatory control of puberty.

Publications resulting from the project:
None

Funding Sources:

Sergio	Ojeda, D.V.M.	NIH/National Institute of Child Health & Human Development
Alejandro	Lomniczi, Ph.D.	R01 HD084542

Project Title: Behavioral Genomics of Alcohol Neuroadaptation
SPID: 0760
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: Human alcohol research and clinical practice demonstrate that, without question, there is a wide range of individual variation in risk for excessive drinking, in sensitivity to alcohol effects, and in response to treatment strategies. Impulsive behaviors are recognized as one risk factor, particularly if the construct of impulsive behaviors encompasses measures of both response inhibition and temporal discounting. A history of heavy ethanol intake appears to be related to increases in these measures of impulsivity. However human studies have been unable to distinguish antecedent baseline measures of impulsivity from the consequential effects of a history of heavy ethanol consumption. Our model of ethanol self-administration in macaque monkeys provides a unique and important model of alcohol abuse, and reflects the individual differences in propensity to drink alcohol noted in the human population. Because of genetic similarities between humans and nonhuman primates, these studies can then be a key step in translating candidate mechanisms of ethanol's effects into the human condition through functional genomics. Thus, our primary focus of this PARC project is to use the monkey model to characterize antecedent and consequent measures of two aspects of impulsivity (response inhibition and aversion to a delay in reinforcement) with genetic factors related to excessive ethanol intake.

Progress during the reporting period: A new cohort of 10 cynomolgus monkeys entered the alcohol self-administration protocol. All baseline measures have been acquired and training on the use of the operant panels is complete. The drinking and hormonal data are being processed.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Tamara Phillips, Ph.D. — NIH/National Institute on Alcohol Abuse & Alcoholism
P60 AA010760

Project Title: Neural Basis Of Tactile Object Perception In SI Cortex
SPID: 3998
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Wigner Research Center for Physics

Project Description: The goal of this proposal is to investigate the organization and circuitry within the hand and digit region of primary somatosensory cortex in nonhuman primates. Hand and digit behavior are defining aspects of object identification in primate behavior, and are central to different types of tool use, typing, texting, and body language. Despite this, little is known regarding the cortical circuitry underlying different stage of sensory (tactile and proprioceptive) processing. This proposal will use multiple anatomical and functional approaches to discover the intra-areal and inter-areal connectivity patterns between functional columns in the hand representation of primary somatosensory areas (3a, 3b, 1, and 2). These approaches will include anatomical tract tracing and functional tract tracing (using optical imaging and fMRI during focal electrical and pulsed near infrared laser stimulation). The role of these circuits during behavior will be examined. These studies will provide invaluable data for incorporation of sensory guidance in manual motor prosthetics, an area in which there is currently little understanding.

Progress during the reporting period: Over the past year, progress towards achieving the scientific goals of these studies have included: (1) setting up of the laboratory's surgical suite, as the PIs have recently moved to the ONPRC; (2) obtained the squirrel monkeys and caging needed to begin work described in Aim 1; and (3) started performing studies in macaque and squirrel monkeys investigating the functional and anatomical tract tracing of primate primary somatosensory cortex (Brodmann areas 3a, 3b, 1 and 2).

Publications resulting from the project:
None

Funding Sources:

Anna	Roe, Ph.D.	NIH/National Institute of Neuro Disorders & Stroke
Robert	Friedman, Ph.D.	R01 NS093998

Project Title: Somatic Aneuploidy in the Aging Brain
SPID: 1064
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: This project aims to study the basis of the differences between high and low levels of aneuploidy with time and uncover key differences that are established between normal (successful) and diseased (unsuccessful) states with the ultimate goal of providing new strategy for diagnosis and targets for therapeutic intervention of such states.

Progress during the reporting period: During this reporting period, we used traditional and novel single-cell sequencing techniques on banked frontal cortex tissue of a young male (4 yr.) rhesus macaque producing 317 *bona fide* single-cell libraries, of which 259 (82%) passed quality filters for copy-number calling. Specifically, we have been able to successfully adapt and optimize a more traditional single-cell sequencing library preparation for more affordable higher-throughput (DOP-PCR). Using DOP-seq and PicoPLEX, an established commercially available single-cell sequencing kit we generated 72 (23%) single-cell libraries. In collaboration with Excluded by Requester novel Single-cell Combinatorial Indexed sequencing (SCI-seq) we were able to generate 245 (77%) single-cell libraries, with comparable results for a fraction of the cost. Currently we are making progress on applying SCI-seq to additional brain samples from older ages, specifically an elderly rhesus macaque.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester
Private Source

Project Title: Effects of Modified Flavonoids on Inflammatory Demyelination
SPID: 4317
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: This project aims to evaluate how intraperitoneal injections of SuBr3 influence disease onset and progression in mice with EAE. Our long-term goal is to determine if SuBr3 or related compounds with similar chemical structures can be safely used to promote remyelination in patients with MS and if they also can contribute to preventing MS attacks.

Progress during the reporting period: This recently completed pilot project demonstrated that SuBr3, a modified flavonoid, promotes remyelination but does not influence inflammatory processes following intraperitoneal injections in mice with experimental autoimmune encephalomyelitis (EAE), a model of multiple sclerosis. This is an important finding, as it indicates that SuBr3 will not worsen inflammatory processes. The data from this study were included in a grant proposal to the Congressionally Directed Medical Research Programs, and will serve as partial rational for non-human primate studies on the efficacy of SuBr3 or related compounds in treating inflammatory demyelination.

Publications resulting from the project:
None

Funding Sources:
Excluded by Requester
Private Source

Project Title: Role of Snf5 Mutations in Schwannomatosis Pain
SPID: 0592
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Oregon Health & Science University

Project Description: Our aims are: (1) To determine if infecting animals with JMRV leads directly to progressive, inflammatory demyelinating disease. We will experimentally infect animals via intracranial injection and follow them longitudinally by MRI, followed by histopathological, immunological, and biochemical analyses. (2) To characterize the specific roles of JMRV-infected B cells in demyelination, axonopathy, and neuron death. For these studies, we will analyze B cells from both infected and spontaneous cases. These studies will define the roles of viral infection and B cells in inflammatory progressive demyelinating disease, and further characterize a unique potential animal model of PPMS.

Progress during the reporting period: We have completed a round of proteomics experiments to identify the secreted proteins expressed by Snf5 mutant Schwann cells. We find that a number of proteins are elevated in the conditioned media of Snf5 mutant Schwann cells and we have validated this expression in the case of the chemokine, CCL2, which has been implicated in pain in previous studies. We are now performing additional experiments to validate other targets and testing if CCL2 is required for the pain phenotypes we observed earlier.

Publications resulting from the project:
None

Funding Sources (PIs and sources):
Lawrence Sherman, Ph.D. DOD/U.S. Army Medical Research Acquisition Activity W81XWH-15-1-0592

Project Title: White Matter Damage in Age-Related Cognitive Decline
SPID: 2202
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester
Oregon Health & Science University
Oregon Health & Science University
Stanford University

Project Description: The goal of this project is to define the molecular and cellular changes that occur in human pre-frontal cortex during age-relate cognitive decline. In particular, we are looking for correlations between oxidative damage, changes identified by diffusion tensor imaging, alterations in gliosis and oligodendrocyte progenitor cell accumulation, and changes in hyaluronan synthesis and catabolism in white matter from subjects in the Adult Changes in Thought study.

Progress during the reporting period: This project was in suspense for a significant portion of 2016 because the P.I., Excluded by Requester moved to Stanford University from the University of Washington. As a result, funding was held until very recently. We are continuing to pursue our studies characterizing HA, now with a focus on deep white matter vessels in patients with vascular brain injury and Alzheimer's disease.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Thomas Montine, Ph.D. NIH/National Institute on Aging R01 AG031892

Project Title: Prenatal Nicotine and Lung Development: Role of CHRNA5, Addiction and Epigenetics
SPID: 3246
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: Maternal smoking during pregnancy remains a major cause of perinatal morbidity and causes lifelong decreases in pulmonary function and increased risk of asthma in offspring. Despite significant efforts to reduce maternal smoking through public health campaigns and smoking cessation interventions, approximately 13% of all women self-report smoking during pregnancy and this effects the lifelong respiratory health of over 400,000 infants each year. Nicotine addiction is clearly a driving force in the inability of some women to quit smoking during pregnancy and both GWAS and genotyping studies have identified a common polymorphism (rs16969968) in the α5 nicotinic acetylcholine receptor (nAChR) that is associated with heavier cigarette use and reduced smoking cessation. Remarkably, our preliminary data suggests that this same polymorphism that increases the likelihood of maternal smoking during pregnancy also increases the degree to which maternal smoking during pregnancy adversely affects offspring pulmonary function. Thus, the primary objective of this proposal is to determine the mechanism by which alterations in the α5 nAChR subunit mediate the effects of maternal smoking during pregnancy on lung development and to assess the relative contribution of nicotine addiction versus the direct effects of nicotine on lung.

Progress during the reporting period: Initial analysis of alpha5 knockout mice shows that loss of alpha5 blocks some of the effects of prenatal nicotine exposure on lung function. Preliminary studies with two-bottle choice of nicotine or water in alpha5 D398N het females demonstrate a wide range of nicotine preference with some mice consuming up to 16 mg/kg nicotine per day and others avoiding the nicotine solution. Combined with our human studies on effects of smoking during pregnancy on infant lung function, our studies to date in transgenic mice emphasize the importance of alpha5 in modulating the effects of maternal smoking during pregnancy on infant lung development and suggest that the combination of addiction and lung development paradigms will be a useful approach in teasing apart relative contributions of maternal versus fetal genotype.

Publications resulting from the project:
None

Funding Sources:

Lyndsey	Shorey, Ph.D.	NIH/National Heart, Lung, & Blood Institute F32 HL123246

Project Title: Campylobacter vaccination to reduce enteric disease and improve infant growth velocity
SPID: 9806
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: The goal of this project is to determine if an effective vaccine against Campylobacter will reduce the incidence of EED and diarrheal disease among outdoor-housed infant rhesus macaques (RM). If successful, this interventional study could provide a roadmap for reducing the burden of Campylobacter-associated enteric disease among children living under conditions of high Campylobacter exposure due to poor sanitation.

Progress during the reporting period: We just received funding a few weeks ago and are in the process of preparing IBC and IACUC documents that, once reviewed and approved, will allow us to begin these vaccine studies.

Publications resulting from the project:
None at this time.

Funding Sources:
Excluded by Requester
Private Source

Project Title: Development of an H2O2-Inactivated Dengue Virus Vaccine
SPID: 8723
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — University of California Riverside

Project Description: This vaccine project encompasses many of the key product development goals listed in RFA-AI-11-014 including, lead vaccine candidate optimization; evaluation of safety, toxicity, and immunogenicity; evaluation of efficacy in appropriate challenge models; evaluation of stability at optimal and elevated storage temperatures; and cGMP manufacturing of vaccine material suitable for completing all IND-enabling preclinical studies. The successful completion of these objectives will result in cGMP-grade vaccine material suitable for future initiation of a Phase I clinical trial, a crucial milestone in the advancement of a human vaccine for this important NIAID Category A Priority Pathogen.

Progress during the reporting period: We have optimized virus growth and purification parameters and have completed cGMP production of the Master and Working virus banks. We are currently testing for adventitious agents and working on a cGMP production plan.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Mark Slifka, Ph.D. — NIH/National Institute of Allergy & Infectious Disease
R01 AI098723

Project Title: Development of NHP Model of Environmental Enteric Disease
SPID: 9233
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: The overall goal of this pilot project is to examine the underlying mechanisms and clinical outcomes associated with naturally occurring EED and diarrheal disease among outdoor-housed rhesus macaques. In contrast to mice, many human enteric pathogens are avirulent in rodents because it does not represent a natural host-pathogen interaction. Mouse models also require experimental infection that may or may not mimic the conditions (or dose) that is encountered during natural exposure by the fecal/oral route of transmission that is occurring in locations of poor sanitation/hygiene. Moreover, mice are typically housed under nearly aseptic conditions with unknown consequences on microbiome diversity and this may result in a largely artificial system for analysis of human enteric disease. In contrast, the rhesus macaque model provides the opportunity to directly study enteric disease transmitted by fecal/oral transmission and this mimics many aspects of human disease, ranging from inapparent clinical illness (e.g., EED) to acute, chronic/relapsing diarrhea, to dysentery. Interventional studies will not be performed at this stage but the objective will be to establish this as an NHP model for future testing/down-selection of preventative and therapeutic strategies to reduce the burden of enteric disease among children living under conditions of poor sanitation

Progress during the reporting period: We have followed 40 animals longitudinally and are in the process of comparing the microbiomes of animals that have one or more episodes of diarrheal disease to animals that remain healthy over the same time period.

Publications resulting from the project:
None

Funding Sources:

Excluded by Requester

Private Source

Project Title: Mechanisms of Orthopoxvirus Host Control and Viral Immune Evasion
SPID: 5277
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Washington University-St. Louis
Oregon Health & Science University

Project Description: The goals of this project are to characterize the molecular mechanisms by which cowpox virus (CPXV) and monkeypox virus (MPXV) inhibit T cell stimulation and the impact of these immune evasion mechanisms on viral virulence and the development of anti-viral immune responses. We previously demonstrated that CPXV inhibits MHC-I-mediated antigen presentation thus escaping poxvirus-specific CD8+ T cells. Preliminary data suggest that, in addition, CPXV escapes CD4+ T cell stimulation and inactivates T cells in trans, i.e. without infecting T cells and independent of antigen presentation. The latter mode of T cell inhibition is very similar to our previously reported mechanism by which MPXV inhibits MHC-independent T cell stimulation. We therefore hypothesize that the responsible gene products are conserved between CPXV and MPXV. By analyzing deletion mutants we identified a gene region in the CPXV genome encoding the genes responsible for both CD4+ T cell escape and inhibiting T cell stimulation by anti-CD3. Since both antigen-dependent-and antigen-independent stimulation of T cells requires signal-transduction by the T cell receptor (TCR), it is conceivable that a single gene is responsible for both T cell evasion phenotypes. In three specific aims, we will (I) identify the genes in CPXV and MPXV responsible for inhibiting MHC-I-independent T cell stimulation by CPXV and MPXV, (II) characterize the corresponding gene products of CPXV and MPXV and determine how they inhibit TCR-mediated T cell activation, and (111) examine the role of T cell evasion for CPXV virulence and the impact of these inhibitory mechanisms on the development of antiviral immune responses in vivo: Since T cell inactivation by CPXV and MPXV is unlike any other viral T cell inhibitor mechanism described to date, our studies are expected to uncover novel molecular strategies for viral immune evasion. We further expect that this work will lead to a re-evaluation of the role of T cell evasion in the pathogenesis of zoonotic orthopoxviruses (and potentially smallpox, if the T cell inhibitors are conserved in Variola major) because these evasion mechanisms are absent from the widely studied Vaccinia Virus (W) and the mousepox virus ectromelia (ECTV).

Progress during the reporting period: We completed analysis of a recombinant orthopoxvirus protein developed in Excluded by Requester laboratory and used monkeypox to test different types of antiviral antibodies developed in the paper b Excluded by Requester

Publications resulting from the project:
Excluded by Requester
Excluded by Requester

Funding Sources:
Mark Slifka, Ph.D. NIH/National Institute of Allergy & Infectious Disease
U19 AI1099

Project Title: A Novel Inactivated Trivalent Vaccine to Prevent Infection by VEE, EEEV, and WEEV
SPID: 5244
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Washington University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester — Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: The goal of this project is to develop safe and effective vaccines against biological weapons of mass destruction involving virulent alphaviruses, VEEV, EEEV, and WEEV.

Progress during the reporting period: We have developed growth, purification, and inactivation methods that provide for a highly immunogenic trivalent vaccine against VEEV, EEEV and WEEV. We are now optimizing the final formulations.

Publications resulting from the project.
None

Funding Sources (PIs and sources):
Excluded by Requester — DOD Defense Threat Reduction Agency

Project Title: Novel Subunit Vaccines against Varicella Zoster Virus
SPID: 0735
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

Altravax
University of California Riverside

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Varicella zoster virus (VZV) is a neurotropic alpha-herpesvirus that causes varicella (chickenpox) and establishes latency in the sensory ganglia. Reactivation of VZV leads to herpes zoster (shingles), a painful and debilitating disease that is associated with post-herpetic neuralgia. Most cases of herpes zoster occur in persons over 50 years of age, with immunosuppression being an additional risk factor. Two approved VZV vaccines are available, both based on a live-attenuated strain of VZV. The high-dose version is recommended for adults to reduce the incidence of shingles; this reduction is on the order of 50%. However, the long-term efficacy of these live-attenuated vaccines is inadequate, and improved vaccines are desirable. Reactivation of VZV, with the attendant consequences of herpes zoster, is thought to be due to inefficient T- cell immunity. Because VZV-specific antibody titers do not significantly decline with age, the increased risk of VZV reactivation among older individuals is likely due to an age-associated decrease in T-cell immunity. Improved vaccines should therefore be efficient at inducing a robust cellular immune response. The only animal model that recapitulates the human VZV-induced disease is intrabronchial infection of young rhesus macaques with simian varicella virus (SVV). SVV and VZV are evolutionarily related and are co-linear with respect to genome organization. Immunization of patas monkeys with VZV can protect the animals from SVV challenge, demonstrating substantial antigenic relatedness of the two viruses. Recent studies by Dr. Messaoudi, the Co-PI of this Proposal, have examined the T-cell responses given by each of the nearly 70 open reading frames (ORFs) of SVV in infected macaques. ORFs have been identified that are responsible for strong T-cell responses during acute infection but are only weakly immunogenic in latent infection. We hypothesize that these ORFs are candidates for an effective vaccine to prevent reactivation and thus herpes zoster. In this Proposal, we will create DNA vaccines expressing nine ORFs that are strongly immunogenic in acute infection but weakly so in latency. Initial studies with mice will allow identification of those ORFs that are potent inducers of T-cell responses. We will select three ORFs for immunization of rhesus macaques with DNA vaccines delivered by electroporation. Electroporation can increase the potency of DNA vaccines and is efficacious, safe, and well tolerated in human clinical trials; it represents a realistic product modality for a VZV/HZ vaccine destined for adults. After several immunizations, macaques will be challenged with live SVV and the viral titers evaluated.

Progress during the reporting period: We vaccinated animals and challenged them with SVV to determine if there is protective immunity.

Publications resulting from the project.
None

Funding Sources:

Robert	Whalen, Ph.D.	NIH/National Institute of Allergy & Infectious Disease
Ilhem	Powers-Messaoudi, Ph.D.	R43 AI112141

Project Title: CPAP Drives Lung Growth and Pulmonary Function in Moderately Preterm Primates
SPID: 9060
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Indiana University

Project Description: Preterm delivery at less than 37 weeks of gestation is the most common cause of abnormal lung development and one with potential lifelong sequelae since preterm delivery can limit the ability of the lung to reach its maximum potential. The survival of extremely premature infants (24-28 wks gestation), who frequently develop bronchopulmonary dysplasia (BPD), has shifted focus away from moderate and late premature (MLP) infants (≥ 30 to < 37 wks gestation), who initially require relatively little respiratory support and rarely develop BPD. However, MLP infants are the majority of premature births and develop a high incidence of wheezy respiratory illnesses, hospitalizations, and use of asthma medications compared to infants delivered at term gestation. Therefore, MLP infants contribute to high morbidity, family stress, and health care costs following NICU discharge. Pulmonary function testing of MLP infants show they exhibit reduced expiratory flows compared to age-matched term infants and do not demonstrate catch-up when tested in later life. Continuous positive airway pressure (CPAP), which provides mechanical lung distention, is a standard of NICU care for maintaining functional residual capacity (FRC), avoiding intubation and barotrauma, and decreasing respiratory morbidity. While CPAP is currently used to minimize lung injury, it may also promote lung growth and development, since mechanical stretch of the lung is an important stimulus to lung growth. Supporting this, in studies in ferrets, we have demonstrated that 1-week of CPAP increased lung volume and airway size. In addition, we demonstrated that treatment of adult asthmatics with nocturnal CPAP for 1-week suppressed airway hyper-reactivity, an airway characteristic that is often present in subjects born prematurely. Lastly, we have found that among infants born prematurely (mean 32 weeks gestation) and who didn't develop BPD, those treated with CPAP in the NICU had larger lung volumes and greater pulmonary diffusion capacity compared to non-CPAP treated infants. We therefore hypothesize that CPAP stimulates lung growth, improves lung function, and suppresses airway hyper-reactivity in premature infants. We propose to test this hypothesis in a highly-translatable, non-human primate model in which moderately premature (140 days gestation, = 85% of 165 days term gestation) rhesus monkeys will be treated with 10 days CPAP (5 cmH2O) or sham CPAP (0 cmH2O).

Progress during the reporting period: Initial studies on the benefits of CPAP to moderately premature infants using a non-human primate model have now started with ongoing analysis of lung development and pulmonary function.

Publications resulting from the project:
None

Funding Sources (PIs and sources):
Eliot Spindel, M.D., Ph.D. NIH/National Heart, Lung, & Blood Institute R01 HL129060

Project Title: Nicotine, Nicotinic Receptors and Lung Cancer
SPID: 1601
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester Oregon Health & Science University

Project Description: The overwhelming majority of lung cancers are associated with smoking and most lung cancers express nicotinic acetylcholine receptors (nAChR) that are activated by the nicotine in cigarette smoke. The objective of this application is to characterize how the interaction of nicotine with nicotinic acetylcholine receptors (nAChR) expressed by lung cancers stimulates tumor growth with the ultimate objective of developing new therapeutic approaches to lung cancer by blocking this proliferative pathway. The nicotinic receptors are ligand-gated ion channels composed of 5 subunits, either a mixture of alpha and beta subunits or 5 of the same alpha subunit. Binding of a nicotinic agonist such as acetylcholine or nicotine opens the ion channel allowing entry of Na+ or Ca++ into the cell. While the nAChR are best known for their role as neurotransmitter receptors in the CNS, they are also widely expressed in non-neuronal cells. Our laboratory has been a leader in showing that essentially all lung cancers express nAChR and binding of nicotine to the nAChR stimulates lung cancer growth. The real world importance of nicotine as a stimulus for lung cancer growth has recently been confirmed by multiple genome-wide association studies linking polymorphisms in nicotinic receptors to increased risk of lung cancer even when corrected for numbers of cigarettes smoked. Strongest linkage by far has been with polymorphisms in the 15q25.1 nicotinic receptor gene cluster that encodes the alpha3, alpha5 and beta4 nAChR subunits.

Progress during the reporting period: Tobacco smoke exposure studies with mice bearing the D398N polymorphism are presently in progress to determine the direct effects of the polymorphism on lung cancer development. Preliminary data suggest that the polymorphism does not have a direct effect on sensitivity to tobacco smoke. New studies have shown potential for compounds that target multiple nAChR subunits at the same time to reduce lung cancer cell growth.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Eliot R. Spindel, M.D., Ph.D. NIH/National Cancer Institute R01 CA151601

Project Title: Development of Poly ICLC for Neuroprotection Against Ischemic Brain Injury
SPID: 4833
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: Brain ischemia is a leading cause of morbidity and mortality in the United States. We seek to develop therapeutics to reduce the extent of damage and functional impairment resulting from ischemic injury to the brain, an area of significant unmet medical need. In a mouse model of stroke injury we have demonstrated that the synthetic dsRNA, polyinosinic-polycytidylic acid stabilized by poly-L-lysine and carboxymethylcellulose (PIC, Hiltonol®), is a robust prophylactic neuroprotectant against ischemic injury. PIC given to mice one day prior to transient middle cerebral artery occlusion reduced the area of damage in the brain by ~95%. We recently published that interferon (IFN) receptor signaling is required for PIC-induced neuroprotection against mouse stroke, providing a potential mechanistic biomarker for predicting neuroprotective doses. Based on our studies in mice we hypothesize that preconditioning is medicated through systemic IFN secretion and consequent induction of interferon regulated genes in the brain and that these markers can be used to identify efficacious doses for translation to non-human primates (NHP) studies and ultimately human clinical trials.

Progress during the reporting period: This project has only just begun. So far only a few animals have been tested to ensure that they produce the expected immune response. The various assays have yet to be performed on the collected blood samples.

Publications resulting from the project:
None

Funding Sources:

Mary P.	Stenzel-Poore, Ph.D.	NIH/National Institute of Neurological Disorders & Stroke R21 NS094833

Project Title: Developmental Exposure to Maternal Obesity-Induced Inflammation Impacts Offspring Brain and Negative Valence Behaviors
SPID: 7508
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description: We propose that maternal obesity increases offspring exposure to inflammation, which leads to perturbations in the serotonin system, induces atypical brain connectivity, and increases risk for behavioral abnormalities. Aim 1 defines the long-term impact of exposure to inflammation induced by maternal obesity on offspring temperament and behavior. Aim 2 uses functional brain imaging to identify target regions for histochemical studies and observe the effect of inflammation induced by maternal obesity on brain wide functional neural networks. The use of this non-invasive technique allows our findings to be readily translatable to humans. Aim 3 identifies the site- specific changes in neuroanatomy that underlie the alterations in functional brain imaging and behavioral abnormalities.

Progress during the reporting period: We documented that exposure to maternal high-fat diet consumption increased anxiety in offspring at 11 months of age. Further, post-weaning high-fat diet consumption increased stereotypic pacing. Using resting state functional connectivity MRI we show atypical connectivity with the NAc to specified frontal cortices in offspring exposed to maternal HFD, which was associated with measures of anxiety. Using molecular techniques, we demonstrated a suppression of the central serotonin system in HFD offspring as evidenced by decreased mRNA expression of TPH2 (the rate limiting enzyme for central 5-HT synthesis). We also noted that post-weaning high-fat diet consumption decreased serotonergic projections to the nucleus accumbens and prefrontal cortex in male animals.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Elinor Sullivan, Ph.D. NIH/National Institute of Mental Health R01 MH107508

Project Title: Cognition in Rhesus Macaques in Relation to Age and Endocrine Status
SPID: 6670
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Universidad de Valparaíso, Chile
Universidad de Valparaíso, Chile
University of Munich, Germany

Project Description: In men and male rhesus macaques testosterone (T) and dehydroepiandrosterone (DHEA, an adrenal androgen precursor) show characteristic 24-hour patterns in the circulation, and both show significant age-related decreases. Although the exact physiological consequence of these hormonal changes is unclear, both T and DHEA are thought to act as intracrine substrates for estradiol (E2) synthesis in the brain. Therefore, it is plausible that their age-related decline negatively impacts brain function, either directly through androgen receptors and/or indirectly through estrogen receptors. Using the rhesus macaque as a translational animal model, we propose to test the hypothesis that age-related attenuation of circulating T and DHEA levels negatively impacts centrally-mediated physiological processes, including the circadian sleep-wake cycle and cognition. Moreover, we predict that physiological testosterone supplementation, designed to mimic the circulating 24-hour T pattern of young animals, will ameliorate these age-associated disorders. Specific Aim 1 will use a battery of cognitive tests to assess differences between young and old male rhesus macaques, and between old animals receiving extended treatment with "young" physiological levels of T or placebo. Cognitive assessments will include: 1) the delayed response test of spatial working memory, which is particularly sensitive to aging and prefrontal cortex dysfunction; 2) delayed non-matching-to-sample, a task probing primarily temporal lobe-based memory; 3) a visuospatial cueing test of visual attention that is estrogen-sensitive, and 4) performance in a novel maze to assess spatial learning and memory. In addition, sleep-wake cycles will be continuously monitored using Actiwatches, while morphological and biochemical differences will be examined in targeted brain areas by magnetic resonance imaging (MRI). Specific Aim 2 will use a series of biochemical and histochemical methodologies to elucidate the plasticity that occurs within the central nervous system (CNS) during male aging and after supplementation with T. Rhesus-specific gene microarrays and quantitative real-time PCR will be used to identify genes that are differentially expressed in the CNS among young males, untreated old and the T-treated old males. This integrative systems approach should help to identify plasticity in neurotransmitter systems and synapses and shed light on potential regulatory mechanisms. In situ hybridization, immunohistochemistry, enzymology, and hormone measurements will be used to further corroborate the results. Our current NIH grant (AG-029612) similarly examines the interacting impact of ovarian-adrenal interactions in perimenopausal female rhesus macaques. Consequently, data from the ongoing female study, combined with data from the proposed male study, will disclose important gender-based differences and help to elucidate their underlying mechanisms.

Progress during the reporting period: We found that estrogen supplementation was highly effective at maintaining cognitive function in old animals with low endogenous circulating estrogen levels, thus emphasizing the therapeutic potential of estradiol-based hormone replacement therapy (HRT) in early postmenopausal women. In contrast, supplementation with dehydroepiandrosterone (DHEA), an adrenal

steroid that shows a marked age-associated decline, was found to be ineffective. To help elucidate the cause of perturbed activity-sleep patterns of the elderly, we examined the orexin neuronal system of old animals with either active or sedentary activity patterns but found no significant difference in the number of orexin neurons; however, this does not rule out the possibility that reduced activity in the elderly stems from reduced orexin neuronal projections to arousal centers of the brain, such as the locus coeruleus, or from attenuated release of orexin.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Henryk F. Urbanski, Ph.D. NIH/National Institute on Aging R01 AG036670

Project Title: Establishment of a Primate Model for Menopausal Hot Flushes
SPID: 0783
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
University of Maryland Baltimore

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Menopause is an inevitable consequence of aging in women, and it affects the quality of life of millions of women all over the world. Menopausal symptoms including hot flushes, a decline in cognitive function, sleep disorders, depression/anxiety, cardiovascular disease, genitourinary conditions, and osteoporosis. These symptoms have been shown to be causally linked to a decline in circulating sex steroid concentrations, which is particularly dramatic after menopause. Consequently, menopausal symptoms are considerably more problematic in elderly women than in elderly men. The most immediate and unbearable symptoms of the menopause are hot flushes, which cause not only physical discomfort but also negatively impact mood and behavior and in general, the quality of life. Among current treatments of hot flushes, only estrogen therapy and hormone therapy (estrogens and progestins have satisfactory efficacies. Although estrogens prevent hot flashes, they have unwanted side effects in the periphery, including the stimulation of the uterus and breast, and the increased risk of cancer risk in these organs. Although there has been a great effort to develop safer estrogens, the lack of animal model(s) reminiscent for the symptoms, their pathomechanism, temporal pattern, etc. of women's menopause has had a tremendous negative impact on the success of this effort. We have recently shown that nonhuman primates, such as the rhesus macaque, undergo a menopausal process that is hormonally identical to that of women. They, therefore, hold great promise for studies aimed at elucidating the mechanisms that underlie hot flushes in women, and for the development of safe and effective therapies. Although the use of NHPs for studies aimed at developing novel treatments for menopausal symptoms is critical, due to high costs and technical problems, there have been only two studies utilizing them in the last 30 years. Our primary goal here is to evaluate a primate model of hot flush, by examining the effects of ovariectomy and subsequent treatment with estrogen, on adult rhesus monkey facial skin temperature, using infrared thermal imaging (FLIR T650sc) without restraining the animals.

Progress during the reporting period: Hot flushes are one of the most common complaints associated with the onset of menopause. Using thermal imaging cameras we are developing a remote automated system for non-invasively monitoring skin temperature changes across the 24-hour day. This will enable us to examine how thermoregulatory mechanisms become perturbed when circulating estradiol levels decline, and thus lay a foundation for the development of safe and effective therapies for hot flushes symptoms in postmenopausal women.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Henryk F.	Urbanski, Ph.D.	NIH/National Institute on Aging R21 AG050900
Istvan	Merchenthaler, Ph.D.	

Project Title: Modulation of Immune senescence by androgen treatment in aged male macaques
SPID: 0621
Unit/Division: Neuroscience
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University
University of California-Riverside

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
None

Project Description: Aging results in a progressive decline in immune function, which leads to increased morbidity and mortality related to infections. In men, increasing age also results in significant perturbations in the levels of circulating androgens (testosterone and dehydroepiandrosterone (DHEA)), which has been linked to sarcopenia, osteoporosis, cardiovascular disease and diabetes. Since sex steroid levels modulate immune function, it is likely that the age-related decline in androgen levels will also affect immune senescence. To gain a better understanding of the pleiotropic effects of androgen supplementation in aged men we have developed a novel paradigm of androgen supplementation in which testosterone and DHEA are administered to mimic the natural circadian rhythm of these hormones. This approach can restore both testosterone and DHEA levels to "youthful" 24-hour rhythms in aged male rhesus macaques. The overall goal of this project is to use this innovative paradigm to test the hypothesis that *physiological* testosterone and DHEA supplementation, designed to mimic the circulating 24-hour pattern of young animals, will ameliorate major biomarkers of immune senescence and improve T cell responses to vaccination.

Progress during the reporting period: In this study we evaluated the pleiotropic effects of physiological androgen supplementation in aged males on immune cell subset frequency and response to vaccination. The frequency of naïve CD4 and CD8 T cells declined in aged control animals and those of memory T cells increased, whereas the frequency of naïve and memory T cells remained stable in androgen-supplemented males and levels of inflammatory cytokines were lower than in the controls. Despite these changes, both androgen supplemented and age-matched controls exhibited lower levels of T and B cell response following vaccination compared to the young animals, indicating that physiological androgen supplementation can improve some aspects of immune senescence, but cannot restore age-related decline in immune function.

Publications resulting from the project:
None

Funding Sources:

Henryk F.	Urbanski, Ph.D.	NIH/National Institute on Aging R21 AG043896
Ilhem	Messaoudi Ph.D.	

Project Title: Consortium for AIDS Vaccine Research in Nonhuman Primates, F. Nonhuman Primate Core
SPID: 7413
Unit/Division: Division of Pathobiology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Harvard University
Emory University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester — Oregon Health & Sciences University

Other Core, Affiliate or Visiting Scientists associated with Project:

Excluded by Requester — Oregon Health & Sciences University
Oregon Health & Sciences University

Project Description:
The Nonhuman Primate (NHP) Core is a multicenter Core structured to provide the resources for purpose-bred animals and unique facilities and specialized investigative and technical expertise required to insure successful completion of the Consortium for AIDS Vaccine Research in Nonhuman Primates' (CAVR) multifaceted and extensive NHP research protocols. The Core's performance sites include the Oregon National Primate Research Center (ONPRC) Beaverton, OR, and the New England Primate Research Center (NEPRC), Southborough, MA). Nonhuman primates are unique, long-lived species that share many physiologic similarities with humans. These similarities include body composition, maturation, reproduction, metabolism and close genetic relatedness. Of NHPs available for research, Old World monkey species have the closest evolutionary relationship to humans and they are essential surrogates for biomedical research focused on major human diseases that lack suitable alternative animal models. The organization and function of the NHP immune system closely resembles that of humans. Because of these profound similarities, NHPs have long been recognized for their value as comparative models for human vaccine development, efficacy testing and safety evaluation, and for the investigation of fundamental questions in basic immunology. Because of the similarity of the immune systems of macaques and humans, preclinical HIV vaccine development is heavily dependent on the SIV and SHIV macaque surrogate models. While the value of the macaque-SIV model to advancement of AIDS vaccine research is unquestioned, NHP research is expensive, and requires highly specialized resources and personnel. The role of the NHP Core is to provide management and expertise necessary to affect an integrative, multidiscipline approach for the in vivo assessment of CAVR's NHP studies focused on identifying the early events following mucosal SIV infection and understanding the critical innate and adaptive immune mechanism(s) involved in early interdiction or control of infection.

Project Progress:
The NHP Core site at the Oregon National Primate Research Center (ONPRC) supported a total of 83 rhesus macaques (RM) for Focus 1 studies during the current funding period. These include 24 RhCMV/SIV vector-vaccinated RM that are currently in the CD8 subset-depletion/SIV challenge phase of the experiment (n = 12) or are awaiting subset-depletion and SIV challenge (n = 12). This study also includes 5 unvaccinated RM which are being SIV challenged as unvaccinated controls for the vaccinated RM currently being challenged. An additional 34 monkeys have been assigned to this project for vaccination and experimental use in Year 2. The remaining RM (n = 20) are animals that were used in the past year to ascertain the relative efficacy of strain 68-1 vs. 68-1.2 RhCMV vectors or were RhCMV/SIV vector-protected RM that were subjected to CD8+ or CD4+ cell depletion after the onset of protection, or are protected animals that are being followed for SIV reservoir clearance. All of the RM in this group that are viremic (non-protected) will be taken to necropsy in the coming months. Aviremic RhCMV/SIV vector-protected RM being followed for reservoir clearance will be ether be taken to necropsy to confirm reservoir clearance or will be re-challenged to assess the durability of RhCMV/SIV vector-mediated protection. Services provided by Core to laboratory investigators include assistance with 1) protocol development; 2) development of budgets germane to conduction of nonhuman primate studies; 3) assistance with the preparation of documents for submission to the IACUC and the IBC; 4) animal acquisition/selection; 5) animal housing and general husbandry; 6) experimental procedures and

specimen collection, processing and distribution (blood draws, tissue biopsies, bronchoalveolar lavage, vaccination, mAb treatment, SIV challenge, etc.), 7) clinical management; 8) necropsy studies; and 9) acquisition and management of animal demographic, physiologic, clinical, and pathologic data

Publication:
Nothing to Report

Funding Source:
Dan H. Barouch, M.D., and R. Paul Johnson, M.D. NIH/NIAID 5U19al095985

Project Title: Expanded SPF Rhesus Macaque Breeding Colony for AIDS Research
SPID: 3038
Unit/Division: Division of Pathobiology
Type of Project: Management/Other
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with Project:

Excluded by Requester — Oregon Health & Sciences University; Oregon Health & Sciences University; Oregon Health & Sciences University; Oregon Health & Sciences University

Project Description:
The Indian rhesus macaque (*macaca mulatta*) develops a disease that closely mimics human acquired immunodeficiency syndrome (AIDS) when infected by simian immunodeficiency virus (SIV) or chimeric simian-human immunodeficiency viruses (SHIV), and represents the best animal model for HIV infection. Preclinical vaccine development is heavily dependent on the SIV and SHIV rhesus macaque models. The value and utility of the model are markedly enhanced by improving the level of microbial and genetic characterization. Macaques free of ubiquitous viruses that are homologues of human viruses responsible for opportunistic infections are essential for a growing number of AIDS-related opportunistic infection models and for viral vaccine vector development based on these agents. The utility of macaque models for immunological research has been hindered by the unprecedented complexity of their major histocompatibility complexes. Comprehensive MHC genotyping has the potential to revolutionize the use of macaques in infectious disease research and to guide functional immunology studies. MHC-restricted cellular immune responses are key in protective immunity and resistance to infectious diseases. The comprehensive objective of the project is to increase the capacity of the ONPRC AIDS Research Expanded SPF Breeding Colony to provide genetically characterized Indian-origin rhesus macaques free of a broad number of enzootic and zoonotic agents to enhance the usefulness of the resource for cutting edge opportunistic agent and vaccine research.

Project Progress:
The colony census at the close of 2016 was 212 and comprised of 107 adult breeding animals, 42 juvenile replacements, 30 infants and 33 adult and juvenile animals available for research assignment. Thirty animals were assigned to research projects and one orphaned infant was released to the P51 Breeding Colony. Serologic screening of the colony was completed using a multiplex protein assay, Proprietary Info that we have been beta testing for the past three years. The colony remains free of the nine expanded SPF definition agents with the exception of lymphocryptovirus (LCV). Lymphocryptovirus-positive animals have been isolated from the colony and enhanced LCV serologic testing implemented in negative animals. A plan is in place to re-derive LCV negative infants from LCV-positives dams by weaning them at 180 days and serially testing them at monthly intervals. Several of the established expanded SPF breeding groups are scheduled to move to group housed outdoor sheltered enclosures in the spring of 2017.

Publication: (if none, indicate Nothing to Report)

Excluded by Requester

Funding Source:
Michael K. Axthelm, D.V.M., Ph.D. — NIH Office of the Director 5U24OD023038

Project Title: HIV reservoir clearance by allogenic, CCR5 knockout stem cell transplantation
SPID: 0057
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principle Investigator of the project/ Institutional affiliation:

Excluded by Requester	Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
None

Project Description (one paragraph): With 34 million people currently infected with HIV, stopping the epidemic remains imperative. Timothy Brown (also referred to as the Berlin patient) is the only person in history functionally cured of HIV. It is hypothesized that the allogeneic CCR5Δ32/Δ32 stem cells he received following myeloablative conditioning gave him a reconstituted immune system with a lasting resistance to HIV infection, allowing him to remain HIV-free in the absence of antiretroviral therapy. However, testing this hypothesis is difficult given that CCR5Δ32/Δ32 stem cell transplants are rare. Here, we propose to build an experimental, non-human primate model of allogeneic, CCR5 knockout stem cell transplantation to directly test whether immune reconstitution with CCR5-deficient cells following reduced-intensity conditioning can functionally cure SIV-infected cynomolgus macaques.

Progress during the reporting period (2-5 sentences):
We have successfully edited CCR5 in cynomolgus macaque embryos using CRISPR/Cas9 technology. We are currently performing embryo transfers into surrogate female cynomolgus macaques to induce pregnancies of CCR5 knockout offspring.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):

Excluded by Requester	Private Source

Project Title: A Cytomegalovirus-based Therapeutic Vaccine Against Oncogenic Human Papillomaviruses
SPID: 0177
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester
Oregon Health & Science University

Project Description (one paragraph): High-risk human papillomaviruses (HPV) cause cervical cancer, the second most common neoplasm among women globally, and a large proportion of oropharyngeal cancers. Although prophylactic vaccines to HPV are effective they have no therapeutic effect and thus do not benefit the millions of individuals already infected. Thus, there is both a medical need and a commercial opportunity for an HPV-targeting therapeutic vaccine. The ultimate goal of this project is therefore to evaluate in clinical trials whether sustained HPV-specific effector memory T cell (T_{EM}) responses elicited and maintained by spread-deficient cytomegalovirus (CMV) vectors can overcome the immunological ignorance observed in persistent HPV and terminate the multistep progression through cervical intraepithelial neoplasia (CIN) to cancer. CMV-vectored vaccines have demonstrated unprecedented effectiveness in non-human primate (NHP) model systems for HIV/AIDS including the first documented immune-mediated clearance of an established lentivirus infection. These comprehensive studies in NHP thus strongly suggest that CMV-vectors can provide a therapeutic effect against persistent viruses that integrate into the host genome such as HPV. CMV vectors are the only vaccine platform that indefinitely maintains high frequencies of T_{EM} in circulation and this is observed even with safety-enhanced vectors that have been modified to limit secretion, dissemination and reactivation. Moreover, CMV vectors can be engineered to induce robust immune response to novel epitopes, eliciting CD8+ T cells to sub-dominant MHC-I-, MHC-E- and MHC-II-restricted peptides not found in natural infection or upon conventional vaccination. Importantly, CMV vectors can be used repeatedly and in CMV-positive hosts without loss of immunogenicity, a critical feature given the high prevalence of CMV in the human population. Since failure to clear HPV infection correlates with weak and narrow T cell responses we hypothesize that the extensive breadth, frequency and continuous circulation through non-lymphoid tissues (including the cervix) of T_{EM} elicited by CMV will clear HPV-infected cells over time and provide lasting protection. In a proof-of-principle phase I study we demonstrated in a murine tumor model that murine CMV vectors induce T cells that eliminate tumor cells expressing the HPV oncogenes E6 and E7. In ongoing studies we further evaluate the breadth and restriction of T cell responses elicited by rhesus CMV to E6 and E7 of HPV in NHP. To advance the clinical development of a CMV-based immunotherapy for high risk HPV16 and 18 we propose here to design and construct E6/E7-expressing human CMV vectors displaying multiple safety features. We will compare two proprietary HCMV vector backbones containing patented modifications with respect to their in vitro growth characteristics and their ability to elicit HPV-specific T cell responses in NHP. The down-selected HCMV/HPV vaccine candidate will be further characterized for safety in NHP and used to prepare vector seed stocks for manufacturing under current good manufacturing practice (cGMP) regulations, thus enabling IND-filing and clinical testing.

Progress during the reporting period: We started to generate HCMV-based vectors expressing a fusion protein of HPV16 and HPV16 E6 and E7 proteins.

Publications resulting from the project: None

Funding Sources (PIs and sources):
Klaus Frueh, Ph.D. TomegaVax, Inc./NIH – 2R44 CA180177-02

Project Title: A Therapeutic Vaccine for Cervical Cancer
SPID: 3053
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project:
None

Project Description: The currently approved HPV vaccines are designed to be prophylactic, exhibiting no significant therapeutic effect. This leaves millions of women who are already infected and those not receiving vaccination prior to exposure to HPV at risk. A successful CMV-vectored HPV vaccine will in effect convey both therapeutic anti-HPV and prophylactic anti-cervical cancer functions. It would be made available to HPV-positive individuals to eliminate residual infected or reactivating HPV-infected cells and those expressing HPV antigen progressing along the path to cervical cancer. While the vaccine may not entirely eliminate HPV, we believe that the unparalleled T cell response induced by CMV will be able to prevent spread and potentially reverse the course of cancer progression. The goal of this study is to characterize the T cell response elicited by RhCMV/E7E6 over time in the two well-characterized Rhesus CMV vector backbones. Each of these vector backbones elicits a unique MHC presentation profile and depth of epitope coverage resulting from the presence or absence of immune-modulatory genes within the vector. We will monitor the T cell response to the entire fusion protein, using a pool of overlapping peptides, as well as the response to previously identified immunodominant epitopes.

Approach: We will characterize the T cell response elicited by the RhCMV-HPV vectors to each of the antigens with respect to specificity, kinetics, quantity and phenotype. All animals used in our studies will be naturally infected with RhCMV at the onset of the experiment, thus recapitulating the high CMV prevalence in the human population. Animals will be randomized with respect to weight and age. The first group, Cohort 1, of 4 female RM will receive a subcutaneous (SC) dose containing 1x106 plaque-forming units (PFU) of each of the 68-1RhCMVΔUL78ΔUL82/HPV vectors during weeks 1, 8 and 16. Cohort 2 (n=4) will receive the corresponding 68-1.2RhCMVΔUL78ΔUL82/HPV vectors. Blood will be collected from these cohorts starting three weeks before immunization and then at bi-weekly intervals thereafter to monitor development of HPV-specific immune responses. CD4+ and CD8+ T cell responses to the HPV proteins will be quantified by intracellular cytokine staining (ICCS) using overlapping, consecutive 15-mer peptide mixes constituting the respective antigens. This assay will be applied to lymphocytes obtained from PBMC. In addition to measuring the magnitude of total Ag-specific CD4+ and CD8+ T cells in PBMC as well as their functional and phenotypic characteristics, we will also verify the “unconventional” vs. “conventional” epitope targeting of CD8+ T cells obtained from cohorts 1 and 2, respectively. This will be accomplished by using “blocking” mAbs specific for MHC-I, MHC-II and HLA-E, and the invariant chain-derived, MHC-II-specific binding peptide CLIP to inhibit Papillomavirus-specific CD8+ T cell responses in PBMC as we have done previously. We will measure the breadth of the T cell response by comprehensively de-convoluting the whole specific CD8+ T cell response to at least one HPV antigen down to individual 15mer peptide responses in at least 2 animals per vector backbone.

Progress during the reporting period: This project has been concluded successfully. We were able to demonstrate that CMV vectors elicit T cell responses to all four proteins included in a fusion protein of HPV16 E6, HPV16 E7, HPV18 E6 and HPV18 E7. Moreover, we were able to elicit both conventional and unconventional CD8+ T cell responses to the HPV proteins.

Publications resulting from the project: None.

Funding Sources (PIs and sources):
Excluded by Requester | Private Source

Project Title: A Human Cytomegalovirus-based Immunotherapy for HIV-1
SPID: 5018
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principle Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph):
The ultimate goal of this project is to develop an immunotherapy for human immunodeficiency virus (HIV)-1 based on a spread-deficient cytomegalovirus (CMV)-derived vaccine expressing "tailored" antigens designed for maximal coverage of clade B epitopes. In non-human primate models, rhesus CMV-vectored vaccines demonstrated unprecedented protection against highly virulent simian immunodeficiency virus. In this proposal, we will therefore test the hypothesis that a tailored vaccine cocktail selected from a small vaccine panel containing HIV antigens optimized for T cell epitope coverage of a given HIV clade is superior with respect to inducing "relevant" T cell responses as compared to non-tailored approaches. We will use novel algorithms to design tailored antigens that maximize epitope-matches and we will insert these antigens into a new human CMV-vector backbone developed at TomegaVax during phase I of this proposal. We will monitor epitope-specific T cell responses against specific HIV strains using a recently developed NHP model for HCMV. Based on these results, we will design our final vaccine cocktail. To facilitate manufacturing of HCMV vectors under good manufacturing practices (GMP) we will generate a complementing master cell bank based on preliminary data showing, for the first time, HCMV growth in a cell type previously used for the manufacturing of unrelated viral vaccines. Upon completion of this project, we will have designed, characterized, and developed a manufacturing strategy to generate clinical grade HCMV/HIV vector products.

Progress during the reporting period: Recent data suggest that therapeutic vaccination against SIV requires canonical T cell responses. Based on these results, we have now redesigned our HCMV vectors to lack the US11 gene. Upon completion of vector construction, we plan to study the immune response to these vectors in monkeys.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Klaus Frueh, Ph.D. NIH/NIAID AI100343

Project Title: Evasion of Antigen Presentation by Rhesus Cytomegalovirus
SPID: 9457
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):

Excluded by Requester — University of California, Davis
Oregon Health & Science University
Oregon Health & Science University

Project Description: Human cytomegalovirus (HCMV) is a ubiquitous herpesvirus that persists for life. Although HCMV is generally benign in healthy individuals, the virus can cause disease in immunocompromised populations and HCMV is the leading infectious cause of congenital disease in newborns. The reasons why the immune system is able to control, but unable to eradicate, HCMV are unknown. Our main hypothesis is that immunomodulatory CMV genes, particularly modulators of innate and adaptive cellular immunity, enable the establishment and maintenance of persistent infection in immunocompetent individuals. A better understanding of these immune modulatory processes will be essential for the development of vaccines against HCMV as well as for the optimization of CMV-based vaccine vectors that have recently assumed center stage in the development of vaccines against HIV and TB. Our work in non-human primate models of CMV infection revealed a series of unexpected results that indicate a complex relationship between CMV and the innate and adaptive cellular immune response involving viral evasion, viral recruitment and viral manipulation of the host's immune response. Particularly novel is our finding that CMV-encoded genes enable the virus to control the epitope specificity of the adaptive, CD8+ T cell immune response. We discovered that wildtype RhCMV and HCMV elicit MHC-I-restricted CD8+ responses that are exclusively directed to sub-dominant or "non-canonical" epitopes. However, in the absence of the MHC-I inhibitors Rh189 (in RhCMV) or US11 (in HCMV), additional CD8+ T cells are induced that recognize "canonical" MHC-I epitopes, i.e., epitopes that predominate the CD8+ T cell responses elicited by unrelated viruses or vaccines not based on CMV. Since such stringent control of T cell specificity has not been observed before for any infectious agent, we will elucidate why, how and where primate CMVs prevent the induction of canonical CD8+ T cells. In Specific Aim 1 we will test the hypothesis that canonical CD8+ T cells are particularly efficient in controlling viral dissemination and, therefore, rhesus and human CMV developed specific measures to both prevent their priming and to escape their control. In Specific Aim 2 we will investigate which structural features enable Rh189 to inhibit the induction of canonical CD8+ T cells in comparison to related MHC-I-inhibitory proteins of the same gene family that do not prevent canonical CD8+ T cell priming. In Specific Aim 3 we will test the hypothesis that spreading of Rh189-deficient RhCMV to myeloid cells is required for the induction of canonical CD8+ T cell by a direct priming mechanism. We will examine the role of viral dissemination by deleting Rh189 from single cycle viruses. Moreover, by inserting targeting sites for cell type-specific microRNAs into the 3'-UTR of Rh189 we will identify which cell types need to be infected to enable canonical CD8+ T cell priming in the absence of Rh189, The results of this work are expected to provide new insights into the control of non-canonical CD8+ T cell targeting by CMV that will ultimately lead to improved vaccines for HCMV and improved vaccine vectors based on HCMV.

Progress during the reporting period: We are in the process of generating RhCMV with modified Rh189 genes. Specifically, we are generating chimeras with Rh182 and Rh185. Moreover, we will insert mir-targeting sites into the 3-UTR of Rh189 to determine which cell types are responsible for the induction of canonical, MHC-I-restricted CD8+ T cells.

Publications resulting from the project.
None at this time

Funding Sources:
Klaus Frueh, Ph.D. NIH/NIAID 5R01AI059457

Project Title: Immunological Characterization of a Novel HCMV Vaccine Platform
SPID: 4091
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
TomegaVax, Inc.

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester
Oregon Health & Science University

Project Description: Rationale: Funded by an NIH SBIR, TomegaVax has generated a molecular clone from a novel clinical HCMV isolate derived from the breast milk of a healthy mother with a healthy, asymptomatic infant who showed no signs of HCMV infection. Our clone, VGTI-1, differs from currently available HCMV clones that were derived from symptomatic children or adults. The fact that VGTI-1 was literally fed to a baby should facilitate regulatory approval of a VGTI-1-derived attenuated vaccine or vector. The goal of the project is to establish VGTI-1 as a novel vaccine vector platform. This project takes advantage of our preliminary observation that clinical strains of HCMV-expressing heterologous antigens (SIV) were capable of inducing a lasting T cell response in RM. Given the known species-specificity of CMV this result was quite unexpected. While HCMV infection of RM will most likely not be a suitable model for HCMV pathogenesis, it will allow us to address some fundamental questions regarding the translatability of results obtained in the RhCMV model to HCMV. Specifically, we can determine whether HCMV is capable of super-infection and whether this is dependent on inhibition of antigen presentation conveyed by the viral genes US2-11 as we reported for RhCMV (Hansen, Science 2010). Monitoring serial HCMV infection of RM is facilitated by the insertion of immunological markers. In this project we will use antigens derived from HSV2. This will have the added advantage that vectors generated as part of the HSV2 project funded by Takeda will be examined in vivo. The two projects thus dove-tail with each other. Upon completion of this two-year program we anticipate to have established whether HCMV is capable of super-infection and whether this is dependent on viral inhibition of antigen presentation.

Progress during the reporting period: This project has been completed. We demonstrated that the novel clinical isolate VGTI-1 was able to superinfect animals previously infected with the same vector. These results are important for vaccine development since they show that HCMV-based vaccines using VGTI-1 can be used repeatedly and in individuals that are already immune to HCMV.

Publications resulting from the project:
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: Safety and Immunogenicity of Single-Cycle HCMV in Non-Human Primates
SPID: 4092
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester TomegaVax, Inc.

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester Oregon Health & Science University

Project Description: The ultimate goal of this project is to design and evaluate the engineered safety features built into a vaccine against human cytomegalovirus (HCMV). HCMV pathogenesis is both the reason for developing an effective vaccine and a serious safety concern to be addressed in the design of CMV vectors. HCMV can cause serious disease complications in immunosuppressed individuals, particularly solid organ and bone marrow transplant recipients, and this virus is the leading infectious cause of congenital birth defects. Recently, single-cycle CMVs were shown to induce long-term immune responses comparable to wild-type (WT) CMV in mice Excluded by Requester and Unpublished (our unpublished observations). This suggests that a rationally designed single-cycle HCMV vaccine may be effective against disease caused by this virus. Particularly, this attenuated vaccine should prevent congenital infection and disease in transplant patients, without compromising the immunogenicity needed for protection. The rational design aspect of attenuation is in stark contrast to previous approaches that used traditional methods of tissue culture adaptation. The resulting CMV vaccine (strain Towne) was unable to generate the level of immune response observed in naturally infected individuals, and duration of the response was relatively short-lived. In contrast, preliminary data in rhesus macaques (RM) using rhesus CMV (RhCMV) demonstrates that spread-deficient and single-cycle RhCMV can induce long-term immunity. This project takes advantage of our preliminary observation that clinical strains of HCMV expressing heterologous antigens (SIV) were capable of inducing a lasting T cell response in RM. Given the known species-specificity of CMV this result was quite unexpected. While HCMV-infection of RM will most likely not be a suitable model for HCMV pathogenesis, it will allow us to address some fundamental questions regarding the translatability of results obtained in the RhCMV model to HCMV. Specifically, we can address the question whether single-cycle HCMV is capable of inducing lasting T cell responses as observed for mouse and rhesus CMV and, if so, whether the T cell and antibody response induced by single-cycle viruses prevents super-infection by virus lacking MHC-I inhibitory genes. Monitoring HCMV infection of RM is facilitated by the insertion of immunological markers. In this project we will use antigens derived from HSV2. These vectors, generated as part of the HSV2 project funded by Takeda, will dovetail to provide in vivo data for these constructs. Upon successful completion of this program we will establish whether single-cycle HCMV can recapitulate the immune response observed with WT HCMV, and clear the path to clinical testing of single-cycle HCMV vectors to prevent HCMV disease.

Progress during the reporting period (2-5 sentences): This project was completed. We demonstrated that single cycle vectors based on the novel clinical isolate VGTI-1 are able to elicit lasting immune responses in monkeys that are similar to replication competent VGTI-1. These results are important for the development of HCMV-based vectors since they show that safety can be uncoupled from immunogenicity.

Publications resulting from the project:
None at this time

Funding Sources:
Excluded by Requester Private Source Private Source

Project Title: Evaluating Bromodomain Inhibitors for HIV Cure Therapy
SPID: 9998
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester
Oregon Health & Science University

Project Description:
In this study, we are evaluating whether a class of drugs known as bromodomain and extra-terminal domain inhibitors (BETi) can reverse viral latency in Simian Immunodeficiency Virus (SIV)-infected rhesus macaques that are on effective Antiretroviral Therapy. This proof of concept pilot study is designed to evaluate the safety and potential use of BETi as latency-reversing agents for HIV cure.

Progress during the reporting period:
The account for this study has not been set up as the study is pending institutional biosafety approval. At this time, there is no progress to report.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):
Excluded by Requester
Private Source

Project Title: Epitope-Targeted Vaccines for HIV-1 Prevention
SPID: 1795
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
New York University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Mt. Sinai School of Medicine
Molsoft, L.L.C.
Oregon Health & Science University
New York University
Mt. Sinai School of Medicine

Project Description: The recent RV144 clinical vaccine trial induced modest and transient protection in healthy individuals against HIV-1 infection, and is considered to be a marginal success. We and others have demonstrated that, by focusing the Ab response on V3, cross-clade neutralizing Abs are elicited which are detectable >1 year after immunization. Therefore, we now propose to extend the platform we previously developed for designing and developing V3-scaffold immunogens in order to create and test new epitope-scaffold protein immunogens that will focus the Ab response on two additional sites of vulnerability in Env: the V2 loop and the cluster of quaternary neutralizing epitopes (QNEs) composed of portions of V2 and V3. The HIVRAD will be composed of: Project 1: Vaccines to Induce Functional Abs Targeting the V2 Loop; Project 2: Rational Design of Immunogens Targeting the HIV-1 V2/V3 Quaternary Neutralizing Epitopes; Core A: Administrative Core; Core B: Protein Production Core; and, Core C: Animal Studies Core. The epitope-scaffold immunogens to be developed can be used individually or in combination, and will constitute powerful new tools for inducing broad and potent protective Abs. Many of the participants have worked together for >20 years to develop and characterize >100 human mAbs to HIV and other pathogens. Recently, the team has worked collaboratively and synergistically, preparing and analyzing >25 crystals of monoclonal Abs (mAbs) and mAb/epitope complexes, developing DNA Env primes and epitope-scaffold immunogens, and performing immunization experiments. Our experience places us in a strong position to extend our studies to epitopes that only recently have been recognized as important for protection from HIV infection. By the completion of the proposed Program, we plan to have identified epitope-targeting immunogens and immunization protocols that will generate Abs with protective anti-viral functions directed specifically toward the conserved regions of the V2 loop and the V2/V3 quaternary neutralizing epitopes of HIV-1 gp120.

Progress during the reporting period: In the last year, we have immunized macaques with two promising V2 scaffolds and have generated moderate antibody responses, including Tier 1 neutralizing antibodies. These data will help to inform the next generation of scaffolds for testing.

Publications resulting from the project.
Excluded by Requester

Funding Sources:
Xiangpeng Kong, Ph.D. New York University School of Medicine/ National Institute of Allergy & Infectious Disease P01 AI100151

Project Title: HIV B-Cell Lineage Vaccine Design Based on Replicating Ad and Env Protein in NHP
SPID: 1054
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester PaxVax, Inc.

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester Oregon Health & Science University
Oregon Health & Science University

Project Description:
Development of a HIV-1 vaccine to prevent, or reduce, the rate of infection remains a high priority. The lessons from numerous failed and the recent modestly successful RV144 Thai trial indicate the need to advance new approaches to HIV-1 vaccine design with the goal of inducing immune responses that are the appropriate type, quality, magnitude and active in the appropriate sites in the body. Our strategy is to build upon the RV144 study which implemented a canarypox vector prime (T and B cell immunogens) followed by a recombinant envelope (Env) protein boost immunization. The primary objective of this project is to assess an immunization strategy to induce broadly neutralizing antibodies (BnAbs) in nonhuman primates based on vaccines containing recombinant simian adenovirus (SAd) viral vectors and HIV-1 Env glycoproteins selected from sequential isolates of an HIV-1-infected individual that ultimately developed CD4-binding site BnAbs. The premise of this approach is to engage naive B-cell receptors of BnAbs, and continue to immunize with select immunogens to stimulate somatic mutation that leads to induction of BnAbs. Our central hypothesis is that the combination of replicating adenovirus persistently expressing Envs selected at critical junctions during development of BnAbs will be efficient vaccine immunogens for inducing protective antibodies against HIV-1 infection. It will be evaluated whether serial or swarm immunization with SAds expressing Envs delivered with matching Env glycoprotein immunogens can induce BnAbs. The recombinant SAdEnv vectors will be assessed for immunogenicity in rabbits before proceeding to NHP studies in Year 2. Both antibody (binding, neutralizing, and ADCVI) and Env-specific T cell immune responses will be evaluated. Completion of this SBIR II program may provide sufficient data to determine the utility of the replicating adenovirus vector system for expressing B cell lineage Envs and potentially could yield an experimental vaccine suitable for clinical development.

Progress during the reporting period:
We have completed the immunogenicity phase of this project and included a final boost with SOSIP Env immunogens in the 18 animals under study. Animal samples have been shipped to Duke University and final antibody and T cell assays are in progress at OHSU.

Publications resulting from the project.
None at this time

Funding Sources:
Jeffery Alexander, Ph.D. PaxVax/ National Institute of Allergy & Infectious Disease 5R44AI102787-04

Project Title: Targeting IgM Memory To Establish Protective B Cell Reponses in HIV
SPID: 6617
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester Rochester University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester Oregon Health & Science University
Oregon Health & Science University

Project Description:
Inducing a protective antibody (Ab) response to HIV Envelope (Env) is a major strategy for vaccine-mediated prevention. Defining the developmental queues of bNAb (broadly neutralizing antibody) development and recapitulating their induction and persistence by vaccination remains elusive. Our work has begun to define the B cell features associated with HIV bNAb and protection in humans and non-human primates. The primary focus for studying HIV-specific B cell responses thus far has been IgG and IgA, however relatively minimal investigation has been focused on the contribution of IgM memory to effective HIV-specific responses. Within the human IgM memory population, subsets have been identified in blood including “marginal-zone-like” and “B1-like” B cells, however the inter-relationships between these functionally and phenotypically overlapping populations remains unclear. B cells at mucosal sites include abundant IgM producing antibody-secreting cells (ASC), and half of the mucosal IgA is derived from B-1 B cells. Our previous work has demonstrated the unique characteristics of HIV Env-specific IgM memory B cells in humans and its association with the incidence of bNAbs in HIV-infected subjects and broader Env reactivity in HIV vaccinees. Numerous features of IgM memory suggest that with adequate engagement it could be a valuable contributor to an effective B cell response to HIV. Additionally, IgM antibodies have been shown to contribute to neutralizing Ab responses against many other viruses. The ability of IgM memory B cells to differentiate upon antigen-stimulation into IgG (and IgA) memory and ASC populations may contribute to qualitatively distinct Ab responses. Our central hypothesis is that immunization strategies that induce robust Env-specific IgM memory responses will enhance protection from HIV infection. This hypothesis will be tested by the following specific aims: 1) to optimize strategies for the induction of HIV Env-specific IgM memory utilizing in vivo mouse experiments, 2) to determine the protective activity of HIV Env-specific IgM responses in rhesus macaques through an immunogenicity and challenge experiment and 3) to characterize human HIV Env-specific IgM memory through in-depth phenotypic and functional profiling. This project will significantly advance our insight into preventing HIV transmission and the mechanisms that control the development of protective humoral responses to HIV.

Progress during the reporting period: The work during this period has been performed in Rochester, and we have provided HIV Envelope protein antigens for this work to Excluded by Requester We are in the process of preparing some modified Envelope constructs for this project to use in the coming year.

Publications resulting from the project.
Excluded by Requester

Funding Sources (PIs and sources):
James Kobie, Ph.D. University of Rochester / NIH National Institute of Allergy & Infectious Disease R01 AI007787

Project Title: Passive Transfer Studies in Rhesus Macaques to Investigate the Efficacy of Protection of Anti-V2 HIV-1 mAb
SPID: 0020
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Excluded by Requester **Other Core, Affiliate or Visiting Scientists associated with the Project:**
Excluded by Requester
Mt. Sinai School of Medicine
Oregon Health & Science University

Project Description:
Traditionally, PBMC based 90% neutralization titers have been used for estimating *in vivo* protection in the macaque mucosal challenge model. While neutralization has been associated with antibodies shown to protect in this setting, there is evidence that yet, undefined mechanisms may lead to protection against infection. The immune correlates of the human HIV vaccine trail in Thailand (RV144) revealed a reduction in infection risk associated with IgG antibodies binding to scaffolded HIV1 V1V2, but avidity, ADCC, or neutralizing antibodies did not significantly predict HIV1 infection rate. In order to determine if a V2-specific antibody can protect against SHIV repeated challenge in the absence of neutralizing capability, we will conduct a passive transfer experiment in twelve rhesus macaques. If protection efficacy is achieved, this study will set the stage for future studies to explore undetermined mechanisms that may contribute to protection. The mAb 697D is a valid candidate for testing the protective efficacy of V2 antibodies because it is highly cross reactive with many strains of HIV1 and reacts with gp70V1V2 scaffold which was the only significant inverse correlate of risk identified in RV144. To choose a challenge virus, we will test available SHIVs for neutralization *in vitro* by mAb 697D before starting the *in vivo* phase of the study. Once the *in vivo* halflife of mAb is established, we will begin the passive transfer study to evaluate the protection efficacy of the V2 mAb compared to an isotype control antibody controls. A dose of 50 mg/kg of V2 mAb will be given subcutaneously before the first SHIV exposure and continuing at intervals to be determined from the PK study. Based on animal titration data of the SHIV stock chosen as the challenge virus, we will use a dilution of virus that is expected to infect all control animals within 46 inoculations delivered intrarectally (*i.r.*). Repeated *i.r.* exposures will be applied twice per week. Regular blood draws will monitor for plasma virus and passively transferred antibody concentrations. After a total of 12 challenges, we will assess whether mAb 697D provides protective benefits compared to controls.

Progress during the reporting period: We have shown in the first round of testing small sample sizes (n=6) that the IgG1 anti-V2 mAb 830A, which was more potent than 697D in vitro, is partially effective in controlling viremia and the establishment of viral reservoirs. We have completed expanded challenge studies with the IgG1 form as well as an IgG3, versus a dengue virus human mAb control antibody (n=12 per group), and detailed tissue analyses are completed and undergoing statistical analysis for significant differences.

Publications resulting from the project.
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: Persistent Modulation of Microbiota to Enhance HIV Vaccination
SPID: 8456
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester University of Washington

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
None

Project Description (one paragraph): Given the highly complex nature of HIV, including the challenges of protecting mucosal surfaces from transmission and high variability of the virus, developing innovative vaccination strategies is crucial. Indeed, despite extensive research, a fully efficacious vaccine to prevent HIV transmission remains elusive, and there is limited understanding of correlates of protection, particularly at mucosal surfaces. Recently, the importance of the microbiome in mucosal immunity has become appreciated, and here we hypothesize that we can exploit the microbiome to induce protective vaccine responses. Here we propose a novel HIV vaccination approach that uses persistent probiotic therapy as an adjuvant to enhance immunogenicity and protection induced by a potent combined vaccine strategy. Our vaccine consists of concurrently administered SIV (gag p55) and HIV (gp140) DNA + HIV gp140 trimer protein. Recent studies have provided evidence that combining DNA and protein for vaccination elicits increased vaccine specific cellular and humoral immunity, In addition, our preliminary studies provocatively demonstrated that probiotic treatment in SIV-uninfected macaques results in increased T follicular helper cells in lymph nodes, IgA expressing B cells in mucosal tissues, increased antigen presenting cells in mucosal tissues, and increased multifunctional T cells, as well as decreased proliferation and activation of CD4+ T cells. Thus, we hypothesize that combining the potent immunomodulatory effects of beneficial microbiota manipulation with a novel vaccine platform that should induce robust cellular and humoral immunity will result in unprecedented high levels of vaccine specific responses in both mucosal and systemic tissues, resulting in protection from rectal SHIV challenge. There are several innovative aspects of this vaccine design, including: (i.) Modulation of the microbiota with probiotics to enhance mucosal vaccine responses; (ii.) utilization of a novel dual SHIV DNA-HIV gp140 protein vaccination platform; (iii.) novel measurements of potential vaccination correlates will be measured including microbiome morphogenesis, homeostatic mucosal responses, innate immune responses, and T follicular helper and germinal center B cell responses, in addition to standard correlates of vaccination (antibody and T cell responses).

Progress during the reporting period: We participated in regular conference calls and provided DNA expression vectors and recombinant trimeric Envelope glycoproteins based on subtype C immunogens for this first set of macaque immunogenicity and challenge experiments. These experiments are comparing macaques receiving probiotics and those that are not for serological and mucosal immune responses and vaccine protection. We have measured potent binding and Tier 1 neutralizing antibodies after vaccination.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):
Nichole Klatt, Ph.D. University of Washington and WaNPRC / National Institute of Allergy & Infectious Disease NIH R01AI120712

Project Title: Programming HIV Immunity for Broadly Neutralizing Antibodies by Vaccination
SPID: 8064
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester

Vanderbilt University
Oregon Health & Science University
Vanderbilt University
Oregon Health & Science University
Fred Hutchinson Cancer Research Center
Seattle Biomedical Research Center
PaxVax
University of the Witwatersrand
Johannesburg, South Africa

Project Description: The overall goal is to design novel vaccines based on env genes from HIV-infected subjects who develop broad NAbs (bNAbs) in an accelerated fashion. In Project 1, we identified multiple HIV-1 infected, ART-naive subjects who developed both autologous and bNAbs within the first 2-3 years of infection and characterized the epitope-specificities of these bNAbs. In Project 3, we defined changes that accrue to the subjects' cloned quasispecies Envs from initial infection through broadening. We hypothesized that specific diversification of the quasispecies would drive maturation of bNAbs in vivo, by presenting new epitopes in escape variants, or by focusing the response on more conserved epitopes. In Project 2, we characterized the temporal development and maintenance of functional T-helper (Th) responses that allow B cells to respond to the changes in the Env proteins produced by the patient's quasispecies variants in Project 1. We adapted a novel technology to sort Env-specific B cells from these subjects and characterized NAbs that neutralize diverse isolates, to refine our choice of Env immunogens. Vaccines were based on natural longitudinally derived env variants that arise during broadening. Variants were used singly and in mixtures to "program" humoral immunity in vaccinated rabbits and macaques to elicit broader NAbs than other vaccines to date.

Progress during the reporting period: Clade B immunogens elicit potent Tier 2 autologous neutralizing antibodies and Env-specific Tfh cells in macaques. We have completed a SHIV challenge study that compares Clade C Envs delivered by different vaccine regimens. Combination DNA+protein vaccines have been compared with simian adenovirus 7 vectors plus protein vaccines, each delivering Gag and Env antigens. Data are under statistical analyses for completion of manuscripts.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Funding Sources:

Nancy Haigwood, Ph.D. National Institute of Allergy & Infectious Disease P01AI078064

Project Title: Protective role of V2 antibodies induced at mucosal tissues in macaques
SPID: 1053
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
New York University School of Medicine

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University

Project Description:
The role of antibodies (Abs) in preventing infection with HIV-1 has been firmly established by a multitude of passive immunization experiments in several animal models. In recipients of the RV144 vaccine, high levels of plasma anti-V2 Abs correlate inversely with reduced risk of HIV-1 infection. However, whether the V2 antibodies directly protect against infection or whether the V2 Abs correlate with vaccine efficacy remains unknown. To address these questions, we propose to study the various inhibitory functions of anti-V2 monoclonal Abs (mAbs) and the mechanistic effect of vaccine-induced mucosal anti-V2 Abs in rhesus macaques, i.e., whether these antibodies protect against SHIV challenge alone or in cooperation with other anti-HIV-1 envelope (Env) antibodies. We hypothesize that anti-V2 Abs inhibit the gp120/α4β7 integrin interaction and block binding of HIV-1 to Th17 cells expressing α4β7, CD4 and CCR5. As Th17 cells are mainly located in the mucosal tissues, we predict that induction of anti-V2 Abs locally increases the titer of V2 Abs in mucosal secretions and more efficiently blocks virus binding to target T cells, resulting in protection against HIV-1 infection. To test this hypothesis, we will immunize rhesus macaques with V1V2 fusion protein to induce mucosal and systemic anti-V2 Abs compared to gp120 Abs and challenge the animals with SHIV to determine the protective potentials of V2 Abs. The possible inhibitory functions of anti-V2 Abs, including neutralization, Fc-mediated activities and inhibition the gp120/α4β7 interaction, will be tested using human V2 mAbs produced in our lab in both isotypes IgG1 and IgG3 (Aim 1). These studies will determine the type and range of inhibitory activities mediated by vaccine-induced mucosal and/or systemic anti-V2 Abs. The macaques will be immunized using gp120 DNA prime and protein boost including V1V2-fusion protein administered at mucosal tissues, systemically and compared to systemic gp120 with matching sequence of CM244 virus. The most representative inhibitory functions defined in Aim 1 will be used to monitor the development of vaccine-induced V2 Abs in serum and mucosal secretions (Aim 2). To determine vaccine efficiency, the immunized macaques with detected anti-V2 Abs in mucosal vaginal and rectal secretions will be challenged by multiple low doses of vaginal SHIV-BaL inoculation (Aim 3). The proposed study is designed to test whether anti-V2 antibodies have ability to protect from SHIV challenge or reduce the viral load and whether mucosal V2 antibodies have any advantage over systemic V2 antibodies. The results of this research will have practical consequences to inform the design of HIV vaccine to induce either a high titer of systemic anti-V2 Abs along with other Abs or include intranasal immunization to induce mucosal anti-V2 Abs to increase vaccine efficacy.

Progress during the reporting period: We have completed preparation of immunogens and have initiated the first set of macaque immunogenicity studies in December 2016.

Publications resulting from the project.
None at this time

Funding Sources:
Miroslaw Gorny, Ph.D. New York University School of Medicine/ National Institute of Allergy & Infectious Disease 5R01AI112546-02

Project Title: Reducing Latent Viral Reservoirs in Infant Macaques
SPID: 0459
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester — Oregon Health & Science University

Project Description: While ART is the standard of care for HIV+ mothers and their infants who are exposed to infection risk before, during, and after birth, the field has not addressed an extension of ART therapy that could abate virus expansion and eliminate established latent viral reservoirs. The objective of this project is to adapt an established model of persistent pathogenic SHIV infection in newborn rhesus macaques to study the effects of very early therapies with or without ART. Passively transferred NAbs can provide sterilizing immunity in nonhuman primate models and when present early in infection can change the course of SIV or SHIV infection stabilizing the adaptive immune response to prevent viral divergence. The central hypothesis of this research is that therapeutic treatment with potent neutralizing human monoclonal antibodies (NmAbs) will result in highly controlled or undetectable viral reservoirs in babies born to HIV-infected mothers. Newborn rhesus macaques, when infected orally with SHIV-SF162P3, develop widely dispersed and rapidly diverging viral quasispecies in blood and tissues within the first few days to weeks of infection resulting in high and persistent viremia. However, in newborn macaques that receive passive treatment with neutralizing IgG, disease and death is prevented demonstrating that NAbs present during acute infection can alter the dynamics of infection and reduce viral spread and establishment of the reservoir. Once the timing and characterization of latent viral pools are characterized, the project will define the roles that NmAbs play in (i) controlling virus load, (ii) affecting the size of the integrated viral reservoir, and (iii) influencing the development of effective adaptive immune responses. The project will also examine whether NmAb cocktails can further augment the ability of ART, resulting in more potent and durable reduction in latency.

Progress during the reporting period: We have shown that passive transfer of a dual cocktail of human neutralizing mAbs PGT121 and VRC07-523 given 24 hours after oral viral exposure in one month olds leads to complete viral clearance within 14 days. There is no evidence of adaptive immunity or establishment of permanent viral reservoirs, thus establishing a new paradigm for antibody-based therapy. Additional work this year showed that delaying treatment to 48 post exposure again results in profound viral control and very low virus integration, but results were more variable. We are working to expand these studies with ART.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Funding Sources:
Nancy Haigwood, Ph.D. National Institute of Child Health & Human Development R01HD080459

Project Title: Targeting Neutralizing Epitopes in the MPER of HIV Env
SPID: 3207
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Emory University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Emory University
Simon Fraser University

Project Description: The spread of HIV infection is a major threat to public health worldwide and the development of an effective vaccine strategy is of the highest significance. Currently, the greatest and most pressing challenge to AIDS vaccine research is to develop a vaccine strategy that can induce strong and broadly neutralizing antibodies (bNAbs) against HIV. We have assembled a team of investigators who possess specialized expertise in antigen design, B cell analysis, virology, and vaccine immunology to develop an effective vaccine strategy to induce bNAbs against the conserved epitopes in the membrane-proximal external region (MPER) of the HIV envelope glycoprotein (Env), which are targets for several potent and broadly neutralizing monoclonal antibodies against HIV. This collaborative effort will explore strategies to overcome major obstacles that hinder the induction of bNAbs against the MPER of the HIV Env. Specifically, we will explore different vaccine strategies to present the MPER in its neutralization-competent structure and investigate alternative approaches to overcome the weak antigenicity of MPER for inducing strong bNAbs against HIV. Building on our recent success in eliciting MPER-specific HIV NAbs by a HA/gp41 chimeric antigen and employing multidisciplinary approaches, we will: 1) modify vaccine design and develop new chimeric protein antigens to selectively augment induction of bNAbs against the conserved epitopes in the HIV Env MPER; 2) determine the targets of vaccine-induced MPER-specific neutralizing antibodies and modify vaccine design to selectively augment induction of such antibodies; and 3) optimize the immunization regimens and investigate the use of adjuvant for inducing strong neutralizing antibodies against MPER of the HIV Env. The successful development of these vaccine strategies will be of great significance for HIV vaccine development, and knowledge gained through these studies could also be applied to vaccine design against other conserved neutralizing epitopes in the HIV Env, which are very likely to be conformational sensitive, cryptic, and weakly immunogenic like the epitopes in the MPER.

Progress during the reporting period: To date, this group has explored the design of various HA/gp41 chimeric molecules for immunogenicity in small animals (rabbits and guinea pigs), and plans have been formulated for macaque immunizations with several of the most promising candidates in early 2017.

Publications resulting from the project:
None at this time

Funding Sources:
Chinglai Yang, Ph.D. Proprietary Info National Institute of Allergy & Infectious Disease NIH R01 AI111851

Project Title: Efficacy of Strain 68-1 RhCMV Vectors Expressing 5' Leader Polypeptides
SPID: 4370
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only): None

Project Description: The development of an effective HIV/AIDS vaccine remains a high international health priority as the most cost-effective means to stem the AIDS pandemic. At this point in time, there are very few general HIV/AIDS vaccine strategies that remain viable, that is, have shown promising efficacy in preclinical studies and not been proved ineffective in human clinical trials. Among these is the approach developed by our group in which persistent Cytomegalovirus (CMV)-derived vectors are used to elicit high-frequency, indefinitely persistent HIV/SIV-specific effector memory T cell (TEM) responses. In the preclinical rhesus macaque (RM) – SIV model, we have demonstrated that after mucosal SIV challenge >50% of monkeys vaccinated with strain 68-1 RhCMV/SIVgag, /SIVpol, /SIVenv, /SIVrevtatnef vectors show complete, durable protection and eventual clearance by virologic and immunologic criteria. Protection is likely determined by the ability of TEM cells to intercept a nascent HIV/SIV infection immediately upon acquisition (with no response delay due to requirement for anamnestic expansion and effector differentiation). If this assumption is correct one could speculate that a greater efficacy could be achieved if the earliest HIV/SIV immunogens could be targeted within hours after initial infection. Recently a novel set of 5' leader encoded HIV-1 and SIV polypeptides was discovered, and these polypeptides were expressed very early in HIV/SIV-infected cells and were highly immunogenic. Therefore, the 5' leader polypeptides (5'-LP) are an extremely attractive vaccine target considering that every spliced and unspliced HIV/SIV mRNA contains the 5' leader sequence, and thus polypeptides encoded from this region will be ubiquitously expressed rapidly and early following infection. Thus, the major objective of the research proposed here will be to determine whether RhCMV vectors expressing SIV 5' leader polypeptides can protect a rhesus macaque from highly virulent SIVmac239 mucosal infection and if these vectors in combination with vectors expressing conventional SIV open-reading frames can enhance protective efficacy. These objectives will be accomplished by experimentally addressing the following Specific Aims: (i) to determine the epitope specificity and restriction, function and phenotype of SIV 5' leader sequence polypeptide-specific T cells elicited by strain 68-1 RhCMV/5'-LP vectors; (ii) to determine the efficacy of strain 68-1 RhCMV/5'-LP vectors with vaccination against limiting-dose, mucosal SIV challenge; (iii) to determine the immunogenicity and efficacy of a combination vaccine containing both strain 68-1 RhCMV/5'-LP vectors and strain 68-1 RhCMV vectors expressing SIVgag/pol/nef.

Progress during the reporting period (2-5 sentences): The objectives for this year were to define the T cell immunogenicity of strain 68-1 RhCMV/5'-LP vectors in RM, including 1) the dynamics of CD4+ and CD8+ T cell responses to each 5'-LP RF insert following initial RhCMV/5'-LP vector vaccination and homologous boosting in blood. To this end, we have vaccinated 21 RM and are currently following and characterizing their vaccination-induced immune responses in peripheral blood. The study is only in its first few months, but preliminary data shows robust CD4+ CD8+ immune response to all 3 vaccinated 5'LP-atigens.

Publications resulting from the project: None at this time

Funding Sources:
Scott Hansen, Ph.D. NIH/NIAID AI124370

Project Title: Efficacy and Immunogenicity of 68-1 RhCMV Vectors Expressing Conserved SIV Antigens
SPID: 0645
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
Duke University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester
Oregon Health & Science University

Project Description:
Thus far, all non-human primate efficacy studies with CMV vectors have been with a prime/boost vaccine strategy. In each of these efficacy studies, CMV was administered twice, ~12 weeks apart, with the repeat vaccination designed to provide additional antigen via the same route, and thus re-enforcing micro-environmental regulation of vaccine-elicited T cell differentiation. Interestingly, while we have found that boosting indeed enhances seeding of effector cells to mucosal tissues, our data indicates that robust tissue-resident effector memory SIV-specific T cell responses develop even after the first dose of CMV vectors, suggesting that a clinically-desirable single-dose vaccination strategy may be possible. However, as protection is likely determined by the ability of CMV-elicited SIV-specific T_{EM} cells to intercept nascent SIV infection at mucosal sites, it is critical to determine whether a boost is required to develop the necessary frequencies of effector cells in the mucosal sites to mediate protection. Furthermore, it would be desirable for clinical development of CMV vectors to determine if both the duration post-first CMV vaccination and the boost are both required for effective response development and maturation. In order to inform whether future clinical trials should proceed with a single-dose or prime-boost vaccine strategy, these fundamental questions must be addressed. Therefore, the following aims will be addressed: 1. Compare the specificity and strength of T cell responses after immunization of macaques with 68-1 RhCMV/SIVconsv239 versus a 'conventional' recombinant chimpanzee adenovirus prime (ChAdOx-1-Sivconsv239) with recombinant MVA-SIVconsv239 boost. 2. Determine the efficacy of strain 68-1 RhCMV/SIVconsv239 vaccination against limiting-dose mucosal SIV challenge.

Progress during the reporting period:
We have engineered a 68-1 RhCMV vector to express the SIVconsv239 construct, the SIV homolog of an HIV immunogen (tHIVconsvX) designed to encompass the most conserved and immunogenic Gag and Pol segments. To explore the benefit of combining the CMV vector and conserved immunogen strategy, we compared the immunogenicity of RhCMV-SIVconsv239 vectors to conventional Ad/MVA vectors expressing SIVconsv239, which are known to elicit only MHC-Ia restricted responses. Three groups of RM (n=4 each) have been immunized with (A) two subcutaneous inoculations of 5 $x10^6$ PFU of 68-1 RhCMV-SIVconsv239 given at weeks 0 and 12); (B) a single subcutaneous inoculation of 5 $x10^6$ PFU of 68-1 RhCMV-SIVconsv239; or (C) intramuscular delivery of $5x10^{10}$ virus particles of ChAdOx1-SIVconsv239 at week 0 and $2x10^9$ PFU MVA-SIVconsv239 at week 4. Vaccine-induced SIVconsv239-specific immune responses were followed longitudinally in peripheral blood for 60 weeks for groups A and C (late challenge) and 18 weeks for group B (early challenge). As anticipated, both vaccine modalities elicited and maintained high-frequency SIVconsv239 CD4+ and CD8+ T cell responses in peripheral blood. However, on average, the 68-1 RhCMV/SIVconsv239 vaccinated animals exhibited a higher overall T cell response compared to the ChAdOx1-SIVconsv239 vaccinated animals. Additionally, we have now completely epitope mapped and determined the MHC restriction of every T cell response from each of the identified CD8+ epitopes in 4 animals from both the long-term CMV- and ChAdOx1/MVA-vaccinated groups. Amazingly, both vaccine groups elicited broadly targeted CD8+ T cell responses to the conserved regions of both SIVgag and SIVpol, with an average of 69 epitopes recognized in CMV-vaccinated animals versus 59 in the ChAdOx1/MVA-vaccinated animals. Furthermore, as

previously reported, 68-1 RhCMV vectors elicited both unconventional MHC-II- and MHC-E restricted CD8+ T cells whereas ChAdOx1/MVA-vaccinated animals elicited conventional MHC-Ia-restricted CD8+ T cells as expected. These data strongly indicate that the use of the tHIVconsvX antigen in either an “Unconventional’ or “Conventional” vaccine regimen will likely generate strong HIV-specific CD8+ T cell responses. Low dose mucosal SIV challenge has recently begun and will be the focus of next year's update

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Barton Haynes, M.D. Duke University/NIH/NIAID
5 UM1 AI00645-04 and 5 UM1 AI00645-05

Project Title: HIV Envelope-based Vaccines from Superinfection to Elicit Neutralizing Antibodies
SPID: 4392
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester
Oregon Health & Science University

Project Description (one paragraph):
Many attempts to modify HIV-1 Envelope (Env) for improved immunogenicity have been attempted, with varying rates of success. Some increased potency in neutralizing antibodies (NAbs) has been claimed, but the breadth achieved is very limited and a breakthrough is crucial to make substantial progress towards an effective Env-based vaccine component. Superinfection (SI) provides a unique immunological setting for studying candidate HIV Envs as potential vaccine components. This project focuses on Env sequences derived from superinfected individuals identified to have characteristics of elite neutralization breadth. The Env sequences from these individuals may contain unique determinants that have developed as the result of the persistence of dual antigen presentation during SI. The project objective is to conduct immunogenicity studies using carefully selected panels of vaccine candidates combined with newly emerging vaccine regimens that will result in substantially improved antibody responses - both in time to response and in breadth of neutralization. To achieve the goal of this project, Single Genome Amplification will be used to clone a panel of gp160 Env genes isolated from plasma and targeting time points associated with development of potent neutralization breadth from two intersubtype superinfected elite neutralizers who are members of a well-characterized African sex-worker cohort.

Progress during the reporting period (2-5 sentences): We immunized 12 NHP using cloned HIV-1 Env from the superinfected subject B850. Immunizations consisted of Env DNA plus gp140 trimeric Env protein at 4 different timepoints. The immunizations induced very strong HIV-1 Env-specific antibodies in NHP with moderate neutralizing potency. Modest neutralization of Tier 2, Clade A viruses was also achieved. The project has ended and a manuscript is in preparation.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):
Ann Hessell, Ph.D. NIH/NIAID - AI104392

Project Title: Targeting MAIT Cells for TB Vaccines
SPID: 1709
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph): This proposal is designed to establish whether or not a vaccine targeting Mucosal Associated Invariant (MAIT) can be used to prevent tuberculosis (TB). MAIT cells can recognize cells infected with Mycobacterium tuberculosis (Mtb), are enriched in the human airway, and have effector functions associated with the control of Mtb. MAIT cells recognize small molecules presented by the non-classical molecule MR1. Like CD1, MR1 is on human chromosome 1, and is nearly monomorphic. Known ligands are derived from vitamin B6 and B12 metabolites. At present, those antigens presented in the context of infection with Mtb are not known, and known antigens are highly unstable limiting their utility as vaccine candidates.

Progress during the reporting period (2-5 sentences):

The goal of the project with Excluded by Requester was to develop the tools needed to measure MR1-restricted T cells in the NHP model. With the assistance of Excluded by Requester ad NHP tetramer was developed, and these cells rather extensively characterized. This has resulted in a first publication (see below). As a result, the tools are now in place to measure MR1-directed vaccination strategies.

Publications resulting from the project:

Excluded by Requester

Excluded by Requester

Funding Sources (PIs and sources):

Excluded by Requester

Private Source

Project Title: The Use of HIV-1 Integrase Inhibitors for the Treatment of Multiple Sclerosis
SPID: 6265
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only): None

Project Description (one paragraph):
Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system (CNS) that develops in genetically-susceptible individuals after exposure to an ill-defined trigger(s). A Phase 2 study to determine whether Raltegravir (RALT), an inhibitor of HIV-1 integrase, is effective in preventing progression of relapsing-remitting multiple sclerosis is currently underway in the UK (INSPIRE). The clinical trial is justified by a recent epidemiologic study that found that the incidence rate ratio (IRR) of developing MS in people with HIV, relative to those without HIV, was 0.38 (95%CI 0.15-0.79). The consensus was that ART may be coincidentally treating or preventing progression of MS, although a lack of definitive proof was acknowledged. Authors hypothesized that ART could be inhibiting an infectious inflammatory trigger (e.g., endogenous retrovirus or herpesvirus) or exerting an as yet undetermined protective physiologic influence. Regarding an antiviral effect, HIV integrase inhibitors (INIs) garnered the most interest, hence the INSPIRE trial. INIs are designed to target a catalytic DDE motif in HIV integrase, and this motif is conserved in herpesviral terminases. Indeed, RALT inhibits the replication of several herpesviruses *in vitro*. In light of these data, we considered whether HIV INIs could inhibit the replication of JMRV, a simian herpesvirus that is causally associated with JME (Japanese macaque encephalomyelitis), a spontaneous inflammatory demyelinating disease with clinical, MRI and pathologic similarities to MS, that occurs among genetically-predisposed JM housed at the Oregon National Primate Research Center (ONPRC). A JME-like condition can also be induced in genetically susceptible JM by intracranial injection of JMRV. Our preliminary data show that the IN inhibitor L-870,812 (L812; Merck) inhibits JMRV replication in susceptible cells. We also discovered that L812 could enhance the barrier function of JM brain endothelial cells using an *in vitro* model of the blood brain barrier (BBB). We hypothesize that one of the ways in which cART therapy protects against MS is via exertion of a neuroprotective effect on the BBB. In this application, we will directly test this hypothesis and explore the mechanistic basis of neuroprotection through two Specific Aims. SA 1: To characterize the neuroprotective and antiviral function of HIV integrase inhibitors; and SA 2: To evaluate the therapeutic potential of HIV integrase inhibitors in an NHP model of MS-like disease.

Progress during the reporting period:
Four HIV-1 integrase inhibitors (raltegravir, elvitegravir, dolutegravir and L-870,812) were tested *in vitro* to evaluate (i) ability to inhibit JMRV replication and (ii) neuroprotective activity. While all four drugs reduced JMRV replication and enhanced the barrier function of JM brain endothelial cells, the best combinatorial profile was obtained using L-870,812. Thus, we selected L-870,812 to test in JM *in vivo*. Four JM were used for the *in vivo* portion of this study. All four were injected I.C. with JMRV to induce JME. Two animals received L-870,812 (20mg/kg BID) at -2 through 14 days post-injection. All JM received MRI scans on day 0 and day 7. All JM were euthanized on d14 and blood, CSF and brain tissue harvested. Analysis of these samples is ongoing at present.

Publications resulting from the project: None at this time

Funding Sources (PIs and sources):

Excluded by Requester — Private Source

Project Title: Purging the Latent HIV Reservoir at ART Initiation: A New Eradication Strategy
SPID: 0045
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester U.S. Military HIV Research Program

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
Excluded by Requester Oregon Health & Science University
University of Montreal

Project Description (one paragraph):
This project is based on the hypothesis that there is a window of opportunity during ART initiation where the concomitant use of a latency reversing agent would reactivate latently infected CD4+ T cells (shock) and lead to an enhanced killing of the HIV reservoir by HIV-specific CD8 T cells (kill), as these cells are still present at high frequency at this stage. Therefore, we expect that the addition of a reactivating agent to a traditional ART regimen will lead to a significant decrease in the size of the pool of latently infected cells. We propose to test this new therapeutic approach in the non-human primate model of SIV, specifically in *Mamu-A1*001* rhesus macaques (RM) that have been described to exhibit a potent SIV-specific CD8 T cell response against SIV that is detectable by tetramers.

Progress during the reporting period:
We are continuing with preclinical safety studies, testing the HIV/SIV latency-reversing agent GSK445A, an Ingenol-based PKC agonist. A total of 5 male RM have been assigned to this study and are currently receiving escalating doses of GSK445A to determine the minimum effective dose that induces maximum T cell activation *in vivo*. The optimal dose will be used for a proof of concept study in SIV-infected RM on suppressive antiretroviral therapy.

Publications resulting from the project:
None.

Funding Sources (PIs and sources):

Lydie	Trautmann, Ph.D.	NIH/NIAID R21AI116233-02
Afamefuna A.	Okoye, Ph.D.	The Henry M. Jackson Foundation for the Advancement of Military Medicine 5 R21 AI116233-02

Project Title: Combination Immune Checkpoint Blocker Inhibition to Eliminate HIV Latency
SPID: 0219
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester University of Melbourne

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester Oregon Health & Science University
Oregon Health & Science University

Project Description:
Recent clinical trials in HIV-infected individuals on antiretroviral therapy (ART) of latency-reversing agents (LRA), including histone deacetylase inhibitors (HDACi) and the anti-alcohol drug disulfiram, have demonstrated that activation of latent virus is possible. These interventions did not have a demonstrable effect on the size of the reservoir, perhaps because they do not alone enhance the capacity of the host immune system to clear virus-expressing cells and HDACi may possibly suppress this response. This proposal is based on emerging data that HIV is enriched in cells expressing immune checkpoint blockers (ICB); particularly PD-1, and that inhibitors of ICB such as CTLA-4, can activate HIV or SIV, both *in vitro* and *in vivo* and both anti-PD-1 and anti CTLA-4 can enhance the function of HIV-specific T-cells. Here we will examine whether inhibition of CTLA-4 in SIV-infected rhesus macaques on suppressive ART will activate latent SIV infection and boost SIV-specific CD4+ T-cells in lymphoid tissue leading to a reduction of latently infected cells. In addition, we will examine whether administration of anti-CTLA-4 in combination with anti-PD-1 will act synergistically to eliminate latently-infected cells in the setting of ART.

Progress during the reporting period:
In the last year we have successfully complete all contract negotiation and have received the supply of inilimumab (anti-CTLA-4) and nivolumab (anti-PD-1) from Specific Private Vendor We are also working with Dr. Excluded by Requester (U. Mass.) to make rhesus versions of anti-PD-1. The animal study is due to begin in the second quarter of 2017.

Publications resulting from the project:
None at this time

Funding Sources:
Excluded by Requester
Excluded by Requester

Project Title: Impact of Alemtuzumab on SIV Persistence in Antiretroviral-Treated SIV-Infected Macaques
SPID: 8475
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
University of California, San Francisco

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University
University of Melbourne

Project Description: The primary objective of this Administrative Supplement is to characterize the effects of alemtuzumab on mononuclear cell depletion and recovery in blood and tissue, and to determine whether alemtuzumab results in reduction in (or clearance of) long-lived latently infected T cells in SIV-infected nonhuman primates on suppressive antiretroviral therapy (ART).

Progress during the reporting period (2-5 sentences):
A total of 9 adult rhesus macaques were challenged intravenously with SIV prior to receiving ART starting 12 days post-infection. Once animals achieve full virus suppression (plasma viral loads <15 copies/ml), 6 animals will receive 2 doses of alemtuzumab one week apart, while 3 animals will be untreated controls. Once lymphocyte recovery reaches steady state, ART will be stopped and the impact of alemtuzumab on the size and distribution of the SIV reservoir will be assessed.

Publications resulting from the project.
None at this time

Funding Sources:
Steven G. Deeks, M.D. University of California, San Francisco / NIH/NIAID- 5U19 AI096109

Project Title: Impact of Sirolimus (Rapamycin) on HIV-1 Persistence and Immune Function
SPID: 9035
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester University of California, San Francisco

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester Oregon Health & Science University

Project Description: We are testing whether the transplant drug, sirolimus, will improve SIV-specific immunity, reduce bystander T cell activation and T cell exhaustion, and restore CD8 effector function leading to improved immune surveillance in SIV-infected rhesus macaques (RM) on suppressive antiretroviral therapy (ART). We will also evaluate whether sirolimus treatment can enhance reactivation of latent SIV from CD4 T cells in a combination therapy approach, improving the CD8 T cell's capacity to detect and clear SIV reservoirs.

Progress during the reporting period: A total of 14 adult male RM have been assigned to this study. These RM will be challenged with SIVmac239 prior to receiving ART 12 days post-infection. Once virus suppression has stabilized, RM will be randomized into 2 groups that will receive sirolimus alone (n=7) or sirolimus in combination with an HIV/SIV latency-reversing agent. The impact of sirolimus treatment on SIV reservoir dynamics and viral rebound kinetics will be assessed.

Publications resulting from the project.
None at this time

Funding Sources:
Excluded by Requester University of California, San Francisco / Private Source
Private Source

Project Title: To Determine the Effect of Toll-like Receptor (TLR) Agonists on SIV Production in Effectively Treated SIV-infected Macaques: Module E and Animal Core
SPID: 0159
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

University of California, San Francisco

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
University of California, San Francisco

Project Description:
Achieving a durable state of virus control in absence of antiretroviral therapy (ART) will likely require reductions in the overall reservoir size and an enhanced capacity of the host immune system to control any persistent virus population. We seek a safe and effective strategy that will both "shock" virus out of latency (so it can be depleted) and enhances immune function. We will exploit innate toll-like receptor (TLR) signaling to achieve these goals. In this study we will investigate the safety and potential anti-latency activity of a novel formulation of a TLR7 agonist both alone and in combination with a TLR4 agonist in the macaque model of lentiviral latency. Stimulation of these two TLRs can produce highly synergistic effects both *in vitro* and *in vivo*. To improve potency and reduce toxicity, nanoliposomes will be used to deliver these agonists.

Progress during the reporting period:
At present there is no progress to report, as contract negotiations between OHSU and UCSF are ongoing.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):

Excluded by Requester

Private Source

Project Title: Consortia for Innovative AIDS Research in Nonhuman Primates
SPID: 8936
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Ragon Institute of MGH, MIT and Harvard

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester

Excluded by Requester

Ragon Institute of MGH, MIT and Harvard
Oregon Health & Science University
Leidos Biomedical Research, Inc.
Frederick National Laboratory for Cancer Research
Oregon Health & Science University

Project Description: We have demonstrated that CMV/SIV vectors can 1) re-infect CMV+ rhesus macaques (RM), 2) during re-infection, elicit potent and persistent SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory" (TEM) bias, and 3) completely protect ~50% of vaccinated RM from progressive infection after limiting dose rectal challenge with the highly pathogenic SIVmac239 virus. The protection manifested in these RM is distinct from previous vaccines in its abruptness and extent, with protected RM exhibiting a viral burst in plasma of varying size upon initial infection, followed by immediate control to undetectable levels. Although occasional viral blips in plasma are observed in protected RM, these decline with time, and after 1 year, protection is unaffected by CD8+ or CD4+ cell depletion, and extensive tissue analysis with ultrasensitive nested PCR has shown only rare detection of ~single copy SIV nucleic acid and no viable SIV. Protection correlates with the total SIV-specific CD8+ TEM generated during the vaccine phase, and occurs without an anamnestic response. These data indicate a novel pattern of protection consistent with very early control, likely taking place at the site of viral entry and/or early sites of viral replication and amplification. The current lack of a clear understanding of the cell types and associated mechanisms responsible for this observed protection makes rational improvement of CMV vectors difficult. In project, we will test the hypothesis that specific and definable cellular subsets represent the mechanism of the observed protection with CMV vector vaccines. Two complementary experimental approaches will be used to delineate the contribution of different immune cell populations and immune effector mechanisms to vaccine-elicited protection in rhesus monkeys: correlational (comparing efficacy of RhCMV vectors that fundamentally differ in elicited response type) and interventional analysis using lymphocyte subset-depleting mAbs prior and during challenge to assess the contribution of different lymphocyte subsets to efficacy.

Progress during the reporting period: The major recent progress of this project is the demonstration that efficacy is restricted to vectors (68-1 strain) that elicit unconventionally restricted CD8+ T cells; vectors that show otherwise similar immunogenicity except that CD8+ T cell responses are MHC-Ia-restricted or a mixture of MHC-Ia- and MHC-II-restricted do not protect. A CD8 depletion is currently underway and we expect to directly demonstrate a requirement for CD8+ T cells for efficacy.

Publications resulting from the project:
None at this time

Funding Sources:
Dan Barouch, M.D. NIH/NIAID UM1 AI124377

Project Title: DARE: Delaney AIDS Research Enterprise to Find a Cure. Initial Research Focus 1, Initial Research Focus 3, and Management and Operations
SPID: 6611
Unit/Division: Patho
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph):
Given that many of the clear examples of stringent, long-term, spontaneous and vaccine-associated immune control of HIV/SIV infection are either known, or strongly suspected to be CD8+ T cell-mediated, therapeutic strategies designed to exploit CD8+ T cell immunity hold great promise in contributing to both replication-competent viral reservoir (RCVR) reduction and post-antiretroviral therapy (ART) immune control. However, a major caveat to the exploitation of CD8+ T cells as a 'kill" and/or "control" component of a therapeutic HIV/SIV cure strategy is the fact that HIV/SIV can not only avoid immune recognition by going latent, but even when actively replicating, these viruses evade most natural CD8+ T cell responses by multiple mechanisms, all of which must be countered for any CD8+ T cell-based cure therapy component to be generally effective. In this project we will use the SIV-rhesus macaque (RM) model to investigate the contribution of these HIV/SIV immune evasion strategies to viral persistence during ART and to viral rebound post-ART, and at the same time, to develop strategies for their defeat, with the goal of achieving virologic remission in the absence of ART (e.g., a "functional" SIV cure).

Progress during the reporting period:
Initial studies will determine the effect of CD8+ T cell response modulation on the magnitude and distribution of the SIV RCVR and viral reactivation in ART-suppressed SIV+ RM. A total of 20 RM have been assigned, half of which were selected to express *Mamu* A*01 and the other half *Mamu* B*08. All RM will be intravenously inoculated with SIV and placed on ART 12 days later. Once stable virus suppression is achieved, half of the RM in each group will be given 50mg/kg rhesusized anti-CD8α antibody (Ab), whereas the other half will be given an equal amount of a control rhesusized Ab. The overall goal of these studies is to determine whether the relative level of productive SIV infection (reactivation and cell-to-cell spread, if any, observed as SIV RNA+ cells) is altered by absence of CD8+ T cells, and in RM with intact CD8+ T cells, to determine whether these relative SIV reactivation/spread levels correlate with magnitude and effectiveness of the SIV-specific CD8 T cell responses.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):
Louis Picker, M.D. — Funded by UCSF/NIH/NIAID – 1 UM1 AI126611-01

Project Title: DARE: Delaney AIDS Research Enterprise to Find a Cure
SPID: 6751
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
University of California, San Francisco

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University
University of California, San Francisco
Oregon Health & Science University
Case Western Reserve University

Project Description: The failure to cure HIV infection is believed to result from low-level viral production/ replication, the presence of latent replication-competent provirus in resting CD4+ T cells and T cell dysfunction stemming from persistent immune activation. Current antiretroviral therapies (ART) cannot eradicate the reservoir of long-lived latently infected cells or reverse immune dysregulation. The goal of this project is to determine whether SIV-specific immune responses elicited by RhCMV/SIV vector vaccination results in progressive reduction in (or clearance of) SIV infection, including both viral production and cellular viral reservoirs, in rhesus macaques (RM) on ART over time, and/or result in significant protection against viral rebound after ART cessation.

Progress during the reporting period: This project supported a monkey experiment designed to test the ability of strain 68-1 RhCMV/SIV to reduce the (fully formed) SIV reservoir of, and/or control SIV reactivation in SIV+ monkeys on optimally suppressive combination ART (cART) that was initiated 42 days after the onset of SIV infection. Of the 18 day 42 cART-treated monkeys available for this study, 12 and 6 were randomized to be therapeutically vaccinated with either SIV insert containing or control insert containing RhCMV vectors, respectively. Both sets of monkeys received 2 doses of their respective vectors, and the animals were followed for immune response and reservoir size. Approximately 2 years post-SIV infection, cART was discontinued and the impact of RhCMV/SIV vaccination on the rate and extent of viral recrudescence was assessed.

Publications resulting from the project:
None

Funding Sources:
Steven G. Deeks, M.D. NIH/NIAID - U19AI096109 and 1UM1AI26611-01

Project Title: Development of an Effector-Memory T Cell AIDS Vaccine
SPID: 4417
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester

University of California, Davis
Case Western Reserve University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Leidos Biomedical Research, Inc.
Frederick National Laboratory for Cancer Research
Oregon Health & Science University
Case Western Reserve University
Oregon Health & Science University
University of California, Davis

Project Description: The T cell memory elicited by conventional vaccines (memory responses that, upon pathogen encounter, require effector expansion, differentiation and migration to mediate anti-viral activity) has proved to be of limited effectiveness in HIV/SIV infection. This poor efficacy is likely due to a 'kinetic mismatch' between viral replication and the time necessary to produce and mobilize anti-viral effectors from such vaccine-elicited responses, allowing the systemically distributed and rapidly replicating virus to escape stringent immune control. An alternative approach is to develop a vaccine that elicits tissue-based effector memory T cell responses that can intercept the infection in the first hours and days of infection, when it's most vulnerable to immune control. Work from our group has shown that RhCMV/SIV vectors can elicit potent, long-lasting SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory" (TEM) bias, and completely protect 50% of vaccinated RM from progressive SIV infection after limiting dose, intra-rectal challenge with the highly pathogenic SIVmac239 virus. Protection correlates with peak total SIV-specific CD8+ T cell responses in blood during the vaccine phase, which likely reflects the degree to which these cells are seeded into effector tissues. Taken together, these data indicate a novel pattern of protection consistent with very early control, likely occurring at the site of viral entry or early sites of viral replication and amplification, and mediated by tissue-resident CD8+ TEM. The goal of this HIVRAD is twofold: first, to understand the immunologic basis of this unique protection so as to develop second-generation strategies to increase efficacy towards 100%, and second, to develop vectors that retain optimal efficacy, but have less or no capacity to cause vector-related disease.

Progress during the reporting period: In the past year this project has confirmed the ability of RhCMV vectors to differentially program epitope recognition characteristics of vector-elicited CD8+ T cell responses and has demonstrated the role of cell tropism in mediating this ability, in particular the use of tropism modification to differentially program vectors that specifically elicit CD8+ responses that are MHC-II- vs. MHC-E-restricted.

Publications resulting from the project:

Excluded by Requester

Funding Sources:

Louis Picker, M.D. NIH/NIAID 5P01AI094417

Project Title: Development and In Vivo Characterization of Safety-Enhanced RhCMV/SIV Vectors
SPID: 5113
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester — University of California, Davis
University of California, Davis
University of California, Davis

Project Description: We have demonstrated that CMV/SIV vectors can 1) re-infect CMV+ rhesus macaques (RM), 2) during re-infection, elicit potent and persistent SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory" (TEM) bias, and 3) completely protect ~50% of vaccinated RM from progressive infection after limiting dose rectal challenge with the highly pathogenic SIVmac239 virus. The protection manifested in these RM is distinct from previous vaccines in its abruptness and extent, with protected RM exhibiting a viral burst in plasma of varying size upon initial infection, followed by immediate control to undetectable levels. Although occasional viral blips in plasma are observed in protected RM, these decline with time, and after 1 year, protection is unaffected by CD8+ or CD4+ cell depletion, and extensive tissue analysis with ultrasensitive nested PCR has shown only rare detection of ~single copy SIV nucleic acid and no viable SIV. Protection correlates with the total SIV-specific CD8+ TEM generated during the vaccine phase, and occurs without an anamnestic response. These data indicate a novel pattern of protection consistent with very early control, likely taking place at the site of viral entry and/or early sites of viral replication and amplification, and involving tissue-resident CD8+ TEM. Thus, CMV vectors and the "TEM" vaccine concept offer a powerful new approach to HIV/AIDS vaccine development. However, fully replicative CMV vectors are unlikely to be advanced to human use due to the pathogenic potential of CMV. A central goal is therefore to develop CMV vectors that maintain immunogenicity and efficacy, but are safe to use in humans.

Progress during the reporting period: This project has ended. Over the course of 5 years we have been successful in developing attenuated CMV vector designs that preserve the unique immunogenicity of non-attenuated CMV vectors. This work is currently being prepared for publication.

Publications resulting from the project:
None

Funding Sources:
Louis J. Picker, M.D. NIH/NIAID R01AI095113

Project Title: Development of Attenuated CMV Vectors for an HIV/AIDS Vaccine
SPID: 7409
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Los Alamos National Laboratory

Project Description: The overall goal of this project is the development of an HCMV vector-based HIV/AIDS vaccine (comprised of one or more HIV insert-expressing HCMV vectors) that is optimized for safety, efficacy and manufacturability.

Progress during the reporting period: This project has focused on 3 goals: 1) manufacturing HCMV/HIV vector for a first-in-human clinical trial, 2) setting up clinical and laboratory facilities for performance of the clinical trial, and 3) performance of nonhuman primate studies that support clinical development. With respect to #1, we have recently developed a process for scale-up manufacturing HCMV/HIV vectors in conjunction with a contract manufacturing facility that will produce GMP product. With respect to #2, we have developed the necessary clinical and laboratory facilities and procedures, and are in the process of a pilot observational clinical trial that collects volunteers and determines their CMV status and their willingness to participate in a future CMV vector vaccine trial. With respect to #3, we are in the midst of performing NHP studies that will inform HIV inset design and define the impact of vector attenuation on long-term immune activation status of vaccines.

Publications resulting from the project:
None.

Funding Sources:

Excluded by Requester

Private Source

Project Title: Development of Optimized CMV/TB Vectors: OHSU/AERAS Project 3 Proposal
SPID: 6119
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University

Project Description: Our previous 2 studies show that RhCMV/TB vectors manifest notable, indeed, unprecedented, efficacy against TB disease in highly susceptible Indian-origin rhesus macaques. Although the extent of disease progression in the control groups is higher in Study 1 vs. Study 2, presumably because of the different challenge dose, significant protection is apparent in both studies. These data strongly support the hypothesis that the "in place" or rapidly recruited effector memory T cell responses elicited and maintained by CMV vectors are superior to responses elicited by conventional vaccines, and raise the CMV vector platform as a prime candidate for clinical development as a potentially "better than BCG" TB vaccine. However, without clear understanding of the immunologic basis of protection with this vaccine, the ultimate potential of the CMV-vectored TB vaccine remains uncertain. Given our ability to genetically modify CMV vectors to both enhance safety and differentially program immunogenicity, it may be possible that efficacy can be increased. Also, understanding of the immunologic requirement for complete protection in monkeys will greatly facilitate clinical translation as it will provide an immunogenicity "target" for early phase clinical assessment of HCMV/TB vectors. Thus, in parallel with clinical vector development, we seek to use the Rhesus macaque model to both define the immunologic basis of CMV vector-mediated protection against TB and to optimize both the vector backbone and vector insert design to achieve the highest possible efficacy, while incorporating sufficient attenuation to ensure clinical safety.

Progress during the reporting period: This project has just started.

Publications resulting from the project:
None.

Funding Sources:
Excluded by Requester
Private Source

Project Title: Efficacy of Oral CMV/SIV Vectors
SPID: 1291
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester

Leidos Biomedical Research, Inc.
Frederick National Laboratory for Cancer Research
Immunobiology and Vaccine Design, AIDS Vaccine Design and Development Laboratory, International AIDS Vaccine Initiative
Oregon Health & Science University
Oregon Health & Science University
Case Western Reserve University
Oregon Health & Science University

Project Description: Two large scale nonhuman primate (NHP) efficacy studies have convincingly demonstrated that CMV/SIV vectors can 1) re-infect CMV-seropositive rhesus macaques (RM), 2) during re-infection, elicit potent and persistent SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory bias", and 3) protect ~50% of vaccinated RM from progressive SIV infection after limiting dose rectal challenge with the highly pathogenic, CCR5-tropic SIVmac239 virus. The protection manifested in these RM is distinct from previous vaccines in its abruptness and extent, with protected RM manifesting a viral burst in plasma of varying size upon initial infection, followed by immediate control to undetectable levels. Protection correlates with the extent of total SIV-specific CD8+ T cell generation during the vaccine phase, and is stable in the vast majority of protected RM for at least 6 months. These data indicate a novel pattern of protection consistent with very early control, likely taking place in the site of viral entry and/or early sites of viral replication and amplification, and mediated by tissue-resident TEM.

Progress during the reporting period: This project has ended. The final accomplishment was demonstrating RhCMV/SIV vector efficacy via oral vaccination.

Publications resulting from the project:
None.

Funding Sources:
Louis J. Picker, M.D. NIH/NIDC 5R01DE021291

Project Title: Human CMV-TB Vaccine Early Manufacturing Support – Development of an Attenuated CMV Vector for a TB Vaccine
SPID: 2430
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the project:
Excluded by Requester Oregon Health & Science University

Project Description:
This project is designed to construct, manufacture and validate an HCMV/TB vector for human clinical trials.

Progress during the reporting period: Molecular construction of the selected vector design is ongoing. The GRP manufacturing lab has been set up and is ready for seed stock production,

Publications resulting from the project:
None.

Fundina Sources (PIs and sources):
Excluded by Requester Private Source

Project Title: Induction of Broad Functional Class II Restricted CD8+ T Cell Responses: Translation from NHP to Humans (MHC II- and MHC E-restricted CD8+ T Cells and Control of HIV)
SPID: 8533
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University

Project Description: In the past decade, the Picker research group has designed a novel vaccine approach based upon CMV vaccine vectors that can be genetically programed to generate distinct types of CD8+ T cell responses based on the number and nature of the epitopes recognized and the host MHC molecules that present these epitopes. Since the ability of CD8+ T cells to mediate anti-viral effector function critically depends on the nature (and often, breadth) of viral antigen presentation of the surface of virally infected cells, this response programming is likely to have major influence on vaccine efficacy. Thus, Excluded by Requester and colleagues at Oregon Health & Science University (OHSU) have – in this proposal - joined forces with Excluded by Requester Excluded by Requester of the Ragon Institute of the Massachusetts General Hospital (MGH), Massachusetts Institute of Technology (MIT) and Harvard University, Excluded by Requester of Emory University, and Excluded by Requester of Stanford University to collaboratively determine 1) the mechanisms responsible for generation of unconventionally targeted CD8+ T cell responses, 2) the functional implications of unconventional epitope recognition by CD8+ T cells, and most importantly, 3) whether unconventionally targeted SIV- or HIV-specific CD8+ T cells manifest enhanced in vivo viral control compared to conventionally targeted CD8+ T cell responses.

Progress during the reporting period: We have confirmed the ability of RhCMV vectors to control CD8+ T cell priming with regard to the type of epitopes recognized by vector elicited CD8+ T cells. We are currently defining the viral genes that control this ability.

Publications resulting from the project:
Excluded by Requester

Funding Sources:
Excluded by Requester
Private Source

Project Title: OHSU/AERAS Project 2: Vector Production and Efficacy Experiment #2
SPID: 4097
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester Oregon Health & Science University

Project Description: TB is the most common opportunistic infection affecting HIV-seropositive individuals and it remains the most common cause of death in patients with AIDS. Our previous studies with recombinant RhCMV encoding exogenous antigen inserts have demonstrated the ability of these vectors to elicit and maintain high frequency insert-specific, effector-differentiated CD4+ and CD8+ T cells in both lymphoid tissues and extra-lymphoid effector sites (including, notably, the lung). To explore the possibility that the CMV vector platform would provide anti-TB immune responses with superior efficacy, we entered collaboration with the Private Source in 2011 to use the rhesus macaque model of TB to perform an efficacy trial comparing BCG vaccination, vaccination with RhCMV vectors expressing 9 TB antigens (85A/85B/Rv3407/ Rv1733c/Rv2626c/Rpf A/Rpf C/Rpf D/ESAT6), or a combination of the 2 vaccines (BCG prime; BCG boost). We have completed this initial study and have not only demonstrated superior efficacy of RhCMV/TB vectors over BCG, but have shown that the addition of a BCG prime to RhCMV/TB vaccination partially abrogates the latter's protection. Based on these promising results, we are continuing our collaboration with Private Source to perform a second study designed to confirm the efficacy of the original RhCMV/TB vector set, as well as to potentially optimize efficacy by also investigating a different RhCMV backbone (which we know gives a qualitatively different immune response) and a different TB insert design.

Progress during the reporting period: This project has been completed with demonstration of ~70% efficacy of RhCMV/TB vectors against Erdman strain challenge, compared to unvaccinated controls. This work is being prepared for publication.

Publications resulting from the project:
None.

Funding Sources:
Excluded by Requester Private Source

Project Title: Role of Memory T Cell Dynamics in SIV Infection
SPID: 4292
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester — Leidos Biomedical Research, Inc.,
Frederick National Laboratory for Cancer Research
Oregon Health & Science University

Project Description: HIV and its rhesus macaque (RM) counterpart SIV share a pattern of infection and a constellation of immunologic and pathobiologic features such that the vast majority of susceptible (untreated) people or RM infected with these agents experience unremitting infection and progressive immune deficiency. In work funded by this grant, we pioneered analysis of the *in vivo* immunobiology of naïve vs. memory (TN vs. TM) and central vs. effector memory (TCM vs. TEM) T cells in the RM model (including their homeostatic and functional regulation) and demonstrated the direct relevance of this physiology to SIV pathogenesis and immunity. In particular, we demonstrated that the mechanisms that maintain CD4+ TCM homeostasis and regulate CD4+ TCM differentiation into CD4+ TEM determine the development of immunodeficiency (AIDS) in SIV-infected RM. In addition, we have: 1) shown that IL-7 and IL-15 are critical regulators of CD4+ TCM homeostasis in RM, 2) developed a TN-deficient RM model and used this model to show that CD4+ TN are dispensable for both CD4+ TCM stability and CD4+ TEM production in SIV-infected RM, and 3) developed a method for long-term *in vivo* IL-15 blockade in RM (a "rhesusized" anti-IL-15 mAb) and used this method to show the importance of IL-15 in TEM homeostasis and that complete NK depletion (a second consequence of IL-15 blockade) has little impact on virologic control and disease progression in SIV-infected RM. In the extension of this work, we will use the CD4+ and CD8+ TN depletion models and *in vivo* manipulation of IL-15 and IL-7 to define the fundamental mechanisms underlying: 1) SIV persistence and replication set points (immune evasion vs. immune control), 2) deterioration of CD4+ T cell-mediated and overall immunity leading to AIDS, and 3) the establishment and maintenance of SIV reservoirs and immune reconstitution following pharmacologic control of viral replication (using ART regimens capable of long-term suppression of SIV in RM to <30 RNA copies/mL of plasma and improved methods for monitoring residual viral RNA and DNA in tissues). Identification of these mechanisms will be a crucial step in the development of novel therapeutic approaches aimed at enhancing immune control of HIV replication, and/or augmenting immune recovery and reservoir clearance during anti-retroviral therapy.

Progress during the reporting period: The current focus of this project remains two-fold: 1) the determination of mechanisms by which SIV can maintain persistent replication characterization in the face of highly effective immunity, and 2) the elucidation of the immunobiology of SIV reservoirs after the administration of effective anti-retroviral therapy (ART), including the ability of cellular immunity to influence spontaneous and induced viral reactivation and to limit viral dissemination after ART cessation. A major recent accomplishment was the demonstration that disruption of B cell follicles by anti-CD20 depleting monoclonal antibodies dramatically reduces plasma viral loads (~1 log) in SIV elite controller monkeys, suggesting B cell follicles constitute a barrier against the highly effective SIV-specific CD8+ T cell responses present in these animals. We are currently examining the impact of anti-CD20-mediated B cell depletion on SIV reservoirs and viral rebound kinetics post-treatment interruption in SIV-infected monkeys on ART.

Publications resulting from the project: None.

Funding Sources:

Louis J.	Picker, M.D.	NIH/NIAID R37AI054292

Project Title: A Nonhuman Primate Model of Stem Cell Transplantation to Understand Determinants of Post-transplant SIV Clearance
SPID: 9703
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph): With the most people ever in history currently living with HIV, stopping the HIV epidemic remains imperative. Combination antiretroviral therapy (cART) limits viral replication, but is not curative. Thus, there is an urgent need to design a functional cure via elimination of the viral reservoir. Timothy Brown, aka the Berlin Patient, remains HIV-free in the absence of cART following leukemia-related, MHC-matched, allogeneic hematopoietic stem cell transplantation (HSCT) from a CCR5-deficient donor. The mechanisms underlying this functional cure are not known, but may depend on the immune conditioning regimen, graft-versus-host immunity, or a reconstituted immune system lacking CCR5. Non-human primates are the best model of HIV infection, but previous transplant studies have used autologous or MHC-mismatched allogeneic HSCT due to the complexity of non-human primate MHC. Also, no CCR-deficient macaque donors exist. Thus, no studies have been able to recapitulate the transplant of Timothy Brown. We have built an allogeneic HSCT model using a novel, Mauritian cynomolgus macaque (MCM). MCM have extremely simplified genetics due to a recent bottleneck approximately 500 years ago. Furthermore, we are currently using CRISPR technology to generate CCR5-deficient donors. Therefore, we are uniquely positioned to recapitulate Timothy Brown's transplant in a clinically relevant animal model. In specific aim 1, we will measure the impact of myeloablative chemotherapy on clearing the latent viral reservoir in autologous HSCT transplants. In specific aim 2, we will perform fully MHC-matched HSCT, measure graft-versus host immunity, and correlate it to SIV rebound in the plasma and tissues. In specific aim 3, we will use our CCR5-deficient donors to perform an allogeneic HSCT with stem cells lacking CCR5. Overall, this study will allow us to map the determinants of HIV clearance following HSCT.

Progress during the reporting period: We have identified potential MHC-matched donor recipient pairs for these transplant studies.

Publications resulting from the project.
None.

Funding Sources (PIs and sources):
Jonah Sacha, PhD — Funded by NIH/NIAID – 1 R01 AI129703-01

Project Title: A Novel APOBEC-Based Vaccine Approach for HIV
SPID: 7904
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester George Washington University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
None

Project Description: This project will test the hypothesis that inducing high-frequency T cells against APOBEC3 proteins will protect animals from SIV replication. We will produce two rhesus CMV vectors, each encoding a separate Vif-sensitive APOBEC3 protein, and vaccinate macaques. We will subsequently challenge vaccinated and control animals with low-dose mucosal SIV and measure protection from SIV replication.

Progress during the reporting period (2-5 sentences): We constructed RhCMV strain 68-1 vectors expressing rhesus APOBEC3G, which were immunogenic in macaques. However, no protection from infection or SIV replication was observed.

Publications resulting from the project:
None.

Funding Sources:
Douglas Nixon, M.D., Ph.D. NIH/NIAID - R33 AI93179

Project Title: Graft versus Host Immunity in SIV Clearance following Stem Cell Transplantation
SPID: 2433
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: Three patients remain HIV free in the absence of cART following leukemia-related, MHC-matched, allogenic hematopoietic stem cell transplantation (HSCT). The mechanisms underlying this functional cure are not known, but may depend on graft-versus-host disease in the transplant recipients. Non-human primates are the best model of HIV infection, but no studies have directly assessed the role of graft-versus-host disease in the clearance of the HIV reservoir following MHC-matched, allogenic HSCT. Mauritian cynomolgus macaques (MCM) have extremely simplified genetics, allowing for the identification of fully MHC-matched animals. We intend to define the contribution of graft-versus-host disease to HIV clearance following HSCT using this novel, MHC-matched non-human primate model. In specific aim 1, we will infect 4 MCM with SIV and 4 weeks later administer cART until virus is undetectable in plasma. These animals will then receive MHC-matched HSCT, graft-versus host disease will be measured, and 12 weeks later cART will be lifted. We will monitor animals for an additional 16 weeks to measure SIV rebound in the plasma and tissues. Overall, this study will build a new model of MHC-matched, allogenic HSCT in non-human primates and use this model to assess the role of graft-versus-host disease in HIV clearance following HSCT.

Progress during the reporting period (2-5 sentences): We have successfully established the first nonhuman primate model of fully MHC-matched allogeneic stem cell transplantation. Recipients are fully engrafted with donor cells, including full donor T cell chimerism, without signs of graft versus host disease. Donor chimerism is durable for at least up to one year post transplant, thereby allowing us to now fully test the hypothesis that allo-responses are able to clear the latent viral reservoir.

Publications resulting from the project.
None.

Funding Sources:
Jonah Sacha, Ph.D. NIH/NIAID R21 AI112433

Project Title: Impact of retroviral infection on non-classical, mycobacteria-specific T cells
SPID: 7125
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):

Excluded by Requester

Oregon Health & Science University
University of Chicago
St. Jude's Children's Hospital

Project Description: Over 30 million people are currently infected with HIV, and over 2 million people die from AIDS each year. These numbers are dwarfed only by the number of individuals infected with tuberculosis (TB). Approximately two-thirds of the world's population is currently infected with the bacterium that causes TB, and approximately 10% of those individuals develop active TB. Individuals who are infected with both HIV and TB are up to 31 times more likely to develop tuberculosis than those with TB alone. Thus, there is an inherent need to understand how HIV affects the immune response to TB and whether an intervention can be designed to prevent tuberculosis in co-infected individuals. We have recently identified two unique populations of non-classical CD8+ T cells in rhesus macaques that we believe are critical players in anti-mycobacterial immunity: mucosal associated invariant T cells (MAITs), and MHC-E restricted CD8+ T cells. Thus the goal of this proposal is to characterize these unique T cells following BCG vaccination and understand how SIV infection impacts their anatomical distribution and function.

Progress during the reporting period (2-5 sentences): We have successfully constructed macaque MR1 tetramers and identified nonhuman primate MAIT cells. We are currently mapping T cell responses against BCG to identify MHC-E restricted CD8+ T cells.

Publications resulting from the project.

Excluded by Requester

Funding Sources:

Jonah	Sacha, Ph.D.	NIH/NIAID 5P30 AI027763-22

Project Title: A universal MHC-E- restricted T cell vaccine for HIV
SPID: 7802
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principle Investigator of the project/ Institutional affiliation:

Jonah	Sacha, Ph.D.	Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Jonah	Sacha, Ph.D.

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Louis	Picker, M.D.	Oregon Health & Science University
Helen	Wu, Ph.D.	Oregon Health & Science University

Project Description (one paragraph): With 34 million people currently living with HIV worldwide, developing a prophylactic HIV vaccine that protects against heterosexual transmission remains a top global health priority. We have recently discovered the existence of a novel class of CD8+ T cells recognizing peptide antigen presented by the non-classical molecule MHC-E. In contrast to the staggering diversity of classical HLA-A, -B, and -C alleles present in the human population, only two HLA-E alleles exist, which differ only by one amino acid and are functionally identical. Furthermore, while classical HLA-A and -B molecules are removed from the surface of HIV-infected cells by the Nef protein, HLA-E surface expression increases dramatically. These desirable traits raise the possibility that a vaccine targeting HLA-E could induce a universal T cell response, which would be unaffected by the immune evasion activities of the Nef protein, and shared by all vaccinated individuals. To investigate this intriguing idea, we will define MHC-E-restricted CD8+ T cell epitopes in both humans and rhesus macaques in specific aim 1 of this proposal. In specific aim 2, we will characterize the functionality, TCR usage, and antiviral efficacy of these unusual T cells. In specific aim 3, we will vaccinate macaques with a novel vaccine approach that delivers SIV antigens simultaneously with viral proteins identified to trigger MHC-E presentation. We will subsequently challenge these animals with low-dose SIV to determine the protective capability of MHC-E-restricted CD8+ T cells. Successful completion of these studies could define an entirely new approach to inducing universal protective immunity by mobilizing the monomorphic MHC-E molecule.

Progress during the reporting period (2-5 sentences): We established the existence of and characterized SIV-specific CD8+ T cells that are restricted by the nonclassical MHC-E molecule. To explore MHC-E in a genetically simplified nonhuman primate model we have determined the viral genes critical for cross species infection of Mauritian origin cynomolgus macaques.

Publications resulting from the project.

Excluded by Requester

Funding Sources (PIs and sources):

Jonah	Sacha, Ph.D.	NIH/NIAID AI117802
Helen	Wu, Ph.D.	Salary support only - NIH/NIAID – 1 F31 AI22471-01

Project Title: Reversal of Adaptive Immune Dysfunction in Shock and Kill HIV Cure Strategies
SPID: 2393
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester
University of Hawaii

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
None

Project Description (one paragraph):
Strategies to eliminate the HIV viral reservoir to date have not succeeded. Here, we propose to deplete latently HIV-infected CD4 memory T cells in highly active antiretroviral therapy (HAART)-suppressed patients by targeting the TIGIT and PD-1 immune-inhibitory pathway to restore superior anti-HIV immunity. Our central hypothesis is that co-blockade of TIGIT and PD-1 ligand (PDL-1) synergistically can eliminate or repress HIV and SIV *in vitro* and *in vivo* following reactivation of the latent HIV reservoir. To accomplish these goals, we propose to first extend our preliminary observations demonstrating improvement of HIV and SIV specific CD8 T cell effector activity by combinational blockade of TIGIT and PD-L1 in HIV infection and in non-human primates during SIV infection, and determine whether TIGIT and PDL-1 targeted reagents regenerate potent CD8 T cells capable of eliminating HIV/SIV latently infected cells in an *in vitro* viral suppression assay. We will further test these strategies *in vivo* in the setting of suppressive HAART-treated SIV-infected rhesus macaques. This research is significant because these studies will inform the development of novel strategies for immunotherapeutics to eliminate or suppress latent HIV infection and may identify novel surrogate pathways to target HIV/SIV infection.

Progress during the reporting period: We have obtained the TIGIT antibody expressing hybridoma and are currently expanding this cell line *in vitro*.

Publications resulting from the project.
None.

Funding Sources (PIs and sources):
Jonah Sacha, PhD — Funded by University of Hawaii, NIH/NIAID – 1 R21 AI22393-01

Project Title: UCSF-GVI Center for AIDS Research: Targeting Tim-3 for Elimination of HIV Reservoirs
SPID: 0019
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
University of California – San Francisco

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core. Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester
Kagawa University

Project Description: This project will test the hypothesis that directly targeting the Tim-3:Gal-9 pathway can destroy latently HIV-infected CD4+ T cells. We will administer the most efficacious Tim-3:Gal-9 reagent to HAART-suppressed, SIV-infected macaques to demonstrate proof-of-principle that targeting this pathway is a viable approach to clearing the HIV latent reservoir.

Progress during the reporting period (2-5 sentences): We identified soluble Gal-9 as a potent HIV latency reversing agent. We have administered Gal-9 to healthy, SIV-naïve macaques and demonstrated that Gal-9 can be administered subcutaneously to achieve in vivo levels necessary to achieve latency reversal.

Publications resulting from the project:
Excluded by Requester

Funding Sources:
Lishomwa Ndhlovu, M.D., Ph.D. University of Hawaii/UCSF/NIH National Institute of Allergy & Infectious Disease 5P30 AI027763

Project Title: An Unconventional, Effector Memory T Cell Vaccine for Influenza
SPID: 2837
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester — National Microbiology Laboratory, Canada

Oregon Health & Science University

Project Description: The world may be facing an impending crisis and immediate threat from an uncontrolled influenza outbreak. An influenza pandemic has greater potential to cause large numbers of deaths/illnesses over a shorter time period than virtually any other natural health threat. Antibody-mediated influenza vaccines are extremely strain-specific due to highly variable hemagglutinin (HA) and neuraminidase (NA) antigens. Moreover, influenza vaccines are not effective in the elderly population that is most at risk for developing lethal infection. For this reason, there is an urgent need to develop vaccines that control multiple strains over many years including in the elderly. The clearest means of preventing or minimizing the global catastrophe that will result from widespread infection of a susceptible human population with a new influenza pandemic strain is prophylactic vaccination aimed at inducing broadly reactive, universal immune responses against a range of viral isolates and subtypes. The goal of this project is to demonstrate that effector memory T cells (TEM) induced by CMV- vectors carrying conserved flu antigens will protect against deadly forms of influenza virus. To this end we will design new Rhesus CMV vaccine vectors expressing conserved influenza internal proteins and test the ability of the novel T cells induced by these vaccines to protect against highly pathogenic avian influenza. Successful completion of these studies would lay the foundations for a novel approach to develop a universal influenza vaccine.

Progress during the reporting period: We constructed RhCMV strain 68-1 vectors expressing internal proteins from 1918 influenza. These constructed RhCMV vectors engendered influenza-specific T cells that were nonclassically restricted. Challenge with highly pathogenic 1918 influenza revealed that rhesus macaques are surprisingly resist to highly pathogenic flu viruses as macaques exhibited only minor clinical symptoms.

Publications resulting from the project.
None.

Funding Sources:

Jonah	Sacha, Ph.D.	NIH/NIAID R21AI112837

Project Title: Characterizing the Role of CMV Latency in Solid Organ Transplant Rejection
SPID: 6633
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? (No)

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):

Project Description (one paragraph):
The goal of this project is to determine the mechanisms of Human cytomegalovirus (HCMV)-induced accelerated transplant vascular sclerosis (TVS), which is the hallmark vascular disease associated with chronic rejection (CR) of solid organ allografts. Clinical studies have directly associated HCMV infection with the acceleration of TVS and CR. Approximately 75% of the solid organ donor/recipient population is HCMV+, making it difficult to avoid the negative impact of CMV on CR. HCMV infections persist life-long in a latent form that reactivates during immunodeficiency and under inflammatory conditions like those occurring with transplantation. CMV naïve transplant recipients (R-) of latently HCMV-infected donor grafts (D+/R-) are at highest risk for developing CMV disease and CR. To date the viral mechanisms involved in HCMV reactivation from latency and subsequent acceleration of TVS are unknown. To address this issue, we have developed a rat heart transplant CR model that exhibits all of the hallmarks of human TVS/CR. *We hypothesize that CMV-induced alteration of donor tissue immune profiles prior to transplantation in part mediates the ganciclovir-insensitive accelerated rejection of latently infected donor tissues transplanted into naïve recipients by providing a scaffold for immune activation.* Our first goal is to identify mutations in RCMV chemokines that disrupt chemokine activity while retaining pentameric complex activity and vice versa to characterize the mechanisms by which CMV recruits immune cells into the donor tissues and their role in host transplant rejection. We will characterize the phenotype of the infiltrating immune cells, determine whether they are CMV-specific, as well as identify whether they form tertiary lymphoid structures. We will also characterize the changes in the profiles/antigen specificity of heart resident T cells during latency and determine the role of passenger leukocytes in the development of allograft TVS/CR and viral dissemination.

Progress during the reporting period:
We have constructed a number of mutant recombinant RCMV-containing mutations in R129 and R131 for in vivo characterization as well as made the corresponding recombinant proteins for in vitro characterization. We have made considerable progress on depleting macrophages from latently infected donor tissues and found that their removal prior to transplantation greatly improves graft survival.

Publications resulting from the project.
None.

Funding Sources (PIs and sources):
Daniel Streblow, PhD NIH/NIAID – 1 R01 AI16633-01A1

Project Title: Developing a Model for Determining the Causal Relationship Between Zika Virus Infection During Pregnancy and Fetal Microcephaly
SPID: 1032
Unit/Division: Pathobiology & Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? (No)

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctoral level only):
None

Project Description (one paragraph):
Zika virus (ZIKV), a mosquito-borne flavivirus closely related to yellow fever and dengue viruses, is currently causing a large outbreak in the Americas. Historically, ZIKV was considered a sporadic, relative mild disease. However, current observations with this recent outbreak indicate ZIKV may cause major neurological birth defects such as microcephaly. Microcephaly is characterized by abnormal smallness of the head, a congenital condition associated with incomplete brain development. Studies in humans indicate risk of CNS disruption from exposures to ZIKV that occurs from 8-27wks, emphasizing the importance of assessing ZIKV infection during all 3 trimesters. Our central hypothesis is that maternal ZIKV infection during pregnancy has a deleterious effect on utero-placental perfusion and initiates a fetal and placental inflammatory response that contributes to the development of microcephaly and other aberrations of fetal development. Utilizing our unique non-human primate (NHP) catheterized pregnancy model, the proposed Specific Aims are designed to further our understanding of the pathogenesis of ZIKV infection during pregnancy and the severity of fetal neurological injury in relation to the timing of infection (1st, 2nd or 3rd trimesters).

Progress during the reporting period:
We have infected pregnant rhesus macaques with Zika virus at different points post-gestation. We are currently writing up our results for publication.

Publications resulting from the project.
None.

Funding Sources (PIs and sources):
Daniel Streblow, Ph.D. NIH/NICHD – 1 R21 HD091032-01

Project Title: Investigating the Development of AIDs and non-AIDS Defining Cancers In Aged SIV-infected Rhesus Macaques.
SPID: 6404
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester Oregon Health & Science University\
Oregon Health & Science University

Project Description:
Individuals with an underlying HIV-infection have an increased risk of developing AIDS-defining and non-AIDS-defining cancer. This is a significant healthcare and economical concern as the HIV-infected population is surviving longer and living fuller and productive lives owing to the advent of antiretroviral therapy (ART). Several parameters are associated with this increased incidence in cancer, but two factors that are consistent with cancer development in general are the increasing age of individuals and HIV infection, which suggests there is interplay between aging and HIV infection that leads to an increased incidence of cancer development and progression. Aging is well known to be a risk factor for developing non-AIDS-defining cancer; however, aged HIV-infected individuals are 3x more likely to develop non-AIDS-defining cancer than the comparable normal immunocompetent aged population. Thus, molecular and cellular factors that change over time due to aging and HIV infection must intersected to accelerate the processes that make this population more at risk to develop cancer. Aspects of this can be studied longitudinally in HIV-infected individuals, but this approach has shortcomings and is dependent upon the enrollment of patients that may drop out due to relocation or disinterest. An alternative approach is to investigate an animal model that recapitulates most, if not all, aspects of HIV pathogenesis. Here, we propose to use the widely accepted simian immunodeficiency virus (SIV)-infected nonhuman primate (NHP) model that recapitulates multiple aspects of HIV pathogenesis, including development of AIDS-related malignancies. This outbred model approximates HIV infection and can be surgically and immunologically manipulated to investigate the alterations that occur to lead to cancer. Our studies will be performed through a series of experimental *in vivo* infections and characterization of the host immune response and next generation sequencing of biological samples, including cancer tissues. Combining these types of *in vitro* and *in vivo* experiments to address cancer development and progression will enable researchers to dissect how alterations in the host impacts disease in susceptible populations and how scientists can shift the pendulum in favor of the host.

Progress during the reporting period (2-5 sentences):
We have currently identified and assigned 8 aged rhesus macaques for Specific Aim 1 (SA1) studies, which are underway.

Publications resulting from the project.
None.

Funding Sources:
Scott Wong, Ph.D. NIH/NCI R01CA206404

Project Title: Rhesus HHV-8 Homologue in AIDS-Related Malignancies
SPID: 5922
Unit/Division: Pathobiology and Immunology
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? Yes

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project (doctoral level only):
Excluded by Requester Oregon Health & Science University
Oregon Health & Science University

Project Description: Viruses cause an array of disease manifestations ranging from acute respiratory disease, intestinal diarrhea, hemorrhagic fevers, hepatitis, cancer, and chronic autoimmune disease and, in some instances, death. One virus that was recently identified to be associated with cancer in humans in 1995 is human herpesvirus 8 (HHV8)/Kaposi's sarcoma-associated herpesvirus (KSHV). An accumulation of scientific evidence now substantiates HHV8 as the etiological agent responsible for classical and acquired immunodeficiency disease syndrome (AIDS)-related Kaposi's sarcoma (KS), as well as other lymphoproliferative disorders (LPDs) in immunocompetent and human immunodeficiency virus (HIV)-infected humans. Despite all of this scientific evidence it is difficult to fully understand how the virus causes disease without the ability to follow a natural infection. As such, alternative in vivo models that are readily accessible and can recapitulate HHV8 infection and associated disease are absolutely needed to identify viral determinants of pathogenesis and how these specific determinants, either viral open reading frames (ORFs) or other viral-encoded macromolecules are involved in HHV8-mediated pathogenesis. Here, we propose to utilize a closely related and relevant virus that can manifest similar biological outcomes in its natural host. The genome of the virus, referred to as rhesus rhadinovirus (RRV) has been characterized and shown to be essentially colinear and encodes most of the viral ORFs thought to be associated with pathogenesis. More importantly, in vivo studies show that RRV infection in its natural host recapitulates many, if not most of the properties of HHV8, including persistence and LPDs. The long term goals of the proposed research project are to better understand how HHV8 interacts with its host, utilizing RRV and experimental infection its natural host.

Progress during the reporting period (2-5 sentences):
We have successfully created the RRV microRNA knockout virus (miRNA-ko RRV), which has each individual viral miRNA mutated with sequences to interrupt the stem loop structures required for miRNA processing. The virus has been sequenced and confirmed, and in vitro characterization is underway. Our initial analysis reveals that the recombinant grows slightly less than wild-type BAC-derived RRV in one-step growth assays on primary rhesus fibroblasts, which suggests that either structural alterations impacted this region of the genome involved in DNA replication or that one or more of the viral miRNAs are important for growth.

Publications resulting from the project.
Excluded by Requester

Funding Sources:
Scott Wong, Ph.D. NIH/NCI R01CA075922

Project Title: Postmenopausal Monkey Resource
SPID: 1895
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester

Oregon Health & Science University
University of California - Riverside
Oregon Health & Science University
Oregon Health & Science University

Project Description: The Women's Health Initiative trial (WHI) trial generated considerable controversy because it was interpreted as an indictment of post-menopausal hormone therapy (HT), when in fact, it did not study hormone replacement, which would have required use of the natural hormones, estradiol (E) and progesterone. WHI administered synthetic hormones a decade or more after menopause, raising the questions of whether bioidentical hormones are better and whether there is an optimal time frame for HT.

Progress during the reporting period (a few sentences):
The last measurements containing assessments of the Delayed E group after 2 years placebo + 6 months of ERT were finished and the monkeys have been euthanized. Compared to placebo and DeE animals, females treated with ImE had higher activity levels up to 18 months post-OvH based upon activity collars and behavioral observations. The ImE group learned a spatial maze test significantly faster than the placebo or DeE groups. ImE maintained lower fat mass as well as glucose and insulin regulation significantly better than placebo or DeE treatments at 6 months, but this benefit was lost over the following 18 months and all groups exhibited elevated fat mass and insulin in Glucose Tolerance Tests at 30 months. HOMO-IR was also elevated in placebo and DeE animals. Fenfluramine challenges, expression array analysis of the serotonergic dorsal raphe, MRIs, core body temperature, and immune function tests are completed and the data are being prepared for publication. One placebo-treated animal had a stroke. A competitive renewal of this grant has been submitted and will be funded as soon as congress passes a budget.

Publications resulting from the project.
Nothing to report for this reporting period.

Funding Sources:
Cynthia L. Bethea, Ph.D. National Institutes of Health, Office of the Director - 5R24OD011895-04

Project Title: Effects of CG and VEGF on the Vasculature of the Primate Ovary and Uterus
SPID: 8819
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University
Oregon Health & Science University

Project Description: Studies are proposed to examine the role of a critical local factor, vascular endothelial growth factor (VEGF) in the response to chorionic gonadotropin (CG) during controlled ovulation cycles (COS) in rhesus macaques, an excellent non-human primate model of women's reproductive health. The experiments proposed in this R21 application should discern between the VEGF-dependent and independent actions of CG resulting in early and late onset symptoms of ovarian hyperstimulation syndrome (OHSS). The contribution of CG-induced VEGF to induce the marked ovarian/systemic hyperpermeability associated with onset of OHSS has not been directly investigated in primates. Women with polycystic ovarian syndrome (PCOS~ approximately 5-10% of women in the USA) are at high risk for developing OHSS during COS for infertility treatments~ avoidance of OHSS during COS is a major concern for infertility specialists. To date, investigations into the relationship between vascular structure/function of reproductive tissues and actions of local angiogenic factors have been indirect or static in nature involving single observations after tissue removal. The PI has applied sensitive, minimally invasive techniques enabling repeated measurements of vascular structure-function in the ovaries and uterus of nonhuman primates. Contrast enhanced-Ultrasound (CE-US) and Dynamic Contrast Enhanced- Magnetic Resonance Imaging (DCE-MRI) protocols allow direct quantification of blood flow/volume and tissue permeability of reproductive tissues. Notably, it is possible to simultaneously apply the proposed novel imaging approaches to the uterus, as well as the ovary, to discern the VEGF-dependent versus-independent effects of CG on vascular dynamics in primates. In addition to quantifying the effects of VEGF neutralization on vascular function of reproductive tissues, effects on other angiogenic factors (angiopoietins, ANGPTs) will be quantified as possible therapeutic interventions for OHSS. The results of these experiments will guide future studies investigating novel molecules affecting both ovarian and uterine/systemic vascular function by both imaging and molecular methods. These techniques can be used to identify and evaluate specific therapeutic interventions for women at risk for OHSS and infertility.

Progress during the reporting period (a few sentences):
Females completed final COS cycles followed by simulated early pregnancy to mimic an implanting embryo of early pregnancy (SEP). Neutralization of VEGFA during COS+SEP tended to decrease ovarian blood volume and vascular flow. Additionally, COS+SEP+anti-VEGFA mAb resulted in a significant decrease in vascular flow through the basalis (junctional) zone of the uterus. Minimal effects in SEP cycles were not due to inadequate dosing since VEGFA levels in follicular fluid were reduced 78-fold by anti-VEGF mAb. Media from cultures of granulosa cells from COS cycles demonstrated exposure to VEGFA mAb in vivo also reduced VEGFA levels 4-fold, and reduced production of P4 and ANGPT1 from cultured LGCs; the ratio of ANGPT2/1 increased following VEGFA neutralization in vivo.

Publications resulting from the project:
Excluded by Requester

Funding Sources:
Cecily Bishop, Ph.D. NIH National Institute of Child Health & Human Development R21HD078819-02

Project Title: OHSU Women's Reproductive Health Research K12 Program
SPID: 5809
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:
Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester — Oregon Health & Science University

Project Description (one paragraph):
This application established a multidisciplinary basic, translational, and clinical research training and career development program, the Oregon Health & Science University (OHSU) Women's Reproductive Health Research K12 Program, which will foster and cultivate a cadre of OB/GYN physicians to transition into independent physician-scientists in women's reproductive health. The program builds upon long-standing collaborations between the OB/GYN Department and prominent OHSU Centers, Institutes, and Departments, including the Oregon National Primate Research Center, and Knight Cardiovascular and Cancer Research Institutes, to provide a strong foundation for multidisciplinary training, mentorship, and research. The primary aim of the program is to produce highly-qualified OB/GYN researchers with a specific focus on the reproductive life cycle spanning the preconception period (including family planning) to developmental biology to pregnancy care and complications in both women and their offspring. The specific areas of emphasis would be: (1) contraceptive development, effectiveness, and impact; (2) developmental origins of health and disease (DOHaD) - fetal programming; (3) reproductive biology including ovarian and uterine function/dysfunction, the developing embryo and fetus; (4) maternal physiology, pathophysiology, pregnancy care and complications, and the outcomes of both women and their offspring. Upon completion of the OHSU WRHR K12 Program, scholars will have expertise in research methods and the skills required for success as academic physician-scientists in reproductive health. Scholars will develop expertise relevant to his or her research interests, along with the specific research skills appropriate to that research topic as well as skills in scientific writing including grant writing and academic career development. By the end of the training period, each scholar will be well-prepared to become independently funded physician-scientists. With this in mind, the OHSU WRHR K12 Program has the following Specific Aims: 1) To attract and develop a diverse group of OB/GYN physician-scientists. 2) To train scholars across the span of the reproductive life cycle from contraception, to DOHaD, developmental biology, birth and beyond. 3) To train scholars along the spectrum of basic/translational/clinical research - from bench to bedside to clinical trials to health services research as applied to Women's Health Research.

Progress during the reporting period (one paragraph): Excluded by Requester is servicing as recruitment officer, and Excluded by Requester is serving as scientific director. In the second year of award, two young faculty members are receiving career development assistance as WRHR scholars, Excluded by Requester (September, 2015) and Excluded by Requester (January, 2016). Training plans and career goals are in place with their mentoring teams.

Publications resulting from the project
Excluded by Requester

Funding Sources (PIs and sources):
Aaron B. Caughey, M.D., Ph.D. — NIH National Institute of Child Health & Human Development K12HD085809-02

Project Title: Investigating Pre-Implantation Chromosomal Instability in Assisted Reproduction
SPID: 6073
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description: By applying whole-genome next-generation sequencing (NGS) for comprehensive chromosomal assessment, we will first determine the frequency of aneuploidy and sub- chromosomal errors during meiosis in individual mature rhesus oocytes and zygotes and potential correction upon chromosome-induced polar body extrusion. Using a combination of NGS and non-invasive time-lapse imaging to monitor early cleavage divisions and cellular fragmentation dynamics, we will then evaluate the incidence of mitotic chromosomal mis-segregation up to the ~8-cell stage and reconstruct all whole and sub- chromosomal errors in each rhesus embryo by analyzing the genetic content of both single cells and fragments. Lastly, we will assess the potential contribution of meiotic chromosomal mis-segregation to mitotic errors and subsequent development by performing polar body biopsy on zygotes, allowing the embryo to proceed until the ~8-cell stage, and distinguishing meiotic versus mitotic errors based on chromosomal mosaicism, fragmentation timing, and microsatellite analysis. This work will greatly contribute to our knowledge of normal primate embryogenesis with additional implications for translational application to human infertility and IVF treatment.

Progress during the reporting period (a few sentences):
We determined that the frequency of aneuploidy, micronuclei, and cellular fragmentation in pre-implantation embryos are conserved between primates. By analyzing the chromosomal content of both polar bodies and individual blastomeres, we demonstrated that mitotic errors occur at an equal or greater propensity than meiotic errors. Lastly, we also confirmed that certain embryos contain fragments that encapsulate whole and/or partial chromosomes lost from blastomeres, which become fragile and damaged. We have a manuscript currently in preparation from this research.

Publications resulting from the project:
None at this time

Funding Sources:

Shawn L.	Chavez, Ph.D.	NIH National Institute of Child Health & Human Development R01HD086073-01A1

Project Title: Functional Imaging of Human Placental Structure, Blood Flow, and Oxygenation
SPID: 7182
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/ Institutional affiliation:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Project Description: A fundamental limitation in our understanding of placental function and development is our inability to quantitatively assess basic functional outputs such as blood flow and oxygenation. Our multidisciplinary group has designed a magnetic resonance imaging (MRI) data acquisition and analysis protocol that utilizes endogenous contrast to quantify maternal perfusion of the placenta, has been validated in a pre-clinical animal model and is now ready to be transitioned to human application. The objective of this proposal is therefore to optimize the endogenous contrast MR acquisition protocols for human pregnancy, adapt the 3D analysis tools we previously developed for analyzing contrast-dependent data for modeling of non-contrast perfusion maps in humans, and ascertain fundamental data that will establish the normal variance of placental perfusion in pregnant women longitudinally across gestation in normal and at-risk human pregnancies, focusing on smoking as an environmental perturbation of placental function. We are proposing a longitudinal prospective cohort study of 300 pregnant women across two sites; all study participants will undergo three placental MRI scans across gestation (12-16, 26-28 and 32-34 weeks gestation) and placental tissue will be collected at the time of delivery. Subjects will be recruited based on selection criteria in three cohorts: 1) non-smokers, 2) smokers and 3) high risk for adverse pregnancy outcome. Our scientific approach will allow us to generate data that will demonstrate the normal variance of placental perfusion in pregnant women across gestation. Application of our endogenous contrast MRI protocol in women at high risk for vascular compromise (i.e., smokers and those with a prior history of placental insufficiency) will allow us to test the sensitivity and specificity of this new technique for predicting adverse clinical outcomes.

Progress during the reporting period: All regulatory document preparation and approval, along with study personnel training was completed prior to enrollment opening in October 2016. To date five women have been recruited with first trimester MRI scans completed. In addition, our MRI physicists continue to develop acquisition and post-processing strategies to improve data quality. Preliminary data from these pilot studies are very encouraging for the success of these protocols.

Publications resulting from the project.
None at this time

Funding Sources (PIs and sources):

Antonio E.	Frias, M.D.	NIH National Institute of Child Health & Human Development
Christopher D.	Kroenke, Ph.D.	U01HD087182-01

Project Title: Development and validation of MR imaging methods for in vivo assessment of placental perfusion and oxygenation
SPID: 6331
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:

Excluded by Requester	Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Project Description: Aberrant placental development has been linked to virtually every adverse obstetric outcome including abnormalities in fetal growth, preterm delivery and stillbirth. Adequate blood flow and oxygen delivery are central determinants of placental function and fetal growth. The lack of imaging modalities that facilitate the in vivo study of both normal and abnormal placentas impedes our understanding of placental blood flow and oxygenation. We propose to overcome these limitations using magnetic resonance imaging (MRI) technology. Over the past 5 years we have utilized the nonhuman primate (NHP) to develop a dynamic contrast enhanced MRI (DCE-MRI) method that allows for the quantification of placental blood flow from each spiral artery. Although we recently demonstrated that the level of fetal exposure resulting from maternal administration of gadolinium-based contrast reagent during DCE-MRI is extremely low, the abundance of caution when imaging pregnant patients makes it highly pertinent to develop functional MRI methods that do not rely on contrast reagent administration. We are proposing to use our clinically relevant NHP model for non-contrast MRI sequence development and optimization. Simultaneous use of DCE-MRI in these studies will allow us to utilize our contrast dependent quantitative measure of placental perfusion as a benchmark for non-contrast modeling. The potential clinical benefits of developing MRI protocols for the in vivo assessment of placental blood flow and oxygenation are tremendous; understanding normal placental function will improve clinical monitoring of pregnancy, permit early identification of women at-risk for placental insufficiency, and facilitate intervention to improve fetal outcome.

Progress during the reporting period: These studies are underway with MRI data acquired from 2 completed pregnancies and 5 that are ongoing. We have developed and established methods to modulate oxygen and perfusion. In addition, we have successfully used an iron-based exogenous contrast agent that is considered safe for use in pregnancy to acquire placental perfusion measurements. MRI data analysis is ongoing.

Publications resulting from the project.

In Press

Funding Sources:

Antonio E	Frias, M.D.	NIH National Institute of Child Health & Human Development R01HD086331-02

Project Title: Primate Model of Mid-Gestation Ureaplasma in Utero Infection: Prevention of Neurologic Sequelae
SPID: 9610
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
University of Washington
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
University of Alabama at Birmingham

Project Description: The objectives of this proposal are to assess the therapeutic effect of antenatal maternal antibiotic therapy in preventing or mollifying cerebral white matter damage in the neonate (as a consequence of prolonged U.parvum intra-amniotic infection, IAI) and to correlate neurobehavioral outcomes with neuropathologic findings of neonatal brain injury. Our hypothesis is that treatment of U.parvum IAI with a specific macrolide antibiotic, azithromycin (AZI) will mitigate fetal origins of cerebral white matter injury and decrease the severity of perinatal neurological impairment. We will utilize non-human primate model of IAI, with inoculation of U.parvum (serovar 1) at 105 days gestation. Our new approach will mimic the indolent nature of Ureaplasma spp. infections during human pregnancies by prolonging fetal exposure to these microorganisms and the resultant inflammatory milieu, with the potential for intensified brain injury. Fetal cardiovascular hemodynamic and regional circulatory changes in response to U.parvum IAI, and maternal therapy, will be monitored by Doppler ultrasonography and linked with magnetic resonance imaging (MRI) of the fetal brain during critical periods of development. Neurodevelopmental outcomes such as dysfunctional neuromuscular dexterity, neurobehavioral and cognitive abnormalities will be correlated with neuropathologic findings of perinatal white matter inflammation. A number of mechanistic endpoints will be ascertained that will aid in our understanding of the causal links among Ureaplasma infections, fetal inflammatory responses, and hemodynamic adaptations, which portend cerebral white matter damage and neurological disabilities.

Progress during the reporting period (a few sentences):
We have shown that infants exposed to *U. parvum* IAI require a higher level of clinical intervention compared to control and AZI-treated infants. Cognitive and behavioral development in those infants whose mothers received antibiotic therapy appeared less compromised, suggesting the safety of antenatal antibiotic therapy and improved neonatal health. We provide new data that indicate sexual dimorphism in fetal immune responses to *U.parvum* IAI with a potential lasting effect on male neonates (e.g., persistent brain inflammation and functional neurological impairments). Contre to original hypotheses, our new preliminary data also suggests antenatal treatment with AZI may further potentiate adverse neurobehavioral and cognitive development, particularly in male infants.

Publications resulting from the project:
Excluded by Requester

Funding Sources:
Peta Grigsby, Ph.D. NIH National Institute of Child Health & Human Development, R01HD069610-05

Project Title: Identification of Intrafollicular Determinants Predictive of Oocyte & Embryo Developmental Potential
SPID: 1028
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
None

Project Description: The development of in vitro fertilization four decades ago has provided millions of infertile couples the opportunity to have children. Despite such remarkable advances in our understanding of reproductive physiology and its application toward the treatment of infertility, limitations in efficiency persist as measured by a low live birth rate. The success rate, approximately 35% for women under 37, has only marginally increased since in vitro fertilization appeared in the clinic. A major factor that limits its success is the use of subjective criteria for choosing which oocytes will be fertilized and which embryos that develop will be transferred back to the recipient. Thus, determining the molecular and cellular characteristics that define oocytes with the greatest potential to form embryos capable of yielding a healthy baby is of paramount importance. We hypothesize that in-depth metabolomic analysis of the follicular environment via collection of follicular fluid and the media obtained from embryo cultures shortly after fertilization, as well as non-invasive real-time imaging, will allow us to identify markers of optimal oocyte competency and embryonic developmental potential. Analysis of the follicular fluid and embryonic culture media metabolome will be accomplished through the use of state-of-the-art mass spectroscopy platforms, whereas real-time assessment of cell division parameters and embryo fragmentation will be assessed by recently developed, innovative live cell imaging techniques. These studies will be performed using a clinically relevant and experimentally tractable nonhuman primate model, the rhesus macaque. It is anticipated that the data obtained from these studies will identify molecular markers and cellular parameters that differentiate between oocytes with high versus low developmental potential, thereby limiting the unnecessary fertilization of oocytes unlikely to develop, implant into the uterus, and result in a normal term pregnancy.

Progress during the reporting period (a few sentences):
Ongoing studies include completing the proposed ovarian stimulation protocols and collection of oocytes and the associated follicular fluid from individual follicles. It is anticipated that the necessary samples will be collected at the end of the next 2 to 3 months, at which point all follicular fluid samples will be subjected to metabolomics analyses. The metabolomics profile will then be correlated to developmental outcomes for each oocyte.

Publications resulting from the project.
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: Identification of Intrafollicular Determinants Predictive of Oocyte & Embryo Developmental Potential
SPID: 1028
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
None

Project Description: The development of in vitro fertilization four decades ago has provided millions of infertile couples the opportunity to have children. Despite such remarkable advances in our understanding of reproductive physiology and its application toward the treatment of infertility, limitations in efficiency persist as measured by a low live birth rate. The success rate, approximately 35% for women under 37, has only marginally increased since in vitro fertilization appeared in the clinic. A major factor that limits its success is the use of subjective criteria for choosing which oocytes will be fertilized and which embryos that develop will be transferred back to the recipient. Thus, determining the molecular and cellular characteristics that define oocytes with the greatest potential to form embryos capable of yielding a healthy baby is of paramount importance. We hypothesize that in-depth metabolomic analysis of the follicular environment via collection of follicular fluid and the media obtained from embryo cultures shortly after fertilization, as well as non-invasive real-time imaging, will allow us to identify markers of optimal oocyte competency and embryonic developmental potential. Analysis of the follicular fluid and embryonic culture media metabolome will be accomplished through the use of state-of-the-art mass spectroscopy platforms, whereas real-time assessment of cell division parameters and embryo fragmentation will be assessed by recently developed, innovative live cell imaging techniques. These studies will be performed using a clinically relevant and experimentally tractable nonhuman primate model, the rhesus macaque. It is anticipated that the data obtained from these studies will identify molecular markers and cellular parameters that differentiate between oocytes with high versus low developmental potential, thereby limiting the unnecessary fertilization of oocytes unlikely to develop, implant into the uterus, and result in a normal term pregnancy.

Progress during the reporting period (a few sentences):
Ovarian stimulation protocols were completed, which allowed for the collection of oocytes and the associated follicular fluid from individual follicles. The retrieved oocytes were assessed for their ability to fertilize in vitro and form blastocysts, whereas the corresponding follicular fluid samples underwent metabolomics screening. Several small molecules were identified whose levels correlated with the potential of the oocytes to fertilize and undergo subsequent embryonic development. These molecules may, therefore, serve as markers of oocyte quality and developmental outcome.

Publications resulting from the project.
None at this time

Funding Sources:
Excluded by Requester Private Source

Project Title: Center for development of non-surgical permanent contraception; primate testing contraceptive leads
SPID: 8762
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester Oregon Health & Science University

Project Description: Our long-term goal is to develop a low-cost, nonsurgical approach to permanent female contraception in alignment with the Gates Global Program to improve human health by preventing unintended pregnancy. Although new methods of permanent female contraception (e.g. Essure) have been developed privately, these involve expensive technology and a high level of surgical training, and are not practical technologies to utilize in low resource settings. Our hypothesis is that increased funding for research in permanent contraception would yield one or more approaches that could be studied for feasibility and that a preferred option could then be developed for initial human clinical trials. To support this goal and further investigate our hypothesis, we proposed establishing an Oregon Center for Permanent Contraception Research (OPERM) at the Oregon National Primate Research Center (ONPRC) of the Oregon Health & Science University (OHSU). This project provides funding for planning of a center proposal that will include infrastructure improvements, animal resources, and scientific support and research funds over a 5-year period of funding.

Progress during the reporting period (a few sentences):
OPERM majors activities for the year include 1) conduct of research projects funded in year 1 and 2 evaluating novel approaches to permanent contraception using the baboon model; 2) release of RFP #2 Solicitation to fund development of a nonprimate animal model, followed by SAB review of the projects and award of a new project to Excluded by Requester for development of a guinea pig model; 3) RFP #3 Solicitation of pilot and foundation projects for year 3, with SAB review of projects and award of new projects to Excluded by Requester for liquid-based sclerotherapy and a novel delivery system, and Excluded by Requester for study of combined doxycycline/polidocanol foam; Excluded by Requester for a polidocanol delivery system, and Excluded by Requester (Univ of Washington) for drug-eluting fibers; 4) Progress meeting with scientific presentations from Year 1 and Year 2 projects; 5) RFP #4 Solicitation of pilot and foundation projects; SAB review and award of new projects to Excluded by Requester Excluded by Requester and 6) Outreach activities for pre-IND discussions leading to human clinical trials of polidocanol foam.

Publications resulting from the project.
Excluded by Requester

Funding Sources:
Excluded by Requester Private Source

Project Title: Changes in vaginal impedance in normal cycling Cynomolgus Monkeys
SPID: 5099
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:
None

Project Description: Nonhuman primates are the most suitable animal models for identifying new contraceptives that target the reproductive tract. Intravaginal changes in micro-electrical impedance can be used to monitor the hormonal cycle and to predict the LH/Estrogen-surge based changes in vaginal mucus. The Draminski ovulation detector is a hand-held device that is marketed to measure vaginal impedance in dogs. We will test the use of the Draminski device in macaques, determine the variability of measurements across the menstrual cycle, and determine if impedance measured by this device correlates to changes in steroid hormone levels. Non-invasive detection of ovulation and or the effects of steroid hormone on vaginal mucus will facilitate the development of new on-demand contraceptives that target the reproductive tract.

Progress during the reporting period (a few sentences): Cynomolgus monkeys were trained to present for unrestrained sampling with the Draminsky device. After collecting repeated measurements, we found that the Draminsky device identified non-cycling females (e.g. animals with no E_2 surge or luteal phase; n=3) and cycling animals (both E_2 surge and luteal phase; n=12). Animals with a clear E_2 surge had decreased impedance on approximately day 9 through day 12 of the cycle. A third group of animals (n=3) was also identified with an uncertain E_2 surge, but a clear rise in progesterone. This group displayed variable vaginal impedance measurements mid-cycle.

Publications resulting from the project.
None at this time

Funding Sources:
Excluded by Requester
Private Source

Project Title: A macaque model for endometriosis induced pelvic pain and infertility
SPID: 2377
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project: None
Excluded by Requester
Oregon Health & Science University

Project Description: Nonhuman primates (NHPs) constitute the most suitable animals for preclinical studies on endometriosis. We demonstrated that endometriosis can be created by inoculating menstrual endometrium in artificially-cycled hormone treated rhesus macaques. In Specific Aim 1, we propose to refine and validate a protocol for creating endometriosis in naturally cycling macaques. In Specific Aim 2, we will document the growth of induced endometriotic lesions and assess the effects of lesion abundance and size on the presentation of pain in the animals. Based on our pilot data, we designed a pain and discomfort scoring system, which will be combined with activity monitoring, to quantify discomfort in animals with induced disease and guide the prescription of pain relief for the animals. Like women, NHPs with endometriosis are expected to display reduced fertility compared to endometriosis-free subjects. In Specific Aim 3, we will assess the effect of the induced lesions on fertility. This research will provide a definitive assesment of techniques required to create endometriosis in the macaque for future studies, and characterize the progression of the disease with specific emphasis on assessment of pain and infertility in this useful NHP model.

Progress during the reporting period (a few sentences):
We refined methods for inducing endometriosis in macaques. Success rate for inducing disease was 55% after one procedure, and 90% after 3 procedures (n=20). Most (16) out of 18 animals with the disorder were asymptomatic for pelvic pain. Histological analysis revealed abundant nerve fibers in the lesions, but there was no correlation between nerve fiber density and the presentation of abdominal pain.

Publications resulting from the project.
None at this time

Funding Sources:
Ov D. Slayden, Ph.D. National Institutes of Health, Office of the Director 1R21OD012377-02

Project Title: Contraception by Blockade of Periovulatory Events in Primates
SPID: 5744
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester Excluded by Requester Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester
University of Minnesota
Oregon Health & Science University
University of South Florida
Oregon Health & Science University
Oregon Health & Science University

Project Description: This NIH-funded Contraceptive Development Research Center targets the discovery and development of novel contraceptive agents that prevent one or more periovulatory events in adult, female primates during the menstrual cycle. Three research projects and one animal core utilize Old World (macaque) monkeys to generate new information and proof-of-concept regarding potential modalities for preventing oocyte fertilization, and hence fertility, in women. Project I, "Control of Oocyte Maturation" addresses the hypothesis that novel follicle (granulosa) cell- and oocyte-derived proteins control nuclear and cytoplasmic maturation of the oocyte, and can be exploited to prevent egg maturation. Project II, "Control of Follicle Rupture and Cumulus-Oocyte Activities" tests whether specific antagonists of granulosa- or oocyte-derived proteins disrupt cumulus-oocyte expansion or ovulation. Project III, "Control of Gamete Transport and Fertilization" investigates reversible and nonreversible methods to prevent sperm and oocyte transport in the reproductive tract, and hence fertilization and fertility. Promising agents will be tested in the Nonhuman Primate Contraceptive Core for contraceptive efficacy, reversibility and side effects. Collaborations with colleagues at the University of Minnesota and Excluded by Requester facilitate drug discovery, nonhuman primate testing, and ultimately early (Phase I) clinical trials.

Progress during the reporting period (a few sentences): Project I continues collaborations with Excluded by Requester Excluded by Requester at the University of Minnesota to evaluate two non-hormonal contraceptive targets; a) the selective phosphodiesterase (PDE) 3 inhibitor ORG 99356, and b) the oocyte specific WEE2 (WEE1b) kinase. Studies with WEE2 identified critical structural configurations that maximize specificity. Project II continues to determine the role that proteolytic processes and prostaglandin E2 receptor (PTGER) subtypes play in primate ovulation. Delivery of an antagonist to PTGER3 or an inhibitor of select metalloproteinase enzymes that degrade chondroitin-sulfate proteoglycans into the follicle prevented ovulation, indicating that PGE2 signaling and proteoglycan remodeling in the primate follicle are critical events necessary for ovulation. Project III completed an assessment of eF-MENT released by vaginal ring (IVR) on fertility. eF-MENT releasing IVR that produced serum levels >100 ng eF-MENT/ml blocked sperm passage through the reproductive tract and was contraceptive. Animals became pregnant when levels of eF-MENT dropped below 100 ng/ml indicating that the contraceptive effect is reversible. Also, a protocol for noninvasive collection of macaque cervix epithelial cells by cytobrush was developed. RNA analysis revealed that IVR treatment of macaques with contraceptive agents, including progesterone, levonorgestrel and eF-MENT, suppressed epithelial cell expression of mucins MUC1 MUC5B and OVGP1 (MUC9). This novel technique provides a rapid non-invasive method of assessing the effect of contraceptive compounds that target the cervix.

Publications resulting from the project

Excluded by Requester

Funding Sources: Richard L. Stouffer, Ph.D., NIH Natl Institute of Child Health & Human Dev 5U54HD055744-10

Project Title: Hyperandrogenemia, Diet and Female Reproductive Health
SPID: 1836
Unit/Division: Reproductive and Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester

Sapporo Medical University
Baylor University
Oregon Health & Science University
University of Pittsburgh
University of California at Los Angeles
University of California at Los Angeles
University of California at Los Angeles
University of Oregon
University of California at Los Angeles
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description: A National Center for Translational Research in Reproduction and Infertility (NCTRI) addresses the effects of hyperandrogenemia and obesity on female reproductive health. This interdisciplinary, translational program will discern between the effects of excess androgen exposure and metabolic changes due to a typical Western-style diet (WSD) in female monkeys) on: (1) the hypothalamus-pituitary-ovary-reproductive tract axis, as well as adipose tissue; (2) the impact on fertility; and (3) if the treatment effects are reversible. One project studies a specific population of lean women with polycystic ovarian syndrome (PCOS).

Progress during the reporting period (a few sentences):
After 3 years of treatment, differences in metabolic parameters, plus the structure-function of ovarian, uterine, and adipose tissues are evident between control and T±WSD treated monkeys. A fertility trial was initiated to evaluate fecundity and maternal-fetal-placental function between treatment groups. Pilot studies are also evaluating: (1) the direct actions of vitamin D_3 on primate follicles in vitro, plus the effects of three years of treatment (T±WSD) on (2) skeletal muscle metabolism and (3) the microbiome of the intestinal and reproductive tracts.

Publications resulting from the project

Excluded by Requester

Excluded by Requester

Funding Sources: Richard Stouffer, Ph.D., NIH Natl Institute of Child Health & Human Dev P50HD071836-04

Project Title: Progesterone Receptor and Action in the Primate Ovary
SPID: 0869
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the Project:

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University

Project Description: The goal of this research is to understand the mechanisms whereby luteinizing hormone (LH) either directly, or indirectly via locally synthesized steroids, regulates the structure-function of the peri-ovulatory follicle or corpus luteum (CL) in primates during the menstrual cycle. Recent evidence suggests that specific nuclear progesterone receptor isoforms (PGR-A and -B) regulate different activities in target tissue; and the discovery of nongenomic PGR membrane components (PGRMC1 and 2) adds another dimension to possible P actions in the ovary. Likewise, the PI's evidence that LH and P regulate expression of one estrogen receptor isoform (ER2) reintroduces the concept of local E action in the primate CL. Finally, recent whole genome analyses of the dynamics of the transcriptome in the macaque ovary provide the basis for manipulative studies to unravel the cellular and molecular events, prominently in immune cell-mediated processes, that are LH-dependent and steroid (P or E)-dependent in the primate ovulatory follicle or CL.

Progress during the reporting period (a few sentences):
In vivo protocols, using an adenoviral vector-RNAi to “knockdown” expression of the membrane progesterone receptor PGRMC1 in the preovulatory follicle of rhesus monkeys, were completed. Prevention of the PGRMC1-mediated actions of progesterone blocked ovulation and oocyte release, likely secondarily to causing follicular degeneration and microvascular disruption. This contrasts with our earlier evidence that prevention of nuclear progesterone receptor (PGR)-mediated actions blocks ovulation by disrupting specific processes (e.g., protease activity) required for ovulation and luteal development.

Studies were also completed to analyze cytokine production by immune cells within the primate (macaque) corpus luteum, with the focus on cells migrating into the regressing luteal tissue after the decline in progestogenic activity. Putative (CD11+) macropages produced numerous pro-inflammatory cytokines with chemoattractant (e.g., MCP-1) and chemotaxis (e.g., MDC) activity, whereas the numerous NK (CD16+) cells produced few cytokines. In a P-depleted milieu (functional regression), the increased cytokines from macrophages and cytotoxic activity of NK cells are likely critical for structural regression of the corpus luteum.

Publications resulting from the project.

Excluded by Requester

Funding Sources:

Richard L. Stouffer, Ph.D. — NIH National Institute of Child Health & Human Development, 5R01HD020869-29 (no-cost extension)

Project Title: Acetylcholine/acetylcholinesterase (Acetylcholin/acetylcholineestase) in the ovary
SPID: 1060
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester
Tianjin Central Hospital of Gynecology and Obstetrics, China

Project Description (one paragraph):
The goal of this research is to investigate the role of an acetylcholine (ACh)-acetylcholinesterase (AChE) system in the ovary, and to explore the importance of the newly discovered form of cell death, necroptosis, in the female gonad. Previous study indicated that cholinergic influences involving ACh were mainly trophic in human granulosa cells (GCs). Inhibiting AChE activity by Huperzine A enhanced the influence of ACh. Evidence also suggested that AChE induced necroptosis in cultured human GCs, which could be prevented by necrostatin-1. Therefore, the ONPRC collaborative project is proposed to study the role of AChE and the effect of pharmacological interference with the cholinergic system during primate follicular development in vitro. Primate follicle culture will be used to examine: (Aim 1) inhibiting AChE activity on follicular development and function. Huperzine A will be added into the follicle culture media. Follicle survival, growth and function will be analyzed; and (Aim 2) inhibiting necroptosis on follicular development and function. Necrostatin-1 will be added into the follicle culture media. The same follicular parameters will be analyzed as described above. The experiments are to test the hypothesis that enhancing the trophic action of ACh and/or preventing necroptosis improves the follicular cell viability, which promotes follicle survival, growth and function. The proposed study has the potential to increase our knowledge about the regulation of ovarian follicular development in primates. AChE and necroptosis could be potential targets for pharmacological intervention to maintain follicular cell health and detain the depletion of the ovarian follicle pool during aging, and thus delay menopause.

Progress during the reporting period (one paragraph):
The project was initiated in April, 2016. Rhesus macaque ovaries have been collected via the ONPRC Tissue Distribution Program for in vitro protocols. Protocols for the one-year experiments are expected to be completed in March, 2017. Data will be analyzed and reported in abstracts and manuscripts.

Publications resulting from the project:
None at this time

Funding Sources (PIs and sources):
Excluded by Requester
Excluded by Requester

Project Title: Activin A Function in Primate Ovarian Follicular Development and Fertility Preservation
SPID: 1031
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:

Excluded by Requester — Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester — Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph):
The goal of this research is to understand the role of activin A in regulating preantral follicle growth and antral follicle maturation in primates, and to apply the findings to promote human follicle development and oocyte competence in vitro. Previous studies in nonprimate species suggest that activin A promotes preantral follicle growth and inhibits steroid hormone production by antral follicles in vitro. Therefore, translational studies are proposed to evaluate the role of activin A in regulating primate follicle growth and maturation in vivo during spontaneous menstrual cycles (Aim 1). Activin A ablation experiments will be conducted in rhesus macaques through intraovarian infusion during the natural menstrual cycle. Activin A will also be examined as a noninvasive biomarker to predict follicle development and oocyte competence during in vitro follicle maturation (IFM) (Aim 2). Activin A concentrations in the culture media will be analyzed to identify a cutoff value for activin A levels associated with follicle growth and/or oocyte competence. Finally, data generated from the nonhuman primate research will be applied to human IFM to examine activin A function in improving the coordinated development and maturation of human follicles, and its potential to serve as a predictor of successful IFM (Aim 3). It is hypothesized that activin A repletion during the preantral stage and depletion during the antral stage will promote follicle development and oocyte maturation during human IFM.

Progress during the reporting period (one paragraph):
I successfully completed this pilot study in May, 2016. The data suggest that blocking activin A actions limits the growth and maturation of ovarian follicles in vivo. Follicles developed in vitro can be divided into distinct cohorts based on their production of activin A. The differential productions of activin A are also observed during human follicle culture. Therefore, active activin A production by cultured follicles may have a potential to serve as a marker for selecting follicles for further culture and egg maturation to offer fertility preservation options to women. The findings were reported in an abstract and published. The study also contributed to establishing a database comparing the mRNA expression profiles between in vivo- and in vitro-developed follicles, which has been published in a manuscript.

Publications resulting from the project:

Excluded by Requester

Funding Sources (PIs and sources):

Excluded by Requester — Medical Research Foundation of Oregon

Project Title: Anti-Mullerian hormone actions to control primate folliculogenesis
SPID: 2208
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:

Excluded by Requester

Oregon Health & Science University

Principal NPRC Core Scientists affiliated with the Project:

Excluded by Requester

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University

Project Description (one paragraph):
The goal of this research is to understand the mechanisms whereby anti-Müllerian hormone (AMH) regulates preantral follicle growth and antral follicle maturation in the stag-dependent manner in primates. Increasing evidence suggests that AMH alters preantral follicle growth and antral follicle function. Therefore, studies are proposed in rhesus monkeys to test the hypotheses that: (Aim 1) AMH promotes preantral follicle growth, but inhibits antral follicle maturation in vitro and (Aim 2) AMH promotes preantral-to-antral follicle growth, but prevents further maturation and selection of the dominant follicle in vivo. AMH addition and ablation experiments will be conducted. Follicular morphology and histology, as well as function in steroidogenesis and local factor production, oocyte maturation and competence in fertilization and preimplantation development, plus genome-wide mRNA levels and selected AMH-regulated genes (Aim 3) will be analyzed. AMH will also be examined as a noninvasive biomarker for further follicle growth and oocyte maturation in vitro. Finally, data generated from the nonhuman primate research will be applied to human follicle culture with the hypothesis that AMH manipulation improves the coordinated development and maturation of human follicles and their enclosed oocytes (Aim 4). These experiments will provide valuable information on the heterogeneous expression and stage- dependent actions of AMH in ovarian follicles, as well as mechanisms of AMH controlling follicular development, in primates. New insight will emerge on the potential of AMH to serve as a biomarker for follicle growth and oocyte competence during in vitro follicle maturation.

Progress during the reporting period (one paragraph):
I successfully completed the first-year experiments of this project. Data obtained suggest, for the first time, that AMH effects are stage-dependent during primate follicular development. AMH directly promotes preantral follicle growth while inhibits antral follicle maturation. AMH, co-expressed with its type II receptor, was produced heterogeneously by preantral follicles in primates with levels correlated positively with follicle growth and oocyte maturation. Therefore, AMH may serve as a biomarker for primate follicular development in vitro. The study also contributed to establishing a database comparing the mRNA expression profiles between in vivo- and in vitro-developed follicles. The findings and conclusions were summarized in abstracts and manuscripts.

Publications resulting from the project.

Excluded by Requester

Funding Sources (PIs and sources):
Jing Xu, Ph.D. NIH National Institute of Child Health & Human Development, R01HD082208-02

Project Title: Contraceptive testing for semen availability in male monkeys
SPID: 6009
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principle Investigator of the project/ Institutional affiliation:
Excluded by Requester Eppin Pharma Inc.

Principal NPRC Core Scientists affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the project (doctorial level only):
Excluded by Requester Oregon Health & Science University

Project Description (one paragraph):
Nearly half of all pregnancies in the US and worldwide are unplanned. Surprisingly, in half of these unintended pregnancies, women reported using a contraceptive. Thus, there is a critical need for better contraceptive options that fit the needs of women and men throughout their reproductive lives. In the current environment where commercial pharmaceutical companies have terminated male contraceptive R&D, our efforts with the support of NIH are vital to address this health need. Although there are a spectrum of contraceptive choices for women, choices for men are much more limited. The ideal contraceptive should be safe and highly effective. Male monkeys immunized with the male-specific protein EPPIN (official symbol, SPINLW1) develop high titers of anti-EPPIN antibodies and become reversibly infertile. EPPIN is a receptor for the seminal plasma protein, semenogelin (SEMG1), which is present in primates, but not in rodents. Anti-EPPIN antibodies, when bound to the sperm surface, mimic SEMG1 binding, thereby effectively inhibiting progressive sperm motility and rendering the spermatozoa infertile. The aim of this grant is to evaluate in the rhesus monkey a new sperm motility inhibitor, TZ4_121, which selectively binds to specific regions of EPPIN, for development as potential male contraceptive.

Progress during the reporting period (one paragraph):
Adult male rhesus monkeys (n=4) were trained for semen collection. Baseline sperm counts were obtained for each male 3 weeks prior to treatment. Three of four males received TZ4_121 (8 mg/kg, iv) starting at week 4. Semen was collected at 6, 30, and 78 hours post-treatment (during week 4). Sperm motility in all males was suppressed within 30 hours post-treatment, and sperm were completely immotile at 78 hours. The males were rested for weeks 5 and 6, and semen was collected again for baseline (weeks 7 and 8). In week 9, three of four males received 16 mg/kg, and semen was collected at the same time intervals described above. Following treatment with the higher dose, sperm motility was also suppressed by 30 hours and sperm remained immotile at 78 hours. No adverse effects of treatment have been noted. Frozen semen samples are being shipped to Excluded by Requester to test for the presence (quantity) of compound and for assay of TZ4_121 activity.

Publications resulting from the project.
None at this time

Funding Sources (PIs and funding sources):
Michael G. O'Rand, Ph.D. NIH National Institute of Child Health & Human Development, 1R41HD084077-01

Project Title: Cryopreservation and Transplantation of Ovarian Cortical Tissue for Fertility Preservation
SPID: 3930
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
University of Saskatchewan
University of Missouri
Catholic University of Louvain, Belgium
St. Marianna University, Japan
Center for Human Reproduction, New York City
Cook Regentech

Project Description: The long-range goals of this proposal are to develop robust and reproducible methods for ovarian tissue cryopreservation and transplantation as options for fertility preservation in survivors of cancer or other benign conditions wherein ovarian function is compromised. Cryopreservation of ovarian tissue remains the only option for prepubertal, adolescent and young women with cancer as well as adult patients for whom immediate cancer therapy is required. We successfully devised a method for vitrification of rhesus monkey ovarian tissue in a closed system, and demonstrated post-thaw function in vivo and in vitro. When transplanted to heterotopic sites, vitrified tissue resumes ovarian function, and yields mature oocytes capable of preimplantation embryonic development. Using the rhesus monkey, we propose to identify the transplantation site for optimal fertile function of both peripubertal and young adult ovarian cortical tissue, improve long-term transplant function via local administration of factors important for revascularization as well as follicular survival, and optimize vitrification of isolated preantral follicles and their ability to yield competent oocytes following 3D culture in vitro. Live births in nonhuman primates after these controlled studies will establish the safety and feasibility of experimental therapies prior to clinical translation so girls and young women can be offered the best chances of becoming mothers after surviving cancer.

Progress during the reporting period (a few sentences):
The project began in October 2016; animals are being monitored for normal ovarian/menstrual cyclicty. Beginning in January 2017, ovaries will be obtained for vitrification and pieces of cortical tissue will be subsequently transplanted to various sites in the absence or presence of biomaterials designed to enhance vascularization. Resumption of ovarian cyclicity will be evaluated. Oocytes from resulting antral follicles will be aspirated, assessed for maturation, inseminated in vitro and resultant embryos cultured in vitro to the blastocyst stage. Excluded by Requester and his graduate student are developing an “optimal theory” mathematical model for diffusion of various cryoprotectants into individual primary and secondary follicles, including their enclosed oocytes. The best candidates will be tested for vitrification of follicles followed by 3D culture in March 2017.

Publications resulting from the project:
None at this time

Funding Sources:
Mary B. Zelinski, Ph.D. NIH National Institute of Child Health & Human Development R01HD083930-01A1

Project Title: Efficacy and Pharmacokinetics of Intramuscular DMAU to Male Rhesus Macaques
SPID: 0008
Unit/Division: Reproductive & Developmental Sciences
Type of Project: Research
Percent P51 Dollars: 0%
AIDS related? No

Principal Investigator of the project/Institutional affiliation:
Excluded by Requester
Oregon Health & Science University

Principal NPRC Core Scientist affiliated with the Project:
None

Other Core, Affiliate or Visiting Scientists associated with the Project:
Excluded by Requester
SRI International
SRI International

Project Description: World Health Organization statistics show that 122 million planned pregnancies occur worldwide per year. Yet, in spite of the availability of many different female contraceptive methods and of condoms, an additional 87 million pregnancies were unintended (representing 42% of all pregnancies), and 46 million pregnancies were terminated by abortion. In the U.S., the unintended pregnancy rate is 49% of all births, and about half of these are terminated by abortion. Surprisingly, in 50% of unintended pregnancies, women reported using a contraceptive. Thus, the development of novel, reversible, oral male contraceptive agents has been identified as a major advance needed to address this worldwide reproductive health issue by the National Institutes of Health, Institute of Medicine, and World Health Organization. In order to move any new male contraceptive agent into human clinical trials, efficacy and safety must be demonstrated in at least two non-primate species and in nonhuman primates. Preliminary studies conducted at the Contraceptive Branch of the National Institute of Child Health and Human Development show suppression of sperm numbers (via epididymal collection) after a single intramuscular (IM) dose of the compound, dimethandrolone (DMA), in cynomolgus male monkeys. DMA, the 17β-undecanoic acid ester of dimethandrolone (DMAU; 7α,11β-dimethyl-19-nortestosterone) is a potent androgen currently under development for therapeutic uses in men. Cleavage of the 17β-ester bond liberates the biologically active DMA. In addition to the anabolic and androgenic potency of DMAU and DMA, high bioavailability after oral administration (rodents, rabbits) or injection (primates) makes them attractive candidates for a male contraceptive.

Progress during the reporting period (a few sentences):
Four adult male animals were trained for semen collection and have received a single IM dose of DMA with subsequent biweekly semen collections. Sperm concentrations decreased to levels <1 million sperm/ml in one male 176 days post-treatment and remained suppressed until day 400. Sperm levels decreased 10-fold in the other 3 males by day 100. Sperm levels remained suppressed in one male between Days 113-590, and between Days 176-400, Days 204-386 and Days 274-359 in the other three males respectively. Although sperm levels did not completely return to pre-treatment values, they remained well above those considered to be fertile. Unexpectedly, severe abnormalities in sperm motility were observed in all 4 males 100 days post-treatment, and were sustained through Day 688 in one male, and up to Day 583 in the remaining 3 males. Unilateral testicular biopsies were obtained on Days 611-612 in two males, and Days 746-748 in two males; tissues are currently being analyzed. No adverse effects were noted throughout the post-treatment interval based on blood chemistries, complete blood counts and lipid analyses. Body weights remained normal. Thus, a single dose of DMA partially suppressed sperm concentrations, leading to infertile levels in 1 of 4 males. DMA treatment had a more profound and sustained effect on inhibiting normal sperm motility. Effects of DMA on both sperm levels and motility were reversible.

Publications resulting from the project:
None at this time

Funding Sources:
Excluded by Requester
Private Source
NIH National Institute of Child Health & Human Development

OVERALL: TRAINING AND PROFESSIONAL DEVELOPMENT

P51 RPPR	
Training Summary	**Jan. – Dec. 2016**
Postdoc Trainees	7
Postdoc Researchers	13
Graduate Students - TG	3
Graduate Students	16
Undergrads	12
School Teachers	0
Total	51

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Excluded by Requester
N/A: Not NIH Funded	
Complete	
N/A: Not NIH Funded	
Complete	
Complete	
Complete	
N/A: Not Journal	
Complete	
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N/A: Not NIH Funded	
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N/A: Not NIH Funded	
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N/A: Not NIH Funded	
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In Process at NIHMS	
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In Process at NIHMS	Excluded by Requester
Complete	
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PMC Journal - In process	
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In Process at NIHMS	
In Process at NIHMS	

	Excluded by Requester
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In Process at NIHMS	
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N/A: Not NIH Funded	
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PMC Journal - In process	
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In Process at NIHMS	
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In Process at NIHMS	
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PMC Journal - In process	
In Process at NIHMS	
PMC Journal - In process	

	28069920.
PMC Journal - In process	Excluded by Requester
N/A: Not NIH Funded	

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Category	Explanation
Other	http://nprcresearch.org/primate/ The purpose of this website is to provide investigators, collaborators and program managers from funding organizations such as the NIH with an informative resource to help facilitate research collaborations.
Other	http://www.ohsu.edu/xd/research/centers-institutes/onprc/ This is the publicly available home website for the Center within the OHSU website.

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period?

No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Other	See Section G. Special Reporting

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Component(s)	Country	SS
eRA Commons User Name	Y	ROBERTSON, JOSEPH E	PHD,MD	PD/PI	EFFORT						NA
	N	Excluded by Requester		Animal Technician							NA
	N			Cost Accountant							NA
	N			Animal Technician							NA
	N			Unit Manager							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Technician							NA
	N			Grants/Contracts Mgr							NA
	N			LAM Resident							NA
	N			Res Asst							NA
	N			Admin Coordinator							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N		PhD	Sr. Research Informatics							NA
	N			Sr Res Asst							NA
	N			Research Assistant							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Animal Technician							NA

		Excluded by Requester			EFFORT				
	N			Admin Coordinator					NA
	N			Unit Supervisor					NA
	N			Animal Technician					NA
	N			Admin Coordinator					NA
	N			Animal Technician					NA
	N			Research Assistant					NA
	N			Business Analyst					NA
	N			Resident					NA
	N			Animal Technician					NA
	N			Animal Technician					NA
	N			Sr. Research Assoc					NA
	N			Research Assistant					NA
	N			Animal Technician					NA
	N		DVM	Assoc Vet					NA
	N			Animal Technician					NA
	N			Financial Analyst					NA
	N			Research Assistant					NA
	N			Animal Technician					NA
	N			Resident					NA
	N			Assistant Scientist					NA
	N			Animal Technician					NA
	N			Animal Technician					NA
	N			Research Assistant					NA
	N			Asst Vet					NA

		Excluded by Requester			EFFORT				
	N		PhD	Asst Vet					NA
	N			Admin Assistant					NA
	N		PhD	Staff Scientist					NA
	N			Research Assistant					NA
	N			Research Associate					NA
	N			Animal Technician					NA
	N			Research Assistant					NA
	N			Medical Assistant					NA
	N			Animal Technician					NA
	N			Research Assistant					NA
	N		PhD	Assistant Scientist					NA
	N			Animal Technician					NA
	N			Admin Coordinator					NA
	N			Assoc Biostatistician					NA
	N			Animal Technician					NA
	N			Sr Res Asst					NA
	N			Research Assistant					NA
	N			Research Assistant					NA
	N			Research Assistant					NA
	N			Education Outreach Specialist					NA
	N			Business Analyst					NA
	N			Research Assistant					NA
	N			Animal Technician					NA

		Excluded by Requester			EFFORT				
	N			Admin Coordinator					NA
	N			Asst Vet					NA
	N			Research Associate					NA
	N			Research Assistant					NA
	N			Research Assistant					NA
	N			Research Assistant					NA
	N		PhD	Staff Scientist					NA
	N			Research Assistant					NA
	N			Sr. Research Assoc					NA
	N		PhD	Research Assistant			Core-5553 (Research Library)		NA
	N			Clinical Technician					NA
	N			Occupational Health Nurse					NA
	N			Animal Technician					NA
	N			Admin Coordinator					NA
	N			Clinical Technician					NA
	N			Animal Technician					NA
	N			Animal Technician					NA
	N			Unit Supervisor					NA
	N			Clinical Technician					NA
	N			Sr Res Asst					NA
	N			Research Associate					NA
	N			Animal Technician					NA
	N			Sr Res Asst					NA
	N			Research Assistant					NA
	N			Research					NA

				Associate							
	N	Excluded by Requester		Research Assistant	EFFORT						NA
	N			Research Assistant							NA
	N			Research Assistant							NA
	N			Research Assistant							NA
	N			Chief Operating Officer							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Clinical Technician							NA
	N			Animal Technician							NA
	N			Research Assistant							NA
	N			Mgr, Res Informatics							NA
	N			Research Assistant							NA
	N			Clinical Technician							NA
	N			Admin Coordinator							NA
	N			Project Manager							NA
	N			Animal Technician							NA
	N			Research Assistant							NA
	N			Animal Technician							NA
	N			Research Associate							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Asst Vet							NA
	N			Unit Manager							NA

		Excluded by Requester									
	N			Animal Technician	EFFORT						NA
	N			Unit Supervisor							NA
	N			Animal Technician							NA
	N		DVM	Asst Vet							NA
	N			Research Associate							NA
	N			Animal Technician							NA
	N			Unit Manager							NA
	N			Research Assistant							NA
	N			Animal Technician							NA
	N			Research Assistant							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Research Associate							NA
	N			Research Assistant							NA
	N			Unit Head							NA
	N			Clinical Technician							NA
	N			Research Assistant							NA
	N			Sr. Research Assistant							NA
	N			Unit Manager							NA
	N			Research Assistant							NA
	N			Animal Technician							NA
	N			Financial Analyst							NA
	N			Financial Analyst							NA

	N	Excluded by Requester		Research Assistant	EFFORT				NA
	N			Research Assistant					NA
	N			Unit Manager					NA
	N			Admin Coordinator					NA
	N			Sr Res Asst					NA
	N			Animal Technician					NA
	N			Research Associate					NA
	N		PhD	Staff Scientist					NA
	N			Animal Technician					NA
	N			Research Associate					NA
	N			Research Associate					NA
	N			Program Coordinator					NA
	N			Animal Technician					NA
	N			Admin Coordinator					NA
	N			Admin Coordinator					NA
	N			Unit Manager					NA
	N			Animal Technician					NA
	N			Unit Manager					NA
	N		DVM	Assoc Vet					NA
	N			Research Assistant					NA
	N			Unit Supervisor					NA
	N			Research Assistant					NA
	N			Project Coordinator					NA
	N			Research Assistant					NA
	N			Animal					NA

		Excluded by Requester									
				Technician							
	N			Animal Technician	EFFORT						NA
	N			Animal Technician							NA
	N			Sr Res Asst							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Animal Technician							NA
	N			Clinical Technician							NA
	N			Animal Technician							NA
	N			HR Manager							NA
	N			Animal Technician							NA
	N			Training Lead							NA
	N		PhD	Assistant Scientist							NA
	N			Grants/Contracts Coord							NA
	N			Admin Coordinator							NA
	N			Research Assistant							NA
	N			Surgical Technician							NA
	N			Surgical Technician							NA
	N			Animal Technician							NA
	N			Research Assistant							NA
	N			Surgical Technician							NA
	N			Animal Technician							NA
	N			Research Associate							NA
	N			Clinical Technician							NA
	N			Research							NA

		Excluded by Requester			EFFORT						
				Assistant							
	N			Animal Technician							NA
	N		DVM	Unit Head							NA
	N			Sr. Research Assoc							NA
	N			Research Associate							NA
	N			Office Specialist							NA
	N			Research Associate							NA
	N			Research Assistant							NA
	N			Clinical Technician							NA
	N			Staff Scientist							NA
	N		DVM	Asst Vet							NA
	N			Research Assistant							NA
	N			Surgical Technician							NA
	N			Clinical Technician							NA
	N			Research Assistant							NA
	N			Animal Technician							NA
	N		PhD	Assistant Scientist							NA
	N		PhD	Staff Scientist							NA
	N			Animal Technician							NA
	N			Clinical Technician							NA
	N			Division Chief							NA
	N			Animal Technician							NA
	N			Sr. Research Assoc							NA
	N			Research Assistant							NA

	N	Excluded by Requester		Research Librarian	EFFORT				NA
	N			Animal Technician					NA
	N			Clinical Technician					NA
	N			Animal Technician					NA
	N			Animal Technician					NA
	N			Administrative Director					NA
	N			Animal Technician					NA
	N			MRI Technician					NA
	N			Animal Technician					NA
	N			Unit Manager					NA
	N			Animal Technician					NA
	N			Animal Technician					NA
	N			Clinical Technician					NA
	N			Research Assistant					NA
	N			Research Assistant					NA
	N			Animal Technician					NA
	N			Research Assistant					NA
	N			Clinical Technician					NA
	N			Unit Supervisor					NA
	N			Animal Technician					NA
	N			Animal Technician					NA
	N			Research Assistant					NA
	N			Research Assistant					NA

		Excluded by Requester			EFFORT				
	N			Assistant Scientist					NA
	N			Animal Technician					NA
	N		DVM	Asst Vet					NA
eRA Commons User Name	N		PhD	Assoc Scientist					NA
	N		PhD	Senior Scientist					NA
	N		PhD	Sr. Staff Scientist					NA
	N		PhD	Unit Head					NA
	N		PhD	Staff Scientist					NA
	N		PhD	Assoc Scientist					NA
	N		PhD	Assistant Scientist					NA
	N		PhD	Division Chief					NA
	N		DVM	Unit Head					NA
	N		MD,BA	Division Chief					NA
	N		PhD	Division Chief					NA
	N		PhD	Senior Scientist					NA
	N		PhD	Unit Head					NA
	N		PhD	Unit Head					NA
	N		PhD	Unit Head					NA
	N		PhD/DVM	Unit Head					NA
	N		PhD	Assistant Scientist					NA
	N		PhD	Assistant Scientist					NA
	N		PhD	Senior Scientist					NA
	N		PhD	Assoc Scientist					NA
	N		PhD	Senior Scientist					NA
	N		PhD	Senior					NA

				Scientist							
eRA Commons User Name	N	Excluded by Requester	PHD,AB	Assoc Scientist	EFFORT						NA
	Y		PhD	Center Director							NA
	N		PhD	Senior Scientist							NA
	N		PhD	Senior Scientist							NA
	N		PHD	Senior Scientist							NA
	N		PhD	Faculty							NA
	N		PhD	Assistant Scientist							NA
	N		PhD	Senior Scientist							NA
	N		PhD	Assoc Scientist							NA
	N		PhD	Senior Scientist							NA
	N		PHD,BS	Senior Scientist							NA
	N		PhD	Senior Scientist							NA
	N		PhD	Staff Scientist							NA
	N		PhD	Interim Division Chief							NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: OtherSupport_RPPR_Y57.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

No

OTHER SUPPORT

Excluded by Requester

Excluded by Requester

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

OTHER SUPPORT

ROBERTSON, J.E

ACTIVE

P51 OD011092-57 Robertson (PI) 05/01/14 - 04/30/19 EFFORT
NIH/ORIP
Support for the Oregon National Primate Research Center
The major goal of this project is to provide the support for specialized facilities, scientific and technical personnel, and NHP species needed for the conduct of biomedical research.

Oregon Health & Science University – Host Institution 07/01/08 – 06/30/17 EFFORT

OVERLAP

No overlap

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Major Infrastructure Improvements and Capital Equipment (Supported by ORIP)

Water Line Replacement, Administration Building: $245,000
Colony Annex Remodel: $68,199
ASA Building HVAC Panel Replacement: $33,121
ASB 3 Building Fan Replacement: $26,739
ASB 1 Building Fan Replacement: $17,808
Building One, ONPRC Remodel: $9,133

Sub-total Expense: $400,000

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

File(s) uploaded:
Yr57-RPPR-OVERALL_OtherProducts.pdf

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: Oregon National Primate Research Center	096997515	OR-001	505 NW 185th Ave Beaverton OR 97006
Oregon Health Sciences & University	096997515	OR-003	3181 SW Sam Jackson Park Rd Portland OR 97239

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

Yes

Anticipated Amount	Source(s)
14374504	animal lease, per diem, support core fees

G.12 F&A COSTS

Not Applicable

OVERALL: G.1 SPECIAL REPORTING

YR 57 (2016-2017) P51 RPPR
v02/15/2017

C.5. OTHER PRODUCTS

1. **Colony Statistics Tables**
For animal colonies at a National Primate Research Center (NPRC). For the Reporting Period, include:

Census Date: 12/31/16

A. Nonhuman Primates housed at ONPRC supported partially, or in part, by the P51 grant.

	Breeding Colony			Not in Breeding Colony			Total Colony Census
Species	**Female**	**Male**	**Total**	**Female**	**Male**	**Total**	
Macaca mulatta	1612	938	2550	1046	872	1918	4468
Macaca fuscata	145	80	225	72	39	111	336
Macaca fascicularis				47	34	81	81
Papio hamadryas				24	1	24	25
Papio anubis					8	8	8
Saimiri boliviensis					6	6	6
U42 and U42 ESPF included in P51 grant numbers							
U42	276	155	431	199	135	334	765
U42 ESPF	39	24	63	92	82	174	237

B. NHPs housed at the NPRC, but not supported by the P51 grant1.
Not Applicable

C. NHPs housed at the NPRC, irrespective of source of support.

Species	Total Colony Census
Macaca mulatta	4468
Macaca fuscata	336
Macaca fascicularis	81
Papio hamadryas	25
Papio anubis	8
Saimiri boliviensis	6

2. Tissue Distribution Program Information

Dates covered: 1/1/2016 – 12/31/2016

Sample type	Number of samples distributed
Type #1 (e.g., tissues)	2037
Type #2 (e.g., genetic material)	0
Total	2037

Tissue Distribution Program Information
The Tissue Distribution Program (TDP) is administered by the Pathology Services Unit to maximize the availability and use of NHP tissues and minimize the number of NHPs required for research. As part of the NHP TDP, 37 ONPRC/OHSU investigators received 6,199 tissue specimens and 15 non-OHSU investigators received 296 specimens prepared according to their specifications. An additional 1210 tissues were distributed for use in tissue banks administered at ONPRC. Of 6,495 total tissue samples distributed, 4,458 tissues were received by investigators from animals assigned to them as part of terminal research protocols

3. Project Summary Table

P51 APR Y57	
Project Type	**Number of Projects***
Management/Other	4
Research	148
Pilot	5
Total	157

*based on project not multiple grants or funding sources for same project

4. Percentage of AIDS-related P51 Grant Dollars

P51 supports 29% AIDS sponsored projects.

5. Types of Investigators

Type of Investigator	Number
Core Scientist	35
Affiliate Scientist	109
Visiting Scientist	4
Other	78*
Total	**226**

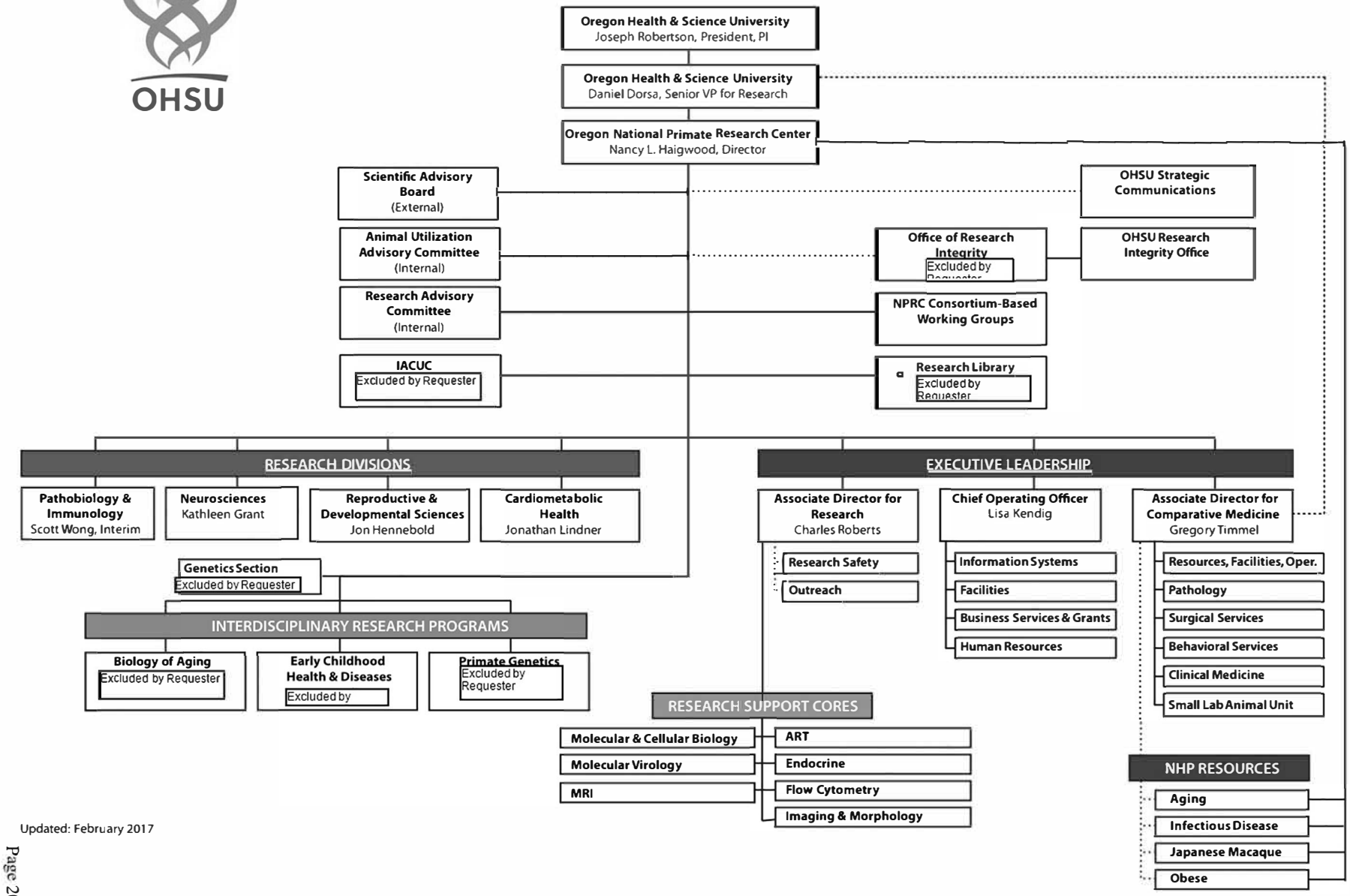
* External Collaborators and ONPRC/OHSU scientists who do not qualify as Core, Affiliate or Visiting Scientists

6. Peer Reviewed Publications Directly Attributed to P51 Activity.

Peer reviewed publications are attributed to P51 activity and included in this section: if they cite the P51 grant in the article; or if the P51 grant is included in the PubMed entry for that article; or in a limited number of cases if the article is authored by a ONPRC core scientist or affiliate and describes using P51 funded resources without citing the grant number.

Oregon National Primate Research Center

Organizational Chart



Updated: February 2017

8. Outreach Activities Statement

ONPRC provides multiple outreach opportunities to showcase ONPRC and NPRC capacities. These opportunities target both the research community and the general public. In terms of the research community, ONPRC researchers are active in writing abstracts and papers for publications, providing presentations, and creating content for OHSU/ONPRC and NPRC Web sites.

In order to more widely disseminate the important discoveries that are made by ONPRC researchers, ONPRC works closely with the Department of Strategic Communications at OHSU to highlight these discoveries and other Center activities to the media and to state and federal legislators. We interact closely with OHSU's Government Relations Office to invite Oregon State representatives to visit the Center and meet with key personnel (Director, scientists, Outreach Coordinator).

With grant support, ONPRC provides two 4-part Science Café series each year (usually in the spring and fall) featuring various Center scientists discussing their work and the importance of the NHP model to that work. Clinical colleagues from OHSU are invited to participate in order to provide a translational discussion of our work. In addition, many ONPRC scientists participate in science talks organized by non-ONPRC entities, including "Science on Tap," "Science Pub," the "Brain Awareness lecture series," and the OMSI/OHSU "Brain Fair." These venues offer additional opportunities for us to dialog with large audiences around the topic of biomedical research.

ONPRC is represented at the annual meetings of the Oregon State Science Teachers' Association and the Washington State Science Teachers' Association; the OHSU/OMSI "Brain Fair;" the OHSU "Brain Awareness Lecture Series," and continues to participate as an active member in OHSU's "SOAR" Committee (Science Outreach and Resources).

Lastly, ONPRC hosted over 4000 visitors to our center during 2016, mostly through our popular tour program for school groups.

9. Financial Support for the Resources

Resource	Direct Cost from ORIP Grant	Program Income Support	NIA Support	B-Rate Program Income Support	Total Support of the Resource
Director's Office	714,414	Proprietary Info		Proprietary Info	
Business Services	973,518				
Research Library	200,218				
Research Safety/Occupational Health	147,531				
Division of Comparative Medicine (DCM) - Admin	147,717				
DCM - Resources, Facilities, and Operations	1,106,292				
DCM - Pathology Services	139,453				
DCM - Surgical Services	102,701				
DCM - Behavioral Services	119,939				
DCM - Clinical Medicine	324,108				
Obese Resource	400,000				
Aging Resource	115,887		273,228		
Infectious Disease Resource	335,975				
Japanese Macaque Resource	350,780				
Assisted Reproduction Core	278,469				
Endocrine Core	97,714				
Flow Cytometry Core	122,771				
Imaging Core	116,728				
Molecular and Cell Biology Core	187,151				
Molecular Virology Core	178,671				
MRI Core	40,000				
Primate Genetics	400,000				
Division of Neuroscience	912,779				
Division of Reproductive and Developmental Sciences	644,450				
Division of Pathobiology and Immunology	437,267				
Division of Diabetes, Obesity and Metabolism	181,466				
Interdisciplinary Program	20,000				
Pilot program	200,000				
Improvement and Modernization	500,000				
Outreach	118,737				
Consortium (Computational, Genetics, Training)	179,212				
Facilities	15,466				
Information Systems	15,756				
Total	**$ 9,825,170**		**$ 273,228**		

10. Feedback from Users

Assisted Reproduction Technology Core

Category	Description
Methods for soliciting feedback	A survey was sent to all ART Core users via email 8/12/2016 with 60% returning feedback.
Topics covered	Staff accessibility and usefulness, adequate range/scope of offered services, satisfaction of services provided, projection of future use, suggested additional services.
Most significant results	The ART Core is highly regarded and its users are very satisfied with all aspects of the ART Core. All indicated continued use of ART Core services.
Lessons learned	The Core provides a valuable service to ONPRC investigators.
Changes made	None

Biostatics & Bioinformatics Unit

Category	Description
Methods for soliciting feedback	A web-based survey was sent to all BBU users both recent and old (going back 2 years).
Topics covered	Quality of the analyses, turnaround time, customer service, and overall satisfaction.
Most significant results	Overall satisfaction is very high but a few improvements can be made.
Lessons learned	- We need to better communicate with the scientists we serve and make sure that they receive timely updates. - Users realize that this is a very important resource and that it needs to be able to grow. - Most users would recommend our unit to others - Retention of valuable personnel is needed.
Changes made	This was our first survey and we received the results on November 30 so we did not have time to implement changes yet. We are definitely planning to improve communication with scientists by sending weekly emails during active projects.

Computational Methods

The purpose of the Computational Methods and Resources (CMR) activity is to identify and implement more efficient work designs that also enhance discovery, animal care and job satisfaction. Our method is to explore how work can be partitioned between people and machines, and to find those balances of cognition (people) and computation (machines) that outperform existing workflows in one or more of the aforementioned dimensions. Given a particular workflow, such as an animal procedure performed by the ONPRC Surgical Survives Unit, we begin by asking users (i.e. workflow participants) to describe how they might design their work in an “ideal world.” This initial feedback (“how does your work work?”) becomes the basis for rapidly constructing one or more software tools that move the work system in the direction described by users. Now

given something that addresses directly some of their work needs, they are highly motivated to provide a next round of feedback on these "first-cut" tools (e.g., procedure-focused intra-operative data entry forms), describing how tools might better adapt to their refined ideas of how they can work best. From this a second generation of tools is constructed from refinements and additions to the initial prototype, in turn generating additional (round 3) feedback. This is nothing more than selection by users over the heritable variation intrinsic to any software system; user feedback is the engine that drives CMR work, in the way that environment steers evolution. (This is in contrast with surveys that solicit perception, and that are often only weakly, if at all, coupled to any mechanisms to change that perception.) The CMR process has reliably produced higher-performing workflows, reducing variations that can hinder discovery or present regulatory issues, while rebalancing work between people and machines to dramatically reduce cost and increase job satisfaction.

There are two other sources of feedback we consider, in addition to that provided by users during the work design process. The first is unsolicited feedback, often provided on conclusion of the development process. This exists in auditable form as emails, but also comes by less formal channels in conversation. The other feedback channel, perhaps the most relevant in a Darwinian view, are requests for additional work that arise from users and groups as a result of prior success with CMR methods. These are likewise auditable in email traffic, and evident in practice as the growing number of CMR-enable workflows in place; these are in turn auditable as server configurations that reflect, and server logs that track, usage of CMR tools and resources over time.

Category	Description
Methods for soliciting feedback (really feedback channels)	• As part of the tool development process • Solicited as in "how did that work for you?" • Unsolicited, voluntary • Return clients
Topics covered (really dimensions of measure)	• Economic efficiency, cost • Level of animal care • Pace of discovery, science • Job satisfaction
Most significant results	• Reduce cost of surgical operations by 35% • Reduce cost of weight management by 50% • Reduce interaction with electronic health record from 40%/day to 15%/day • Return clients
Lessons learned	• There is always a better way to work • Simply ask the user
Changes made	• Many, documentation available on request

In the most recent grant year we have continued the application of these methods to other workflows at ONPRC, and at other NPRCs. For instance, a clinical weight management system has been developed that reduces the time to manage a case from 9 to 4 minutes. This tool synergizes our institutional record system (PRIMe) with other sources of data and was developed directly from user descriptions of particular individual needs. Our infectious disease workflow has been extensively "scaffolded" with computational tools that collectively yield a more efficient and reliable workflow that reduces employee stress, allowing staff to focus on professional objectives and animal care. Three applications (blood-draw, procedure–counting and weigh-alert related) are running at the Tulane NPRC supporting the post-approval monitoring activity there. Numerous other CMR applications are available on request to all the NPRCs. Our colony population modeling application is now a standard part of the colony management workflow at the Tulane and Yerkes NPRCs.

Endocrine Core

Category	Description
Methods for soliciting feedback	The ETSC has not formally requested feedback from users during the current Year 57 [Excluded by Requester] s frequently in contact with the investigators who use the core, and in this way, receives feedback on an almost continuous basis.
Topics covered	Discussion of current services offered, satisfaction with staff and services provided, projection of future use, potential future need for additional services, need for expanding current services.
Most significant results	Discussions with investigators indicate an overall high level of satisfaction by users of the ETSC.
Lessons learned	The ETSC provides a valuable and necessary service to ONPRC investigators.
Changes made	None

Flow Cytometry

Category	Description
Methods for soliciting feedback	The Flow Cytometry Core maintains a list of users, which is used for sending email alerts regarding equipment issues (e.g., service-related downtime, operational changes, etc.) This list has also been used to solicit feedback. In addition, I regularly visit the instruments, and when I find one in use, I make it a practice to ask whether they need help, or have any requests regarding Core operations.
Topics covered	Instrument performance, core supplies, training opportunities
Most significant results	The most common feedback I get is interest in more training.
Lessons learned	Many users would take advantage of formal training sessions, but usually don't think to ask for them.
Changes made	Although any user can request training or assistance at any time, I now make it a practice to offer a 'Flow 101' class approx. every three months.

Genetic Services

Category	Description
Methods for soliciting feedback	We informally request feedback from users of the macaque ancestry analysis and MHC expressed allele analysis, as well as from our oversight committee. We also receive unsolicited feedback.
Topics covered	MHC Analysis, macaque ancestry analysis, MATRR tissue processing, custom genotyping, value of the services.

Most significant results	The feedback has been very positive, including comments on the value of the work for selecting appropriate subjects for research or breeding. We have received multiple unsolicited requests for custom MHC analyses. Our oversight committee has suggested additional expansion of services such as MHC class II sequencing.
Lessons learned	There is expanding need for both in depth MHC analysis and custom MHC analysis. Demand for ancestry analysis has also increased this last year for both internal and external customers. We are occasionally asked to do custom work on a short time-line, and we need to factor all of this increased work load into staffing in the future to maintain quality customer service.

Imaging Morphology

The Imaging Morphology Research Support Core typically solicits user feedback on an annual basis. The survey was created using Survey Monkey and the link e-mailed to all users/ potential users of the facility.

Molecular Cell Biology

Category	Description
Methods for soliciting feedback	Emailed survey link using Survey Monkey
Topics covered	Quality of delivered services, desires for new services
Most significant results	High level of satisfaction and a request for a whole slide scanner
Lessons learned	Important to continue to innovate and develop new techniques for imaging and image analysis. Request for a whole slide imaging slide scanner was over-whelming
Changes made	More training implemented. Will be working to apply for a Shared Instrumentation S10 Grant towards purchasing a slide scanner

Molecular Virology Support Core

Category	Description
Methods for soliciting feedback	In the spring of 2016, an anonymous, web-based survey was emailed to all virology core users.
Topics covered	Usage, service quality, overall rating, general comments
Most significant results	Good to excellent levels of satisfaction with service quality and technical support. 86% of respondents would recommend the virology core to others. Service pricing was unanimously rated competitive. A few users commented that during the Winter 2015/2016 they had experienced longer than usual turnaround times for AAV vector productions.
Lessons learned	The virology core is a valuable and essential resource for investigators and continues to grow in popularity. The available services and pricing are meeting current user needs.
Changes made	The increase in AAV turnaround times was temporary due to rapidly increasing demand and was addressed by hiring additional staff.

MRI Core

Category	Description
Methods for soliciting feedback	• Day-to-day communication with users. Users interact extensively with the MRI core facility staff because MRI procedures require the presence of a member of the PI's laboratory to either log physiological data on the anesthetized monkey, or to control the MRI system. Users additionally interact with MRI facility staff when scheduling the instrument. Throughout these times, users provide continual feedback and suggestions for improving the core. • Annual campus-wide user group meeting to review changes to computer support, and plan for timing of system upgrade. • Discussions during bi-annual core oversight committee meetings.
Topics covered	Operations of the MRI facility (services provided, animal procedures, convenience of e.g. the calendar system, etc.), as well as capabilities of various MRI experiments in scientists' research. Usage plans over the coming year.
Most significant results	Identified time to plan for system upgrade. Communicated plans for future development of computer resources associated with the core. Continual optimization of animal handling and MRI procedures.

Lessons learned	Discussions with users of long-term plans for the analysis of the data, in addition to the feasibility of data acquisition, are extremely valuable at early stages of a new research project.
Changes made	No major changes in the past year. Preparations for major MRI system upgrade next year are underway.

Scientific Retreat

Category	Description
Methods for soliciting feedback	Survey Monkey
Topics covered	Which portions were attended, program format preferences (poster session, keynote, early stage investigators), collaboration establishment questions, venue questions, OHSU/ ONPRC affiliation
Most significant results	The attendees had positive feedback on the format and content of the current retreat and future retreats, as well as being thankful for the opportunity to learn about other projects and collaborations.
Lessons learned	The attendees appreciate having an annual scientific retreat.
Changes made	Expanding the invitation to include all scientists on West Campus, and additional scientists from VGTI.

Tissue Distribution Bank

Category	Description
Methods for soliciting feedback	For internal TDP recipients: Face to face meetings with lab groups prior to project start and request to follow up via phone or email with feedback on how new or existing procedures are going For external TDP recipients: Direct email and phone contact with customer Request for feedback regarding how the package arrived and if the tissues were prepared and shipped in the manner requested is included with shipping information for each shipment
Topics covered	For internal TDP recipients: Quality of tissue after dissection, methods for collecting challenging samples, priority of tissue needs, new collections for investigators. For external TDP recipients: Quality of tissue upon arrival, tissue collection and preparation methods
Most significant results	Innovative dissection and perfusion methods, pre-meeting discussions provided more opportunity to help investigators with their complex sampling Improved customer satisfaction

Lessons learned	Challenges associated new dissection or perfusions, understanding variation in collections between different animals
Changes made	For internal TDP recipients: Adoption of new techniques and training material to assist technicians For external TDP recipients: Development of new collection methods with input from recipients and opportunities for training before investigators collection occurs

Composite Application Budget Summary

Categories	Budget Period
Salary, Wages and Fringe Benefits	6,455,079
Equipment	0
Travel	53,980
Participant/Trainee Support Costs	0
Other Direct Costs (excluding Consortium)	3,589,338
Consortium Costs	0
Direct Costs	10,098,397
Indirect Costs	2,687,550
Total Direct and Indirect Costs	12,785,947

Component Budget Summary

Components	Categories	Budget Period
5549-001 (Admin Core)	Salary, Wages and Fringe Benefits	274,849
	Equipment	0
	Travel	23,600
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	415,965
	Consortium Costs	0
	Direct Costs	714,414
	Indirect Costs	200,036
TOTALS	Total Direct and Indirect Costs	914,450
5553-001 (Core)	Salary, Wages and Fringe Benefits	89,968
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	110,250
	Consortium Costs	0
	Direct Costs	200,218
	Indirect Costs	56,061
TOTALS	Total Direct and Indirect Costs	256,279
5552-002 (Core)	Salary, Wages and Fringe Benefits	15,756
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	15,756
	Indirect Costs	4,412
TOTALS	Total Direct and Indirect Costs	20,168
5551-003 (Core)	Salary, Wages and Fringe Benefits	15,466
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	15,466
	Indirect Costs	4,330
TOTALS	Total Direct and Indirect Costs	19,796
5550-004 (Core)	Salary, Wages and Fringe Benefits	480,180
	Equipment	0
	Travel	2,519
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	481,300
	Consortium Costs	0
	Direct Costs	963,999
	Indirect Costs	269,920
TOTALS	Total Direct and Indirect Costs	1,233,919

5572-005 (Core)	Salary, Wages and Fringe Benefits	279,152
	Equipment	0
	Travel	2,240
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	118,608
	Consortium Costs	0
	Direct Costs	400,000
	Indirect Costs	112,000
TOTALS	Total Direct and Indirect Costs	512,000
5571-006 (Core)	Salary, Wages and Fringe Benefits	25,088
	Equipment	0
	Travel	100
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	14,812
	Consortium Costs	0
	Direct Costs	40,000
	Indirect Costs	11,200
TOTALS	Total Direct and Indirect Costs	51,200
5570-007 (Core)	Salary, Wages and Fringe Benefits	130,542
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	48,128
	Consortium Costs	0

	Direct Costs	178,670
	Indirect Costs	50,028
TOTALS	Total Direct and Indirect Costs	228,698
5569-008 (Core)	Salary, Wages and Fringe Benefits	112,052
	Equipment	0
	Travel	1,080
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	74,019
	Consortium Costs	0
	Direct Costs	187,151
	Indirect Costs	52,402
TOTALS	Total Direct and Indirect Costs	239,553
5568-009 (Core)	Salary, Wages and Fringe Benefits	70,346
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	46,382
	Consortium Costs	0
	Direct Costs	116,728
	Indirect Costs	32,684
TOTALS	Total Direct and Indirect Costs	149,412
5567-010 (Core)	Salary, Wages and Fringe Benefits	62,909
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	59,862
	Consortium Costs	0
	Direct Costs	122,771
	Indirect Costs	34,376
TOTALS	Total Direct and Indirect Costs	157,147
5566-011 (Core)	Salary, Wages and Fringe Benefits	58,598
	Equipment	0
	Travel	260
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	38,855
	Consortium Costs	0
	Direct Costs	97,713
	Indirect Costs	27,360
TOTALS	Total Direct and Indirect Costs	125,073
5565-012 (Core)	Salary, Wages and Fringe Benefits	186,259
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	92,210
	Consortium Costs	0
	Direct Costs	278,469
	Indirect Costs	77,971
TOTALS	Total Direct and Indirect Costs	356,440

5564-013 (Core)	Salary, Wages and Fringe Benefits	31,151
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	319,629
	Consortium Costs	0
	Direct Costs	350,780
	Indirect Costs	98,218
TOTALS	Total Direct and Indirect Costs	448,998
5563-014 (Core)	Salary, Wages and Fringe Benefits	302,658
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	33,317
	Consortium Costs	0
	Direct Costs	335,975
	Indirect Costs	94,073
TOTALS	Total Direct and Indirect Costs	430,048
5562-015 (Core)	Salary, Wages and Fringe Benefits	186,443
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	200,672
	Consortium Costs	0

	Direct Costs	389,115
	Indirect Costs	108,952
TOTALS	Total Direct and Indirect Costs	498,067
5561-016 (Core)	Salary, Wages and Fringe Benefits	209,905
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	188,095
	Consortium Costs	0
	Direct Costs	400,000
	Indirect Costs	112,000
TOTALS	Total Direct and Indirect Costs	512,000
5560-017 (Core)	Salary, Wages and Fringe Benefits	305,980
	Equipment	0
	Travel	816
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	17,312
	Consortium Costs	0
	Direct Costs	324,108
	Indirect Costs	90,750
TOTALS	Total Direct and Indirect Costs	414,858
5559-018 (Core)	Salary, Wages and Fringe Benefits	115,736
	Equipment	0
	Travel	510

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	3,693
	Consortium Costs	0
	Direct Costs	119,939
	Indirect Costs	33,583
TOTALS	Total Direct and Indirect Costs	153,522
5558-019 (Core)	Salary, Wages and Fringe Benefits	82,844
	Equipment	0
	Travel	300
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	19,557
	Consortium Costs	0
	Direct Costs	102,701
	Indirect Costs	28,756
TOTALS	Total Direct and Indirect Costs	131,457
5557-020 (Core)	Salary, Wages and Fringe Benefits	131,468
	Equipment	0
	Travel	540
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	16,965
	Consortium Costs	0
	Direct Costs	148,973
	Indirect Costs	41,712
TOTALS	Total Direct and Indirect Costs	190,685

5556-021 (Core)	Salary, Wages and Fringe Benefits	659,363
	Equipment	0
	Travel	1,540
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	445,389
	Consortium Costs	0
	Direct Costs	1,106,292
	Indirect Costs	309,762
TOTALS	Total Direct and Indirect Costs	1,416,054
5555-022 (Core)	Salary, Wages and Fringe Benefits	137,100
	Equipment	0
	Travel	2,475
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	8,142
	Consortium Costs	0
	Direct Costs	147,717
	Indirect Costs	41,361
TOTALS	Total Direct and Indirect Costs	189,078
5554-023 (Core)	Salary, Wages and Fringe Benefits	122,456
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	23,075
	Consortium Costs	0

	Direct Costs	147,531
	Indirect Costs	41,309
TOTALS	Total Direct and Indirect Costs	188,840
5581-001 (Other)	Salary, Wages and Fringe Benefits	130,645
	Equipment	0
	Travel	10,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	38,567
	Consortium Costs	0
	Direct Costs	179,212
	Indirect Costs	50,179
TOTALS	Total Direct and Indirect Costs	229,391
5580-002 (Other)	Salary, Wages and Fringe Benefits	111,237
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	5,500
	Consortium Costs	0
	Direct Costs	118,737
	Indirect Costs	33,246
TOTALS	Total Direct and Indirect Costs	151,983
5579-003 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	500,000
	Consortium Costs	0
	Direct Costs	500,000
	Indirect Costs	0
TOTALS	Total Direct and Indirect Costs	500,000
5578-004 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	200,000
	Consortium Costs	0
	Direct Costs	200,000
	Indirect Costs	56,000
TOTALS	Total Direct and Indirect Costs	256,000
5577-001 (Project)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	20,000
	Consortium Costs	0
	Direct Costs	20,000
	Indirect Costs	5,600
TOTALS	Total Direct and Indirect Costs	25,600

5576-002 (Project)	Salary, Wages and Fringe Benefits	179,966
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	1,500
	Consortium Costs	0
	Direct Costs	181,466
	Indirect Costs	50,810
TOTALS	Total Direct and Indirect Costs	232,276
5575-003 (Project)	Salary, Wages and Fringe Benefits	423,698
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	13,569
	Consortium Costs	0
	Direct Costs	437,267
	Indirect Costs	122,435
TOTALS	Total Direct and Indirect Costs	559,702
5574-004 (Project)	Salary, Wages and Fringe Benefits	627,086
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	17,364
	Consortium Costs	0

	Direct Costs	644,450
	Indirect Costs	180,446
TOTALS	Total Direct and Indirect Costs	824,896
5573-005 (Project)	Salary, Wages and Fringe Benefits	896,178
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	16,601
	Consortium Costs	0
	Direct Costs	912,779
	Indirect Costs	255,578
TOTALS	Total Direct and Indirect Costs	1,168,357
TOTALS		**12,785,947**

Categories Budget Summary

Categories	Components	Budget Period
R&R Budget - Senior/Key Person Funds Requested	5549-001 (Admin Core)	101,620
	5553-001 (Core)	86,725
	5552-002 (Core)	15,756
	5551-003 (Core)	15,466
	5550-004 (Core)	135,388
	5572-005 (Core)	19,803
	5571-006 (Core)	4,136
	5570-007 (Core)	34,499
	5569-008 (Core)	16,243
	5568-009 (Core)	63,653
	5567-010 (Core)	49,673
	5566-011 (Core)	17,943
	5565-012 (Core)	24,480
	5564-013 (Core)	17,419
	5563-014 (Core)	0
	5562-015 (Core)	106,205
	5561-016 (Core)	46,440
	5560-017 (Core)	25,937
	5559-018 (Core)	22,172
	5558-019 (Core)	18,736
	5557-020 (Core)	18,772

	5556-021 (Core)	18,327
	5555-022 (Core)	37,099
	5554-023 (Core)	78,914
	5581-001 (Other)	0
	5580-002 (Other)	111,237
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	145,449
	5575-003 (Project)	336,122
	5574-004 (Project)	469,500
	5573-005 (Project)	709,452
TOTALS		2,747,166
R&R Budget - Other Personnel Funds Requested	5549-001 (Admin Core)	173,229
	5553-001 (Core)	3,243
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	344,792
	5572-005 (Core)	259,349
	5571-006 (Core)	20,952
	5570-007 (Core)	96,043
	5569-008 (Core)	95,809
	5568-009 (Core)	6,693
	5567-010 (Core)	13,236

	5566-011 (Core)	40,655
	5565-012 (Core)	161,779
	5564-013 (Core)	13,732
	5563-014 (Core)	302,658
	5562-015 (Core)	80,238
	5561-016 (Core)	163,465
	5560-017 (Core)	280,043
	5559-018 (Core)	93,564
	5558-019 (Core)	64,108
	5557-020 (Core)	112,696
	5556-021 (Core)	641,036
	5555-022 (Core)	100,001
	5554-023 (Core)	43,542
	5581-001 (Other)	130,645
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	34,517
	5575-003 (Project)	87,576
	5574-004 (Project)	157,586
	5573-005 (Project)	186,726
TOTALS		3,707,913
R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	5549-001 (Admin Core)	274,849

	5553-001 (Core)	89,968
	5552-002 (Core)	15,756
	5551-003 (Core)	15,466
	5550-004 (Core)	480,180
	5572-005 (Core)	279,152
	5571-006 (Core)	25,088
	5570-007 (Core)	130,542
	5569-008 (Core)	112,052
	5568-009 (Core)	70,346
	5567-010 (Core)	62,909
	5566-011 (Core)	58,598
	5565-012 (Core)	186,259
	5564-013 (Core)	31,151
	5563-014 (Core)	302,658
	5562-015 (Core)	186,443
	5561-016 (Core)	209,905
	5560-017 (Core)	305,980
	5559-018 (Core)	115,736
	5558-019 (Core)	82,844
	5557-020 (Core)	131,468
	5556-021 (Core)	659,363
	5555-022 (Core)	137,100
	5554-023 (Core)	122,456
	5581-001 (Other)	130,645

	5580-002 (Other)	111,237
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	179,966
	5575-003 (Project)	423,698
	5574-004 (Project)	627,086
	5573-005 (Project)	896,178
TOTALS		6,455,079
R&R Budget - Section C. Total Equipment	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0

	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Domestic Travel	5549-001 (Admin Core)	23,600
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	2,519

	5572-005 (Core)	2,240
	5571-006 (Core)	100
	5570-007 (Core)	0
	5569-008 (Core)	1,080
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	260
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	2,000
	5561-016 (Core)	2,000
	5560-017 (Core)	816
	5559-018 (Core)	510
	5558-019 (Core)	300
	5557-020 (Core)	540
	5556-021 (Core)	1,540
	5555-022 (Core)	2,475
	5554-023 (Core)	2,000
	5581-001 (Other)	10,000
	5580-002 (Other)	2,000
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0

	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		53,980
R&R Budget - Foreign Travel	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0

	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Section D. Total Travel	5549-001 (Admin Core)	23,600
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	2,519
	5572-005 (Core)	2,240
	5571-006 (Core)	100
	5570-007 (Core)	0
	5569-008 (Core)	1,080

	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	260
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	2,000
	5561-016 (Core)	2,000
	5560-017 (Core)	816
	5559-018 (Core)	510
	5558-019 (Core)	300
	5557-020 (Core)	540
	5556-021 (Core)	1,540
	5555-022 (Core)	2,475
	5554-023 (Core)	2,000
	5581-001 (Other)	10,000
	5580-002 (Other)	2,000
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0

TOTALS		53,980
R&R Budget - Tuition/Fees/Health Insurance	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0

	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Stipends	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0

	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Trainee Travel	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0

	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0

	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Subsistence	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0

	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Other Participants/Trainee Support Costs	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0

	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0

	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Section E. Total Participants/Trainee Support Costs	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0

	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Materials and Supplies	5549-001 (Admin Core)	5,000
	5553-001 (Core)	750
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	42,916
	5571-006 (Core)	550
	5570-007 (Core)	45,900
	5569-008 (Core)	48,600
	5568-009 (Core)	4,290
	5567-010 (Core)	0

	5566-011 (Core)	30,412
	5565-012 (Core)	24,000
	5564-013 (Core)	35,000
	5563-014 (Core)	1,000
	5562-015 (Core)	5,600
	5561-016 (Core)	63,414
	5560-017 (Core)	11,452
	5559-018 (Core)	3,263
	5558-019 (Core)	15,825
	5557-020 (Core)	13,256
	5556-021 (Core)	377,699
	5555-022 (Core)	3,910
	5554-023 (Core)	4,500
	5581-001 (Other)	24,000
	5580-002 (Other)	3,000
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	1,500
	5575-003 (Project)	2,375
	5574-004 (Project)	1,800
	5573-005 (Project)	2,500
TOTALS		772,512
R&R Budget - Publication Costs	5549-001 (Admin Core)	0

	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0

	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Consultant Services	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0

	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - ADP/Computer Services	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0

	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0

	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Subawards/Consortium/Contractual Costs	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0

	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		0
R&R Budget - Equipment or Facility Rental User Fees	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0

	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0

TOTALS		0
R&R Budget - Alterations and Renovations	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	0
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0

	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	500,000
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		500,000
R&R Budget - Other Direct Cost 1	5549-001 (Admin Core)	3,900
	5553-001 (Core)	109,500
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	94,500
	5572-005 (Core)	75,692
	5571-006 (Core)	14,262
	5570-007 (Core)	2,228
	5569-008 (Core)	25,419
	5568-009 (Core)	42,092
	5567-010 (Core)	59,862
	5566-011 (Core)	8,443
	5565-012 (Core)	27,790

	5564-013 (Core)	240,000
	5563-014 (Core)	32,317
	5562-015 (Core)	186,254
	5561-016 (Core)	124,681
	5560-017 (Core)	5,860
	5559-018 (Core)	430
	5558-019 (Core)	3,732
	5557-020 (Core)	3,709
	5556-021 (Core)	67,690
	5555-022 (Core)	4,232
	5554-023 (Core)	18,575
	5581-001 (Other)	14,567
	5580-002 (Other)	2,500
	5579-003 (Other)	0
	5578-004 (Other)	200,000
	5577-001 (Project)	20,000
	5576-002 (Project)	0
	5575-003 (Project)	11,194
	5574-004 (Project)	15,564
	5573-005 (Project)	14,101
TOTALS		1,429,094
R&R Budget - Other Direct Cost 2	5549-001 (Admin Core)	407,065
	5553-001 (Core)	0
	5552-002 (Core)	0

	5551-003 (Core)	0
	5550-004 (Core)	386,800
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	32,070
	5564-013 (Core)	44,629
	5563-014 (Core)	0
	5562-015 (Core)	8,818
	5561-016 (Core)	0
	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0

	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		879,382
R&R Budget - Other Direct Cost 3	5549-001 (Admin Core)	0
	5553-001 (Core)	0
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	0
	5572-005 (Core)	0
	5571-006 (Core)	0
	5570-007 (Core)	0
	5569-008 (Core)	0
	5568-009 (Core)	0
	5567-010 (Core)	0
	5566-011 (Core)	0
	5565-012 (Core)	8,350
	5564-013 (Core)	0
	5563-014 (Core)	0
	5562-015 (Core)	0
	5561-016 (Core)	0

	5560-017 (Core)	0
	5559-018 (Core)	0
	5558-019 (Core)	0
	5557-020 (Core)	0
	5556-021 (Core)	0
	5555-022 (Core)	0
	5554-023 (Core)	0
	5581-001 (Other)	0
	5580-002 (Other)	0
	5579-003 (Other)	0
	5578-004 (Other)	0
	5577-001 (Project)	0
	5576-002 (Project)	0
	5575-003 (Project)	0
	5574-004 (Project)	0
	5573-005 (Project)	0
TOTALS		8,350
R&R Budget - Section F. Total Other Direct Cost	5549-001 (Admin Core)	415,965
	5553-001 (Core)	110,250
	5552-002 (Core)	0
	5551-003 (Core)	0
	5550-004 (Core)	481,300
	5572-005 (Core)	118,608
	5571-006 (Core)	14,812

	5570-007 (Core)	48,128
	5569-008 (Core)	74,019
	5568-009 (Core)	46,382
	5567-010 (Core)	59,862
	5566-011 (Core)	38,855
	5565-012 (Core)	92,210
	5564-013 (Core)	319,629
	5563-014 (Core)	33,317
	5562-015 (Core)	200,672
	5561-016 (Core)	188,095
	5560-017 (Core)	17,312
	5559-018 (Core)	3,693
	5558-019 (Core)	19,557
	5557-020 (Core)	16,965
	5556-021 (Core)	445,389
	5555-022 (Core)	8,142
	5554-023 (Core)	23,075
	5581-001 (Other)	38,567
	5580-002 (Other)	5,500
	5579-003 (Other)	500,000
	5578-004 (Other)	200,000
	5577-001 (Project)	20.000
	5576-002 (Project)	1,500
	5575-003 (Project)	13,569

	5574-004 (Project)	17,364
	5573-005 (Project)	16,601
TOTALS		3,589,338
R&R Budget - Section G. Total Direct Cost (A thru F)	5549-001 (Admin Core)	714,414
	5553-001 (Core)	200,218
	5552-002 (Core)	15,756
	5551-003 (Core)	15,466
	5550-004 (Core)	963,999
	5572-005 (Core)	400,000
	5571-006 (Core)	40,000
	5570-007 (Core)	178,670
	5569-008 (Core)	187,151
	5568-009 (Core)	116,728
	5567-010 (Core)	122,771
	5566-011 (Core)	97,713
	5565-012 (Core)	278,469
	5564-013 (Core)	350,780
	5563-014 (Core)	335,975
	5562-015 (Core)	389,115
	5561-016 (Core)	400,000
	5560-017 (Core)	324,108
	5559-018 (Core)	119,939
	5558-019 (Core)	102,701
	5557-020 (Core)	148,973

	5556-021 (Core)	1,106,292
	5555-022 (Core)	147,717
	5554-023 (Core)	147,531
	5581-001 (Other)	179,212
	5580-002 (Other)	118,737
	5579-003 (Other)	500,000
	5578-004 (Other)	200,000
	5577-001 (Project)	20,000
	5576-002 (Project)	181,466
	5575-003 (Project)	437,267
	5574-004 (Project)	644,450
	5573-005 (Project)	912,779
TOTALS		10,098,397
R&R Budget - Section H. Indirect Costs	5549-001 (Admin Core)	200,036
	5553-001 (Core)	56,061
	5552-002 (Core)	4,412
	5551-003 (Core)	4,330
	5550-004 (Core)	269,920
	5572-005 (Core)	112,000
	5571-006 (Core)	11,200
	5570-007 (Core)	50,028
	5569-008 (Core)	52,402
	5568-009 (Core)	32,684
	5567-010 (Core)	34,376

	5566-011 (Core)	27,360
	5565-012 (Core)	77,971
	5564-013 (Core)	98,218
	5563-014 (Core)	94,073
	5562-015 (Core)	108,952
	5561-016 (Core)	112,000
	5560-017 (Core)	90,750
	5559-018 (Core)	33,583
	5558-019 (Core)	28,756
	5557-020 (Core)	41,712
	5556-021 (Core)	309,762
	5555-022 (Core)	41,361
	5554-023 (Core)	41,309
	5581-001 (Other)	50,179
	5580-002 (Other)	33,246
	5579-003 (Other)	0
	5578-004 (Other)	56,000
	5577-001 (Project)	5,600
	5576-002 (Project)	50,810
	5575-003 (Project)	122,435
	5574-004 (Project)	180,446
	5573-005 (Project)	255,578
TOTALS		2,687,550
R&R Budget - Section I. Total Direct and Indirect Costs (G +H)	5549-001 (Admin Core)	914,450

	5553-001 (Core)	256,279
	5552-002 (Core)	20,168
	5551-003 (Core)	19,796
	5550-004 (Core)	1,233,919
	5572-005 (Core)	512,000
	5571-006 (Core)	51,200
	5570-007 (Core)	228,698
	5569-008 (Core)	239,553
	5568-009 (Core)	149,412
	5567-010 (Core)	157,147
	5566-011 (Core)	125,073
	5565-012 (Core)	356,440
	5564-013 (Core)	448,998
	5563-014 (Core)	430,048
	5562-015 (Core)	498,067
	5561-016 (Core)	512,000
	5560-017 (Core)	414,858
	5559-018 (Core)	153,522
	5558-019 (Core)	131,457
	5557-020 (Core)	190,685
	5556-021 (Core)	1,416,054
	5555-022 (Core)	189,078
	5554-023 (Core)	188,840
	5581-001 (Other)	229,391

	5580-002 (Other)	151,983
	5579-003 (Other)	500,000
	5578-004 (Other)	256,000
	5577-001 (Project)	25,600
	5576-002 (Project)	232,276
	5575-003 (Project)	559,702
	5574-004 (Project)	824,896
	5573-005 (Project)	1,168,357
TOTALS		12,785,947

A. COMPONENT COVER PAGE

Project Title: Director's Office

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Director's Office provides leadership and oversight to the overall management of the ONPRC. Both the Director and the Associate Director for Research contribute to the overall liaison with the various units of the Center and units of the host institution (Oregon Health & Science University; OHSU) that affect research. The office serves as a centralized nexus for communication within ONPRC as well as OHSU, NIH, other NPRC Directors, and the scientific and lay communities. As noted in the Overview, the ONPRC utilizes a strategic planning process to develop strategies and tactics for the Director's office that are aligned with overall ONPRC strategic goals:

Specific Aim 1. Provide leadership in setting scientific and strategic priorities by leading the strategic planning process and its integration across the Center. Efforts will continue to integrate the current five-year plan of the Center with those of the OHSU's strategic planning and outcomes, linked through the Office of the Senior Vice President for Research. Project management is the mechanism used to track strategic progress and specific activities under Task Forces assigned yearly. Integrated leadership across the Center will be accomplished by scheduled and agenda-driven weekly meetings of the Director and Associate Directors, bimonthly meetings with the Division Chiefs, quarterly meetings with an expanded group of leaders, and regular monthly meetings with the Director of the Vaccine & Gene Therapy Institute, and meetings of key committees to accomplish animal allocation, policy setting, and goals as noted in the Administrative Overview. Finally, the Director's office will continue to plan, coordinate, and sponsor scientific retreats and symposia in collaboration with the Division Chiefs and Interdisciplinary Research Program managers to identify shape opportunities for joint scientific ventures, joint recruitment, and new research initiatives.

Specific Aim 2. Promote and assure fair external and internal access to nonhuman primates and support cores for research. This aim is accomplished via the linked operations of the Research Advisory Committee (RAC), the Collaborative Research Unit (CRU), the Pilot Project Program, and the ONPRC animal allocation process (which includes participation and prioritization by Division Chiefs) and the Division of Comparative Medicine, as well as through linkage with the NPRC Consortium. The CRU will continue to assure that all inquiries from external sources are directed to the appropriate internal collaborator for scientific leadership and expertise. Both the CRU and the Pilot Program have the goal of increased collaboration with outside investigators. The Associate Director for Research will continue to oversee the operation of the Research Support Cores, including procedures for access and peer oversight and review. Rates are set yearly with guidance from the Chief Operating Officer.

Specific Aim 3. Assure stable funding for the Center. This aim will be accomplished primarily via administration, oversight, and management of the submission of the P51 grant and its yearly progress reports. The office will continue to serve as the communication point for the National Scientific Advisory Board (NSAB) and arranges all meetings and reviews by this group for the purposes of advancing the P51 aims and goals. In addition, the Associate Director for Research will serve as the major liaison with the OHSU Foundation and the OHSU Office of Technology Transfer and Business Development, to align strategic funding initiatives and to promote and manage research interactions with industry and public-private partnerships.

Specific Aim 4. Provide effective communication within ONPRC and with OHSU, NIH, and the broader scientific and lay communities. The Office will continue to maintain minutes for all meetings on SharePoint, to publish the electronic newsletter, and to hold quarterly All-Campus meetings to inform employees of ongoing activities and initiatives. This Public Information Officer communicates scientific advances and administrative matters with the Office of Research Infrastructure Programs (ORIP) in DPCPSI at NIH. The Office will continue to work closely with OHSU's Strategic Communications office to publicize scientific breakthroughs internally at OHSU and to the public via press releases. The Director will hold monthly meetings with the Senior Vice President for Research and biannual meetings with the other NPRC Directors and senior staff and NIH staff. The Director's office oversees the ONPRC Outreach program, which is directed to scientists of all ages and the public to enhance science education and knowledge about the role of nonhuman primates in biomedical research.

Specific Aim 5. Provide oversight and linkage to key regulatory functions that are integral to interactions with OHSU and state and local governments. The Director's Office will continue to provide a liaison with the Offices of Research Integrity and Research Safety. The Office coordinates Emergency Response Planning in close collaboration with the Departments of Public Safety and Emergency Planning, working with local law enforcement and public safety groups. This office serves as the contact for the OHSU Government Relations office, which represents the ONPRC in state, local, and national meetings with elected officials.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DirectorsOffice_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We continue to disseminate our research findings and accomplishments through the ONPRC website and our ONPRC electronic newsletter, CenterPage; both are maintained by the Director's Office. Through our Outreach program, we are invested in sharing our Center's activities and progress with our local communities and educators. The Director has participated in various media interviews that have resulted in articles about NHP research, the NPRC Consortium, and the ONPRC. The Director and the Associate Director of Research play an active role in leadership groups at OHSU, and during the past year have reported to the OHSU Board of Directors, the President's Council, and various other senior leadership meetings and conferences. The Project Manager and the Director are actively involved in the Public Relations program with the NPRC Consortium.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will continue with our regular activities that support our specific aims, and in addition, with the direction of the Director's Office and pursuit of the ONPRC strategic objectives, ONPRC leadership will set the plan for the next year's Task Forces' activities and priorities. Specific new activities and initiatives will include recruitment of new core scientists in areas such as primate immunology and, in conjunction with the OHSU Knight Cardiovascular Institute and the Division of Cardiometabolic Health, NHP cardiology research.

DIRECTOR'S OFFICE: ACCOMPLISHMENTS

1. **Provide leadership in setting scientific and strategic priorities by leading the strategic planning process and its integration across the Center**. Our office continues to manage progress on our strategic objectives outlined during our formal strategic planning for ONPRC. We provide leadership and staffing of the Project Manager for all of the Task Forces executing the strategic objectives, and we assure success through tracking and regular reporting. Via regular meetings of ONPRC leadership, we have assured clear and regular communication of ongoing and new initiatives to all staff. After conducting national searches, we have hired a permanent Division Chief for Reproductive & Developmental Sciences, Dr. Jon Hennebold, as well as a permanent Division Chief for Diabetes, Obesity, and Metabolism (DOM), Dr. Jonathan Lindner, an OHSU cardiology physician-scientist. This appointment was accompanied by designation of DOM to the Division of Cardiometabolic Health in order to encompass an expanded focus on cardiovascular disease as well as existing strengths in obesity and diabetes. The Center Director participated actively in the yearlong process to develop a 20-year Master Plan for the OHSU West Campus, along with leaders from the VGTI, Campus Planning, Design & Construction, and the City of Hillsboro. This plan is now complete and will result in significant enhancements to the campus and the ONPRC over the next 10 years and beyond.

2. **Promote and assure fair external and internal access to nonhuman primates and support cores for research.** We have continued to streamline the process for requesting access to and subsequent assignment of animals for research projects. These procedures are being clarified for all involved groups, including the Animal Utilization Committee and the Resource and Operations staff in the Division of Comparative Medicine. In addition, population modeling tools have been incorporated into assignment discussions in order to make more strategic choices when animals are assigned, especially for long-term studies.

3. **Assure stable funding for the Center.** This office is responsible for overseeing all NIH correspondence and internal construction plans related to the awarded P51, G20s, and CO6 grants. We continue to seek opportunities for investment in research projects from industry and non-profit foundations. We have completed construction on one G20 project for expanded containment NHP housing, and we have completed a G20 remodeling project that was awarded this year to upgrade and enhance NHP behavioral suites. A major initiative this year has been to develop long-range plans for the West Campus and to request multi-year funding for capital projects from OHSU central funds, based upon the 20-year Master Plan. We anticipate major additional investments in the campus as a result of these plans and requests, including a Primate Multimodal Imaging Center (PMIC) to provide expanded NHP imaging using PET and CT, funded in part by a private donation to the Private Source and linked to the existing MRI Core. This latter initiative has been in conjunction with the recruitment of Dr. Lindner described above.

4. **Provide effective communication within ONPRC and with OHSU, NIH, and the broader scientific and lay communities**. We have continued oversight of the Center Library in the Director's Office to allow more accurate, timely, and smoother reporting of publications as part of the P51 progress reports and reports to ORIP. We have continued regular meetings for employees after they have been here for 3-6 months to explain the Center organizational and leadership practices and processes. We continue to host OHSU All Employee visits to introduce those employees from other OHSU sites to the West Campus and the ONPRC, a very popular program. We also hold a yearly Public Tour to invite members of the community to visit and learn about the Center. These programs have improved understanding and communication of the importance of NHP research and have enhanced community awareness. Finally, as part of our strategic initiatives, we have appointed a Task Force to enhance intra- and inter-institutional communications and public relations, improving linkages with OHSU Strategic Communications and Government Relations. We are actively participating in the NPRC Consortium Public Relations efforts to develop a national communication plan to inform the public of the value of the primate centers.

5. **Provide oversight and linkage to key regulatory functions that are integral to interactions with OHSU and state and local governments.** The Director's office has continued to be responsible for Incident Command response and materials on the West Campus as part of emergency planning with law enforcement and government entities. Drs. Haigwood and Roberts have met regularly with local, state, and national representatives to assure that these groups are informed of the progress of the Center in biomedical breakthroughs and as local employers.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5549

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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 luded by Requester				Center Director	Instit ut io n Base Salary	EFFORT			37,020.00	9,255.00	46,275.00
2.						Assoc Director					42,573.00	12,772.00	55,345.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **101,620.00**

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						
2	Unit staff	24.0			136,082.00	37,147.00	173,229.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**173,229.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**274,849.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	23,600.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**23,600.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	5,000.00
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. Miscellaneous rental, memberships, Telecommunication, printing	3,900.00
9. Honorarium, hosting groups & guests, miscellaneous other expense	407,065.00
Total Other Direct Costs	**415,965.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**714,414.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	714,444.00	200,036.00
		Total Indirect Costs	**200,036.00**

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)	**914,450.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Business Services

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

BUSINESS SERVICES: Business Services at the ONPRC provides services and resources to assist faculty and administration in the development and management of grants and other financial resources that fund the accomplishment of the strategic research mission of the ONPRC. The business functions are in accordance with OHSU policy and procedures, and NIH rules and regulations. The business service staff provides support for ONPRC ancillary proposals and awards. This includes from initial planning stages, to mid-project financial management and budget tracking, to close-out and final reporting of all non P51 projects. Business Services provides a single-point-of-contact for ONPRC staff to accomplish all business process tasks, accounts payable, requisitioning, fixed assets inventory, purchase orders and travel reimbursements. This facilitation of these processes helps free ONPRC staff to concentrate on their areas of expertise in research, support cores and other areas, and reduce the distraction that can result from the increased administrative burden in the conduct of research.

Through these functions, Business Services provide:
•Accountability and guidance in coordination with central University resources to internal and external funding guidelines, rules, and regulations, and budgetary and schedule commitments.
•Comprehensive support for all human resources and related systems processes at the university including hiring, on-boarding, union matters, labor distribution, etc.
•Provide single-point-of-contact efficiency for ONPRC staff in performing business processes such as ordering research supplies, obtaining purchase cards, submitting travel claims, processing internal billing charges, tracking fixed assets, submitting accounting adjustment forms, and many other business related processes.
•Budgetary development assistance for ancillary proposals and non-human primate costs.
•Consultation services for financial aspects of project planning.
•Education regarding university and federal systems; and requirements for the conduct of research projects with OHSU Research Grants and Contracts, Sponsored Projects Administration and Central Financial Services.
•Review and evaluation of financial progress and assistance in research project resource management.
•Research Award compliance and close-out in coordination with central University resources.
•Reporting and accounting expertise to provide information for individual projects as well as overall ONPRC financing and future projections.

Specific Aim 1: To provide appropriate levels of support and staffing to provide for the efficient, effective, and compliant conduct of the P51 award. This involved the facilitation of all business processes at the university in behalf of the core award and its budget managers from budget planning and submission to Federal Financial Report (FFR) calculation and providing assistance in progress report writing and submission.

Specific Aim 2: To provide excellent customer service to our ONPRC Divisions while maintaining productive relationships with OHSU Business and Grants Management Departments. Standard Operating procedures are being updated and created to clearly define roles and responsibilities. This will clarify and provide efficiencies in the day to day operations.

Specific Aim 3: Fully implement and utilize a radio-frequency identification (RFID) inventory system to track ONPRC fixed assets and include maintenance agreements and service dates on equipment. This will greatly reduce the time and effort involved in equipment inventory tracking and reducing the burden on lab personnel.

Specific Aim 4: Explore and implement a new system for budget development for the competing and non-competing P51 award. The current system is built on multiple Excel spreadsheets with extensive links. Alterations to the award require extensive manual changes throughout multiple spreadsheets which is error prone. The selection and implementation of a system better suited to the P51 award and the requirements of electronic submission will be necessary in the coming competitive period.

ADMINISTRATIVE SERVICES
The Associate Director for Administration is responsible for the overall infrastructure and financing of the ONPRC. He and his team provide comprehensive support for a safe, productive, and environmentally sound infrastructure to support the administrative and facility related needs of ONPRC research and NHP animal care staff. This includes the oversight and management of Center budgeting and financial planning and implementation, Business Services, Information Technology, Human Resources, Facilities, Construction, and Campus Planning. The Associate Director and his team work with their University counterparts in participatory teamwork that facilitates the infrastructure support and financing of the ONPRC in areas such as grants management, design and construction, purchasing, logistics, budgeting, financial services, F&A rate proposal development and negotiation, and security. The ONPRC Administrative team also works with NIH, local governments, and utilities to provide comprehensive infrastructure support.

Through these functions and support team the Associate Director for Administration:
•Safeguards the resources of the ONPRC in association with OHSU central services.
•Ensures planning, management, and financing for the infrastructure resources that support NHP animal colonies and research.
•Ensures ONPRC services to facilitate the day to day business operation of the center in coordination with central university services.
•Ensures core and ancillary grant compliance in association with central Research Grant and Contracts.
•Ensure Information Systems resources appropriate to the NHP research mission.
•Ensures infrastructure construction and renovation projects are appropriately managed meeting the goals and aims of these projects and that their continued use is consistent with funding sources.
•Ensures compliance with local governments and regulatory agencies in relationship to the physical land and buildings.
•Ensures the security of the physical facilities.
•Ensures financing and managerial support for sustainability related programs/projects.

Specific Aim 1: Ensure the continued provision of the effective and efficient operation of the ONPRC infrastructure resources, both physical and personnel resources, to provide an appropriate environment for the safe and effective conduct of animal care and research at the ONRPC.

Specific Aim 2: Work with the University to strengthen work and financing relationships and make timely and accurate resource requests to ensure that the additional expertise and funding necessary to support infrastructure development appropriate to the ONPRC NHP research endeavor are provided in a timely manner.

Specific Aim 3: Work with the University and local governments to establish a realistic and therefore fundable long-range master plan to provide a growth roadmap for the next ten years for the ONPRC.

Specific Aim 4: Increase engagement with other Administrative Directors in the NPRC consortium to continue work on defining and documenting best practices that can be used within the varied institutional environments throughout the NPRC system.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-BusinessServices_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The university implemented business intelligence software called Cognos to use for the university's budget, financial planning and forecasting. This budgeting platform has not been implemented with grant accounts; it has only been used with non-grant accounts at the university. Due to the host institution priority changes with Cognos, we were put on hold with implementing the budget too. We hope to restart this project in the next reporting period.

We also plan on implementing the changes to the billing process from Internal Audit.

The Business Services office will develop an operational strategic plan that will include measurable goals and regular review and updates. The plan will include human resources, grants management and financial reporting.

BUSINESS SERVICES: ACCOMPLISHMENTS

In the P51 application, Business Services and Administrative Services appeared separately. These units have now been combined but the aims have remained the same.

The Center continues to have a dedicated analyst for the P51, a dedicated analyst cost analyst and a financial analyst that focus on cost based rates and the program income that comes into the Center. They have been instrumental in implementing the new billing system and maintain integrity and compliance with all the charges that flow through the system. They continue to work on new features and enhancements with the Information Systems team.

We requested the host institution's Internal Audit to review and test the new billing system to ensure financial controls were working as designed, as well as compliance requirements. Internal Audit did not have any major "findings". They had minor recommendations.

The Business Services office continues to make progress in standardizing monthly financial reports for the core grant as well as non-core grant portfolio. The host institution has implemented a reporting tool (Cognos) and over the past year we have worked closely with them to convert reports from the old system to the new as well as develop new reports that were not possible in the old system. Standard operating procedures continue to be updated with clearly defined roles, responsibilities and expectations.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5550

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			104,952.00	30,436.00	135,388.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **135,388.00**

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						
7	Unit Staff	39.31			267,281.00	77,511.00	344,792.00
7	**Total Number Other Personnel**					**Total Other Personnel**	**344,792.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**480,180.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,519.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,519.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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. Liquid Nitrogen	94,500.00
9. Telecommunication, Miscellaneous Other Expense	386,800.00
Total Other Direct Costs	**481,300.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**963,999.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	963,999.00	269,920.00
		Total Indirect Costs	**269,920.00**

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)	**1,233,919.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Facilities

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

In support of the Associate Director for Administration, the Facilities and Property (F&P) Manager is responsible for the safe, efficient, sustainable and cost-effective management of ongoing operations, maintenance, upgrades, and security associated with the ONPRC campus buildings, grounds and infrastructure. On a daily basis, the F&P team works directly with the Division of Comparative Medicine (DCM) staff to assure that all animal housing and holding areas are in compliance with the applicable regulatory codes and standards for the proper care and use of laboratory animals. Additionally, the F&P staff provides support to all research laboratories and administrative areas to assure all of these spaces are kept clean, safe, and environmentally controlled, thereby allowing for a comfortable and productive work environment. With the relatively recent addition of a Sustainability Manager to the F&P, all operational approaches to maintaining the campus are being reviewed to incorporate the latest innovations in energy savings measures. The F&P Manager works closely with the University's Design and Construction department to plan, fund, design and construct major buildings on the campus in accordance with the rules for project management and financial accountability. As part of this responsibility, the F&P Manager also works directly with the City of Hillsboro and the city's regulatory agencies to assure that all construction and major renovations on the campus are in compliance with the ONPRC's Master Plan on file with the City of Hillsboro, and associated building codes and standards, including the proper care and treatment of storm water runoff, wetland maintenance, and protection of natural resources on the campus. As part of the campus security program, the F&P Manager works with the University's Public Safety Office and the local police and fire departments to assure that the campus is secure and safe at all times.

•Through these functions, the F&P Manager: Coordinates, with the F&P Operations Manager, to assure that all Heating, Ventilating and Air Conditioning (HVAC) equipment is operational and set to the proper temperature ranges at all times.
•Monitors and tracks necessary building repairs to assure the structural integrity and well-maintained appearance of all campus structures.
•Oversees the care and maintenance of all campus grounds, walkways, paths and roads to assure that the work performed to keep the property fully accessible and in good condition is being performed in a sustainable and cost effective manner.
•Ensures that future construction and tenant improvement projects and those working on those projects are fully versed in applicable standards, such as University, NIH, City (JHAs) and State standards.
•Coordinates with the ONPRC Business Office the University Central Financial Services and Design and Construction departments to assure proper funding exists for all new work on the campus
•Oversees campus security and programs for badging and key control access on campus.
•Coordinates with the Sustainability Manager to develop and implement best practices and energy management strategies for the campus

Specific Aim 1 – Ensure the continued safe, efficient, productive and sustainable operations at the ONPRC, complying will all local, state and federal regulations governing the administrative office spaces, research laboratories, and in particular, areas related to the care and welfare of the research animals.

Specific Aim 2 – Work cooperatively with the Administrative, Research, and DCM staffs to identify campus upgrades and renovations necessary to support the ongoing research goals of the University and ONPRC. This should include infrastructure upgrades to support anticipated changes in research methodology or desired animal housing refinements. Incorporate information into a comprehensive Campus Master Plan that will not only support the future needs of biomedical research but will also meet the requirements of the City of Hillsboro.

Specific Aim 3 – Working with the University's Design and Construction Department and Space Planning Group develop a clear understanding of the capital project planning process to assure timely identification and funding of future projects to support the ONPRC research and animal care mission.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Facilities_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

With the completion of the 20-year Master Plan with the City of Hillsboro, the ONPRC will be focusing on prioritizing the projects on the list and getting them moving forward on campus. The priorities include animal space as well as administrative offices for the DCM employees.

The Center will also be assessing all large equipment and creating a priority list for replacement. We will work closely with the host institution to develop a reasonable implementation plan given the available funding.

The Center is also updating all the emergency planning documents and continues to have a monthly Emergency Management Committee meeting. The Committee is planning an exercise to test the campus process and procedures to identify areas that need enhancement. It will be an all campus exercise that includes the Division of Comparative Medicine, Environmental Health & Radiation Safety, Research, Facilities and Administration.

FACILITIES: ACCOMPLISHMENTS

To continue safe, efficient, productive and sustainable facilities operations, two monthly reports are used to track and monitor physical plant activity on campus. The first report, Facilities and Property Department Preventative Maintenance Schedule, is a comprehensive list that identifies specific area for regular service/testing and the specific employee responsible to do work. A Work Order List for Projects tracks specific project, requestor, preferred completion date and estimated cost.

In addition, ONPRC continues its effort to use energy efficiently and effectively throughout the operations. The Center monitors and tracks monthly electric and gas bills. Year-to-date, the data is proving that our energy usages have been decreasing thus meeting our targets set with the Energy Trust of Oregon to reduce our energy consumption.

ONPRC continues to have regular monthly meetings with the OHSU's Design and Construction (DesCon) department to clarify and agree on a specific capital budget process, identifying high priorities for the Center and stay on target with approved capital projects. During capital budget season for the University, the Center's Chief Operating Officer and the Center's Facilities manager meets with DesCon to update needs and priorities that may have changed. The DesCon representative takes this information to the University's Space Planning committee in order for it to be included in their capital budget request with our priority level assessment. Timelines have been established and communicated by the University's Central Financial Services Budget Office.

The Strategic Planning Facilities Infrastructure Task Force that was established in the prior year completed its charge and disbanded. The work performed by this task force was utilized by the West Campus Master Plan Committee. The 20-year Master Plan was completed in December 2016 and is currently being reviewed and awaiting approval from the City of Hillsboro.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5551

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFO RT			12,083.00	3,383.00	15,466.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **15,466.00**

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)	**15,466.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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. Books & Periodicals, Interlibrary loans	0.00
Total Other Direct Costs	**0.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**15,466.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	15,466.00	4,330.00
		Total Indirect Costs	**4,330.00**

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)	**19,796.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Information Systems

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Information Systems (IS) Manager is responsible for the IS service program at the ONPRC. The IS Program comprises IS staff directly reporting to the IS Manager, and the OHSU Information Technology Group (ITG) staff dedicated to the ONPRC but reporting to ITG Management. IS services include but are not strictly limited to: software applications, computational and database services, intranet websites, and multimedia support for all ONPRC seminars, videoconferences or symposia. ITG provides network and telecommunications infrastructure, workstation support, enterprise-wide core applications, resource hosting-management and customer support for the OHSU enterprise network.

Together, the IS Program is a comprehensive technical resource providing people, processes, and technology with a mission in support of ONPRC scientific, clinical and research programs; maintenance of animal resources; development of business applications; and technical integration with OHSU and other institutions. IS' vision is to achieve the most productive synergy between people and computing technologies.

IS specifically focuses on core strategic responsibilities and functions that provide key capabilities to the ONPRC research endeavor and leverage the OHSU IT infrastructure:
Software application support and development in line of business applications such as the integrated research and clinical information
Proprietary Info
stem platform called PRIMe; for office productivity workflows using Microsoft SharePoint; Research laboratory support in areas such as server/system configuration and hosting consultation; and Lab Information System (LIMS) or lab instrumentation interface development and integration
•Business process analysis to achieve improved informational and computational workflows
•Database administration; database and report design, consultation and migration
•Security and privacy of data along with business continuity, disaster recovery and capacity planning
•Service, quality and project management
•Audio-visual, conferencing and training content development support for local and offsite meetings
•NHP Consortium Participation including ONPRC representation for the Data Access Guidelines Group (DAGG) working group

Specific Aim 1. Continue progress in adoption of operational and industry best practices to deliver higher quantity and quality of service delivery to ONPRC and other stakeholders. Focusing on quality improves output. Becoming more efficient helps to lower or create more sustainable operating costs. Systems engineering and technology is getting more complex, not less, requiring prioritizing the highest value efforts.

Specific Aim 2. Leverage and exploit existing technology resources while adding technologies only as strategically needed. This will maximize the return on investments in technology resources, reduce risk in areas such as staffing, and to create a synergistic effect between systems resulting in more agile and scalable technical infrastructure, and ultimately more effective and efficient research, clinical and administrative operations that lead to better research.

Specific Aim 3. Provide support and expertise leadership for research and colony management informatics internally and at the national NHPRC level. Efforts such as creating interfaces to instrumentation allow for the streamlined and automatic capture of data. Facilitating the development of simulations and modeling, for example, help colony managers optimize a limited resource.

Specific Aim 4. Foster effective communications and collaboration internally and externally to, among other things, make it easier for stakeholders to find and use the right quality data in innovative ways. The future success of the NPRCs as a consortium will be increasingly based on collaborative work supported by Information Systems technologies.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-IS_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Specific Aim 1 and 4: Metrics are being established to help measure the center's activity and performance against industry best practices. Regular contact with the other NPRC information technology groups will help us standardize processes and platforms where appropriate and provide insight and support across the NPRC IT community.

Specific Aim 2: As the University supported applications continue to grow and change, our efforts to utilize what is available will help to leverage our resources in the most successful and cost effective way.

Specific Aim 3: Development of viable remote data entry options and the deployment of wireless devices will facilitate the entry of animal health data at its source. This will heighten our ongoing success in reducing errors and improve efficiency throughout the organization.

INFORMATION SERVICES: ACCOMPLISHMENTS

Specific Aim 1: Our testing and development processes continue to be refined, providing improved accuracy and reducing the need adjust programming after it has been moved to our production environment. Engaging representatives of our user community in regularly scheduled meetings has provided excellent opportunities to discuss current concerns as well as future needs.

Specific Aim 2: The Center continues to work with the University's Information Technology Group (ITG) to make sure the use of technology resources available at the enterprise level are leveraged before looking to third party vendors or in-house development. Improved user training, both locally and utilizing University resources, helps to maximize the value of current applications while reducing the need to add new technologies.

Specific Aim 3: Mobile devices are being tested to determine which solutions will provide the flexibility needed and meet the daily needs of the users in a variety of clinical and husbandry situations. Reliability, price, and available support are vital to the decisions about which mobile platforms should be pursued further.

Specific Aim 4: Within PRIMe, the ability to easily connect the animal electronic health record (EHR) with laboratory data is opening lines of communication between the research community and the animal care units. With the use of the Proprietary Info ased EHR expanding to more primate centers, the value of the newly implemented NPRC Information Technology working group is increasing. The IT leaders across the NPRC community meet regularly to discuss common concerns and to explore solutions to the problems that we all face daily.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5552

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			12,120.00	3,636.00	15,756.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **15,756.00**

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)	**15,756.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	**15,756.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	15,756.00	4,412.00
		Total Indirect Costs	**4,412.00**

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)	**20,168.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Research Library

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The ONPRC library provides all library services for ONPRC researchers, veterinarians, behavioral services team and staff with the major emphasis on NHP literature. Services include document delivery and interlibrary loan (ILL) of books and articles and reference services including in depth research projects; active assistance, information and advice ensure compliance with NIH public access policy. The librarian is also responsible for collection development and maintenance of the library's holdings of books and journals. The ONPRC library is closely associated with the OHSU main library to ensure that the needs of ONPRC and its NHP research mission are considered regarding access to e-journals and databases.

Through these functions the library:
•Ensures the ONPRC library collection meets the changing needs of ONPRC patrons and maintains its focus on NHP literature.
•Obtains requested articles and books that are not within the collection.
•Assists researchers and veterinarians in their mission of performing research on and maintaining the health and well-being of NHPs by performing in depth literature searches.
•Assists ONPRC authors to comply with NIH Public Access policy.
•Preserves the areas of the collection of historical significance to the center and unique NHP materials.
•Provides books and articles from its specialized collection of NHP literature to other primate centers, public, government and academic libraries, hospitals and research institutions in Oregon, throughout North America and even worldwide.

Specific Aim 1: Ensure the continued provision of efficient and effective services and maximize resources available for the needs of NHP researchers, veterinarians and support staff.

Specific Aim 2: Work closely with ONPRC Division of Comparative Medicine to provide assistance and support for their expanded educational and research role in Primatology.

Specific Aim 3: Preserve the unique NHP historical resources of ONPRC whilst making them more available to researchers and the wider community.

Specific Aim 4: Help ensure ONPRC authors comply with NIH public access policy in a timely manner.

Specific Aim 5: Develop training methods and techniques using new technologies and resources to effectively meet the needs of the ONPRC community and continue leveraging resources and connections with OHSU main library to ensure that ONPRC has access to any additional resources it needs to efficiently perform its mission of NHP research.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-ResearchLibrary_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Specific Aim 1: The library will continue to provide current services whilst maintaining the high standards of speed and efficiency. Library services will be actively promoted particularly to new employees through brochures in the New Employee Information packets, the CenterPage, or by emails targeted at specific groups. The successful practice of emphasizing communications to and trainings and services for Administrative Assistants will be continued since these are a conduit to researchers and other staff but outreach will be extended to newly established and/or newly appointed researchers.

Specific Aim 2: The library will continue outreach to DCM in order to increase awareness of the availability of current services and actively seek feedback on any unmet education or research needs. The library will expand focus on training and education needs and identify new or existing resources that can support these.

Specific Aim 3: Library outreach has resulted in donations and unearthing of significant historical materials from departments and

individuals which need to be organized and preserved. Items of most value and interest will be digitized and shared with stakeholders.

Specific Aim 4: The librarian will continue to act as a compliance monitor, running monthly checks of new publications and offering training sessions on NIHMS and promoting awareness through articles in the CenterPage, posts on the ONPRC Library Bridge page, and emails to researchers with potentially non-compliant publications and aid authors to resolve problems. The library will continue to offer regular checks of bibliographies in MyNCBI in order to preempt potential compliance problems and will continue to manage the bibliography of the P51 PI, Dr. Robertson. The librarian will provide monthly list of new ONPRC publication to the NPRC website in order to increase the visibility of the latest publications.

Specific Aim 5: The librarian will continue to serve on the Collection Development Committee to represent ONPRC and ensure the needs of ONPRC veterinarians and researchers are met. Strong relations with the OHSU library will be reinforced to ensure the latest trainings and resources are available for ONPRC including areas of data management and even use of social media in research. The Librarian will help guide ONPRC researchers to these resources and sources of assistance.

RESEARCH LIBRARY: ACCOMPLISHMENTS

Specific Aim 1: The library continued to provide literature searches, articles books and electronic resources for research purposes and day to day animal care to researchers, veterinary and support staff. Service goals were met with items obtained through Interlibrary loan (ILL) usually provided within 24 hours and document delivery items (available in the ONPRC library) often within 30 minutes of the request being received, this process has been further improved by the acquisition of a faster, more efficient scanning/copier/color printer. Almost all requests were filled electronically minimizing unnecessary printing and paper wastage. The library also provided articles and books to hospitals, universities, research institutions and public libraries throughout the USA and the world. Non-OHSU researchers and members of the public have accessed the library by appointment to use its specialized resources. To prevent disruption of services during vacations or other absences of the Librarian a member of the business services office staff was cross trained to provide ILL and some other services during these periods.

Specific Aim 2: The library continued to assist veterinarians, interns, residents and other DCM staff in acquiring articles, books and other resources necessary to evaluate potential research projects and to study for professional examinations, including ACLAM. Library access is available 24/7 providing computer access to online resources and quiet study space. DCM requests for new book purchases for the library collection increased and have been met whenever the budget allowed, this has included acquisition of literature on issues such as leadership and conflict management to assist manager and employee education. Additional key reference materials have been added to the small collection of books on departmental loan and housed in the research annex for use by DCM staff and veterinarians. The majority of veterinarians and many of the support staff recognize the library as a resource for animal related or other questions.

Specific Aim 3: The library has continued to add ONPRC related photographs, Ito artwork, and documents to its collection as a result of donations from members of the public and various departments on campus. A new project was undertaken to identify original Ito art on display around campus in order to preserve and protect these valuable works. In collaboration with the Director's office a number of originals have been framed in museum quality glass and have been used to decorate the new Ito conference room. Other pieces housed in areas not conducive to art have been replaced by high quality copies. This project has garnered a great deal of appreciation and interest around campus.

Specific Aim 4: The research librarian has continued the role of Public Access compliance monitor and is proactively alerting authors to non-compliant publications and assisting them in the compliance process. The library has been involved in troubleshooting non-compliance issues, communicating with publishers on behalf of PIs, and assisting them in the NIHMS process or submitting articles on their behalf. The librarian has conducted a number of training sessions for new Administrative Assistants on NIH Public Access Policy and has worked closely with them on resolving problems on behalf of PIs. It is now well established that the librarian is the resource to consult on any issues regarding publications and compliance. The ONPRC librarian continues the responsibility of maintaining the master list of ONPRC publications, including updating the MyBibliography for the PI of the P51 and works proactively through the year to identify and eliminate compliance problems.

Specific Aim 5: The ONPRC Librarian continues to serve on the OHSU Library Collection Development Committee, which ensures continued ONPRC input in the selection of and continued access to resources of special interest to ONPRC, this is especially important when cuts and cancellations are made due to budget cuts. Recently installation materials for OHSU purchased software SAS and SPSS were provided to the ONPRC library (previously these could only be obtained from the OHSU main library circulation desk) which has facilitated access to these resources.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5553

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			61,507.00	25,218.00	86,725.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **86,725.00**

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	Technician	12.0			2,300.00	943.00	3,243.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**3,243.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**89,968.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	750.00
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. Books & periodicals, interlibrary loans	109,500.00
Total Other Direct Costs	**110,250.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**200,218.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	200,218.00	56,061.00
		Total Indirect Costs	**56,061.00**

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)	**256,279.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Research Safety

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Research Safety Program has recently been reorganized and integrated into Oregon Health & Science University's (OHSU) corporate Environmental Health and Radiation Safety (EHRS) Department. This change in organization provides access to the University's wider range of EHRS resources and staff expertise, and allows us to better address safety at the ONPRC. University EHRS oversees enterprise-wide programs and policies (development, administration and periodic review) addressing the entire spectrum of biosafety, chemical safety, radiation safety, hazardous and other regulated waste, worker safety, ergonomics, environmental compliance, emergency response and occupational health programs. During program development, emphasis is placed on program functionality, cost control, and compliance with applicable federal, state, and local regulations. Training for ONPRC personnel is conducted as required by regulations and/or ONPRC Administration. EHRS personnel receive training needed to perform their assigned duties and maintain a network of contacts within the regulatory community. Requested funding is needed to maintain the ONPRC as an environmentally responsible member of the community and as a safe and healthy workplace.

EHRS maintains a dedicated, on-site staff of consisting of the Research Safety Manager/OHSU Biosafety Officer, a Biosafety Officer, two Safety Specialists - Biosafety, and a Safety Specialist – Hazardous Waste. Corporate staff supporting ONPRC also include a Radiation Safety Officer, Assistant Radiation Safety Officer, two Safety Specialists – Industrial Hygiene, Chemical Safety Officer and Safety Specialist – Waste Water Management.

Specific Aim 1. Monitor and evaluate the efficiency and effectiveness of the EHRS organizational structure with respect to ONPRC operations. As the proposed personnel arrangement represents a number of changes in the structure operating in the previous funding period, which itself was organized to address aspects of the previous critique, it will be important to continue assessment of the new organizational structure to ensure optimal levels of research safety.

Specific Aim 2. Improve laboratory safety awareness and compliance. In light of recent high-profile laboratory accidents, and a general increase in regulatory oversight of laboratory safety practices, it is essential that the ONPRC and its investigators and staff are adequately protected from injury and personal and institutional liability. EHRS has begun to expand and improve laboratory safety monitoring and consulting by developing a laboratory safety audit program consistent with that developed by the University of California Center for Laboratory Safety. The goal of this program is to ensure that investigators are adequately informed about safety practices specific to the type of research being performed, and to assist them in maintaining compliance with all applicable federal, state, and local health and safety regulations.

Specific Aim 3. Continue to Strengthen the Occupational Health (OH) and Research Safety Program. The OH has established working relationships with EHRS staff, Department of Comparative Medicine (DCM) staff, and Risk Management.

Specific Aim 4. Continue to strengthen training and injury prevention strategies. The Research Safety Manager represents the ONPRC with the Occupational Health and Safety (OHS) Working Group. The stated goals of the OHS working group are to meet bi-monthly by phone conference and in-person annually to share information critical to protection of personnel working with nonhuman primates and develop common practices between the seven Primate Research Centers.

Specific Aim 5. Continue to strengthen Security and Biosecurity at the ONPRC. EHRS works with OHSU's Department of Public Safety (DPS), DCM staff, facilities, local law enforcement, and first responders to improve Security/Biosecurity at ONPRC.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-ResearchSafety_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-ResearchSafety_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

EHRS will continue to improve our Biosafety and Research Safety Programs using multi-media methods and working with all stakeholders of ONPRC. EHRS reaches out through organizations such as American Biological Safety Association (ABSA) and Campus Safety and Health Managers Association (CSHEMA) to keep in contact with others in similar jobs and to keep up-to-date on current

practices and regulatory changes.

Available trainings are being reviewed by EHRS and other stakeholders for content and best method of delivery; where possible, the trainings are made to be available on-line to ease compliance with training requirements. Additional trainings to cover topics more in depth or as refreshers in response to incident trends are being added to the trainings. Some of these are one-time refreshers and others are considered valuable as annual refreshers.

EHRS is developing a training matrix to ease the burden of staff with completing training requirements for their work.

RESEARCH SAFETY: ACCOMPLISHMENTS

Specific Aim 1: An evaluation process carried out by OHSU central administration has led to the Research Safety Department being folded once again into the EHRS Department. This allows for increased coverage from within EHRS using non-ONPRC dedicated staff for coverage and increased the efficiency of use of ONPRC resources.

Specific Aim 2: The successful OHSU/ONPRC pilot of the laboratory safety audit program (LSAP) has been expanded to include IACUC and IBC regulatory audits allowing researchers a comprehensive regulatory safety audit with a cohesive education and regulatory message. As well as making best use of the EHRS staff time dedicated to the LSAP and implementation of safe practices in the ONPRC laboratories, the LSAP has improved communication and integration of EHRS as subject matter experts within the ONPRC.

Specific Aim 3: A full-time Certified Medical Assistant and apart- time Occupational Health Nurse have been hired with management by the OHSU Occupational Health Department (OH). The collaboration with OHSU OH has led to increased coverage for ONPRC and alignment with the OHSU OH policies. ONPRC and OHSU OH are working to review and update all OH policies applicable to ONPRC to strengthen OH coverage for ONPRC.

EHRS has reached out to [Proprietary Info] providers of medical care for exposures and injuries) in the form of a workshop to review the NHP B virus (Cercopithecine herpesvirus 1) and other experimental infectious agents' exposure response plan.

Increasing collaborations between the ONPRC and researchers at other OHSU campuses has necessitated the expansion of the West Campus NHP tissue distribution program and B virus exposure response plan to include all OHSU campuses and the development of training for OH staff and researchers for exposure response.

Specific Aim 4: The Research Safety Manager, the ONPRC OHN and an OHSU Nurse Practitioner attended the OHP working group meeting at CNPRC in Davis, CA that included discussions of injury rates, PPE choices, and caging design for ergonomic use by workers. The OHP working group is moving to standardize practices and PPE as possible at the NPRCs. The OHP working group has requested the re-establishment of the b virus working group to review initial practices developed by this group and the current state of b virus programs and practices. Additionally, the ONPRC Research Safety Manager is working with the OHP to establish standardized metrics for the NPRCs for ease of communication and understanding of exposures and injuries.

ONPRC has an established incident review process and follow-up on incidents that may include additional training and review of work practices that allows for on-going improvements to exposure and injury response.

The Chemical Safety officer (CSO) has implemented signage for chemical use in animals similar to the biosafety signage previously implemented by the Biosafety Officer (BSO). Also, acute exposure monitoring and baseline exposure monitoring for the use of isoflurane, formaldehyde, and other hazardous volatile chemicals has been established with EHRS safety specialists. Training is in development for other chemical usage at ONPRC for campus employees.

Development of methods to assure compliance with Occupational Health requirements were initiated with the use of the PRIMe database and will eventually tie-in to the electronic IACUC and Occupational Health databases. In-person pre-project meetings for new and repeating projects have been implemented to assure that all participants are aware of project details, health requirements (vaccinations, etc.), and exposure and emergency response.

Specific Aim 5: ONPRC Research Safety staff have participated in local and area disaster response drills coordinated with local law, fire, and emergency responders. The Emergency Response Team continues to review and update their processes for emergency response. On-going FEMA training in National emergency response protocols continues as both on-line and in-person training.

RESEARCH SAFETY: TRAINING & PROFESSIONAL DEVELOPMENT OPPORTUNITIES

The EHRS staff continues to refine and offer training initial and on-going to the ONPRC personnel for biosafety, BSL3, ABSL3, OSHA compliance (such as bloodborne pathogen training and facility safety), chemical safety with new SDS requirements, laboratory safety and biological materials shipping by both in-person and electronic methods.

The EHRS staff continues to receive training to increase their skills as including hazardous materials handling, spill response (chemical, biological, and radiation), conflict resolution, and communication methods.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Protocols	The EHRS works closely with the Occupational Health Working Group to exchange experiences and solutions for safety issues (PPE, Work Processes, engineering controls, and risk assessments) found at the NPRCs. EHRS participates in the ONPRC tissue distribution program by securing biosafety assurances with the exchange of NHP tissues and cells within and without OHSU. Guidance for non-ONPRC collaborators within OHSU for exposure response plans are being developed for exposures to shared NHP tissues and cells.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5554

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			58,168.00	20,746.00	78,914.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **78,914.00**

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 staff	9.6			31,873.00	11,669.00	43,542.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**43,542.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**122,456.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	4,500.00
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. Telecommunications, Radiation licences	18,575.00
Total Other Direct Costs	**23,075.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**147,531.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	147,531.00	41,309.00
		Total Indirect Costs	**41,309.00**

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)	**188,840.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Comparative Medicine

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Division of Comparative Medicine (DCM) provides superior NHP animal models and research support services to the ONPRC by maintaining healthy, specific pathogen free (SPF) nonhuman primate (NHP) breeding and research populations. To ensure physically and psychologically healthy animals free from disease and genetically characterized, DCM also maintains a well-trained and experienced professional, technical and husbandry staff in a collaborative and cooperative posture with the Scientific Divisions.

To successfully accomplish this mission, the DCM will:

Specific Aim 1: Provide a reliable number of healthy, genetically defined and pathogen-free source of NHPs.

Specific Aim 2: Develop improved strategies for the socialization of NHPs.

Specific Aim 3: Train the next generation of veterinarians dedicated to the advances in the understanding and improvement of NHP models.

The DCM will continue to optimize NHP breeding consistent with physical infrastructure and the anticipated need and diversification of the ONPRC scientific programs. The Division will improve management of colony genetics, and continually strive for top quality animal resources by enhanced pathogen monitoring, screening tests and diagnostic technologies, to ensure Specific Pathogen Free (SPF) animals availability. DCM will also implement management strategies to increase breeding efficiencies and provide optimum holding facilities using a systems management approach to identify bottlenecks, leverage points, and potential animal resource management changes to improve breeding program performance.

The Guide has recently been updated and housing standards have been further enhanced for these sentient species. In addition, European Union guidelines will likely expand socialization requirements, which may well influence further such requirements in the U.S. Thus, DCM will explore new opportunities for social compatibility assessment and enrichment, ensure compliance and develop strategies to improve the quality of life for the animals at the Center. Strategies will include innovative and comprehensive approaches to improving the methods of managing medical and behavioral cases, and explore novel use of caging and the design of innovative housing systems to enhance animal welfare and socialization.

Finally, a relatively small number of veterinarians possess the clinical expertise to support NHP research models. Recognizing this fact, the ONPRC has entered into a LAM resident training consortium with OSU veterinary medical school and the OHSU medical center to provide opportunities to veterinarians that wish to pursue the important experience of using the NHP model. This non-NIH funded training program will give residents an integrated and comparative approach to the value and limitations of the wide array of NHP research models, and serve as a continuing education forum for DCM veterinarians and other ONPRC interested professional staff.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We have disseminated the results of our findings through publications in peer-reviewed journals, poster presentations, and presentations at national and international conferences.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In order to advance service support, increase capacity and capabilities, DCM goals for the next grant year are both broad and ambitious:

•Complete P51 Supplement grant funded project to further renovate the Specific Animal Location to provide additional NHP housing space.

•Complete P51 Supplement grant funded project to build examination/procedural space in a sheltered housing unit.

•Continue the planning and design process for the DCM Commons project and Specific Animal Location to increase flex space and staging capacity.

•Continue to refine and validate forecasting model; NHP Resources will continue to utilize this tool to the extent possible for projecting breeding and holding strategies.

•Continue to develop project specific teams consisting of researchers, veterinarians, behaviorists, research technicians and husbandry technicians to facilitate research activities and better integrate DCM and research staff.

•In November, 2016, we received a 3-year, 2.8M grant from the Private Source supporting further development of a Campylobacter vaccination. We will vaccinate and follow infants and dams in the sheltered housing areas, then track changes to microbiome, enteric pathogen distribution, herd immunity, infant growth velocity, and infant cognitive function over time. This study continues our previous work with Excluded by Requester to study the underlying mechanisms and clinical outcomes associated with naturally occurring diarrheal disease among outdoor-housed rhesus macaques. The data collected in 2016 suggest that infant rhesus macaques may provide an excellent model of Environmental Enteric Disease (EED), and will enable us to evaluate potential preventative and therapeutic interventions for our NHP population and human infants.
We received $500,000 in support of our U24 (now U42) eSPF breeding colony. The funds will be used to build a clinical procedure room in one end of our SPF4 Sheltered Housing area. In support of this, and to open 4 sheltered housing spaces for the eSPF breeding colony, we will be consolidating the SPF4 breeding into 28 shelters.

•Work towards bar coding all caging to improve change-out efficiency, monitor cage maintenance, and enhance repair history.

•Conduct veterinary-focused NHP research using data collected via our robust electronic health records and/or pilot grant funds. Continue to pursue projects coordinated with scientific staff where possible and include collaborative input from other NPRC members when appropriate.

•Continue to expand and validate the competency-based training program for DCM and research staff.

•Continue to utilize information technology to increase efficiency for data entry and review.

•Continue to reduce the number of singly housed animals and improve methodologies to avoid breaking established pairs.

•Continue to utilize positive reinforcement techniques to train animals to cooperate with veterinary, husbandry and research procedures in an effort to reduce stress associated with these procedures.

•Continue to implement new enrichment strategies for NHPs, particularly singly housed animals, in an effort to decrease stress and reduce the occurrence of abnormal behaviors.

•Continue to provide timely and valuable pathology support both to our colony resource and the ONPRC research mission.

•Continue to explore strategies for the integration of research and clinical pathology with histopathology to maximize efficiencies and optimize service.

•Continue to provide comprehensive anesthesia, analgesia, and surgical services in support of the research activities on campus. Independent research will continue to be a focus with the development and expansion of research projects DCM veterinarians have initiated.

•Continue to provide, and where possible expand, training opportunities for veterinary students and post-doctoral veterinarians regarding the care and use of nonhuman primates in biomedical research.

•Continue to encourage and provide support for DCM veterinarians pursuing American College of Laboratory Animal Medicine (ACLAM) board certification.

DIVISION OF COMPARATIVE MEDICINE: ACCOMPLISHMENTS

DCM Organizational Changes and Unit Accomplishments. The Division currently consists of eight operational units under the direction of the Division Chief: Resources-Facilities-Operations (Recently divided into two distinct units as described below), Pathology Services (PSU), Surgical Services (SSU), Behavioral Services (BSU), Clinical Medicine (CMU), and the Small Laboratory Animal (SLAU). In addition, during most of the reporting period the Training Manager, Training Lead and Environmental Sanitation Assessment Specialist reported directly to the Division Chief Excluded by Requester In recognition of its importance Training was recently made a distinct unit under the direction of Excluded by Requester (see below). Excluded by Requester was appointed to the newly created position of Assistant Chief, DCM. The Environmental Sanitation Assessment Specialist now reports directly to the Assistant Chief, DCM. Administrative support has been further enhanced by the addition of a Financial Operations Analyst who works closely with the Chief and Assistant Chief, as well as the Administrative Assistant and Administrative Coordinator. Other unit changes and accomplishments reflect a continuing effort to strengthen unit cohesion, facilitate optimization of resources, and provide improved services to the Center as reflected below:

- *Resources-Facilities-Operations Unit (RFO).* To enhance responsiveness and streamline reporting, the RFO unit with the DCM underwent significant restructuring during August, 2016. Specifically, the colony health, breeding, and animal utilization piece were separated from the animal husbandry and operations component.
    - *Resources & Logistics (R&L)* is now a distinct unit headed by Excluded by Requester and managed by Excluded by Requester This unit is responsible for the health and maintenance of the breeding colonies, as well as oversight of short and long term NHP utilization and planning. This includes clinical care of the breeding colonies, breeding colony maintenance and population management, animal selection and allocation for assignment and breeding, sales and acquisitions, and logistics of animal housing. This unit also engages in research for colony health, and in this reporting period supported a study on the development and characterization of a NHP model of Environmental Enteric Disease. Excluded by Requester recently received a 3-year .8M grant from the Private Source supporting development of a Campylobacter vaccination that will begin later in this reporting period. During this reporting period, the R&L assisted in the acquisition of 180 NHPs, including squirrel monkeys, which are a new research resource for the ONPRC. To support the high number of ONPRC animal purchases, R&L recently created a new assistant veterinarian position, whose primary duties will include direct liaison with vendors and agents for the sale and purchase of animals, management and veterinary care of domestic and international quarantine, and veterinary care in support of our breeding colony.
    - *Operations* is now a distinct unit headed by Excluded by Requester and managed by Excluded by Requester Excluded by Requester This change took place in August, 2016.Operations is responsible for all aspects of husbandry for nonhuman primates housed at ONPRC as well as supporting the research endeavor. This unit also monitors animal facilities and equipment repair, maintenance and operations. During this reporting period, Operations received $750K in funding for both the purchase of new NHP housing and associated equipment, and modernization improvements to existing caging and racks. Many significant improvements were made to the ONPRC facilities, including purchasing of new cages, modifications to the existing inventory of cages, racks, and equipment, modifications to corrals and social group housing, resurfacing of the floors and walls of social housing units, remodeling of an indoor behavioral suite, remodeling of a surgery suite, and remodeling of four rooms in our colony annex for long term caged housing.
- *Pathology Services Unit (PSU).* Managed by Excluded by Requester continues to provide pathology support for the animal resource and research mission through necropsies, tissue distribution and clinical pathology laboratory services. The Tissue Distribution Program is administered by PSU to maximize the availability and use of NHP tissues and minimize the number of NHPs required for research. During the current reporting period, Excluded by Requester completed her one-year fellowship

and has begun a residency in veterinary anatomic pathology at the University of Connecticut. One of the two current trainees Excluded by Requester has been accepted to the residency in anatomic pathology at North Carolina State University to begin in July 2017, at the end of her one-year fellowship. Excluded by Requester is completing the third year of anatomic pathology residency training and is studying in preparation for the American College of Veterinary Pathology certifying examination in August 2017.

- *Surgical Services Unit (SSU).* Directed by Excluded by Requester the SSU is projected to complete approximately 7000 surgical cases by the end of this reporting period, a decrease from the previous year. This decrease resulted from the completion of several Pathobiology projects. Offsetting this decrease in the number of cases, additional effort was necessary in model development for new CPAP and NICU procedures as well as neuromuscular blocking agent use during MR imaging. Additional new projects are funded and underway and we anticipate an increase in surgical case load next fiscal year. Approximately 80 procedures were performed over this reporting period in support of colony health maintenance and not as part of any experimental protocol. The surgical training program remains very active and has provided training to 95 individuals. The SSU veterinary staff continues to conduct considerable independent research. Excluded by Requester continues proof-of-concept testing of a prototype medical device that was developed via the Biomedical Innovation Pilot Grant from the Oregon Clinical and Translational Research Institute. A provisional patent has been filed and an OHSU start-up company is currently forming around the device. Excluded by Requester continues collaborations with a research group evaluating the neuroapoptotic effects of commonly-used anesthetics on fetal and neonatal brain development. Excluded by Requester s also a co-investigator on a study developing a small mammal model for contraceptive testing prior to testing in an established baboon model. These studies contribute information intended to significantly refine current practices for the betterment of animal welfare and science.

- *Behavioral Services Unit (BSU).* Managed by Excluded by Requester (NHP Behaviorist), the BSU attempted to pair house approximately 1600 caged monkeys in 2016 (approximately 1000 from May 1-Dec 31, 2016), with a success rate of over 80%. Positive reinforcement techniques were successfully used to train over 300 monkeys to voluntarily cooperate with typical noninvasive procedures such as vaginal swabbing. The BSU continues to modify and improve the “Human Interaction Program” for caged animals. This program has been successful in reducing fear towards caretakers and anxiety behaviors in some animals. The unit continues to modify and improve upon the “Foster Program”, in which abandoned or orphaned infants are reared by a non-lactating female trained to allow the infant to drink from a bottle. BSU also increased enrichment for single housed animals, and has increased behavioral assessments for all caged animals. The ONPRC “Alopecia Working Group”, comprised of members from BSU, PSU, RFO, and scientific staff, made huge advances in their goal of identifying factors underlying alopecia, including behavioral factors. Results from the alopecia study and the Foster Program were presented by BSU staff at the 2016 joint meeting of the American Society of Primatologists and International Primatological Society.

- *Clinical Medicine Unit (CMU).* Directed by Excluded by Requester the CMU has five full-time veterinarians and two Laboratory Animal Medicine residents dedicated to the clinical care and preventive medicine of primarily research-assigned NHPs. A software based method of reviewing animal body weight changes and streamlining data entry by technicians for this common health care initiative was perfected and rolled out to all technicians resulting in improved monitoring efficiency and quality of the review. Increasingly, research groups have incorporated pre-grant submission and pre-project discussions involving stakeholders from all DCM groups including CMU. This allows for consideration of specific animal care needs pertinent to the project helping to enhance both research

and animal welfare. During this reporting period, ONPRC welcomed a group of squirrel monkeys as part of a new project. Along with DCM Operations and research staff, CMU played a significant role in developing processes for caring for this group of animals. CMU has continued to refine the formal training process for veterinary technicians, including development of associated didactic and hands-on teaching methods.

- *Small Laboratory Animal Unit (SLAU).* This rodent and rabbit vivarium is an independent university service center not supported by the P51, and thus provides a mechanism for non-NHP animal research performed by ONPRC investigators. Under agreement from OHSU, Excluded by Requester manages this resource. During this reporting period, the SLAU continued its support of translational projects from rodent to nonhuman primate models.

In June of 2016 the ONPRC underwent a two-day long AAALAC, International site visit. There were no mandatory findings and no suggestions for improvement were made. Our Institution was subsequently awarded full accreditation and exemplary status.

Specific Aim 1: Provide a reliable number of healthy, genetically defined and pathogen-free sources of NHPs.

We continue our efforts to enhance the heterogeneity of the breeding colony. In late 2015, we purchased 14 genetically valuable SPF4 Indian origin male rhesus macaques. Following conventional quarantine, these males underwent an additional year of viral serology screening to confirm their SPF4 status. We have begun to integrate them into our breeding groups.

Table 1 displays NHP population by grant year and species, Table 2 presents NHP *(M. mulatta)* production of animals not assigned to a research project, group formation, and disband rates by grant year (all sp.), and Table 3 depicts the survival rate and fecundity of outdoor socially housed animals by year. Table 4 & 5 depict colony growth over time.

Table 1

	Year 51	Year 52	Year 53	Year 54	Year 55	Year 56	Year 57*
Total NHPs	4806	4886	5871	6024	6033	5751	5352
M. mulatta	4348	4437	5259	5335	5436	5175	4853
M. fascicularis	50	87	198	251	172	150	89
M. fuscata	395	352	401	422	416	379	363
Papio Anubis	13	10	9	12	9	10	11
Papio hamadryas	0	0	4	4	0	37	30
Saimiri boliviensis	0	0	0	0	0	0	6
Importation	102	71	160	207	123	72	166
Animal Sales	189	23	75	157	249	17	72
Project Assignments	949	1650	1177	1035	1357	1290	1002

Table 2

	Year 51	Year 52	Year 53	Year 54	Year 55	Year 56	Year 57*
Population (snapshot)	2563	2525	2915	3006	3117	2877	3235
Production #	659	712	679	693	668	672	330
New Groups Formed	12	18	11	31	38	26	26
Disbanded Groups	7	35	10	27	34	35	22

*Year 57 numbers are calculated through 12/31/2016, lacking January through April data. These months fall within peak birthing season, and commonly account for 60% of births for the year.

Table 3

	2010	2011	2012	2013	2014	2015	2016
Survival rate up to 1 year old	0.82	0.8	0.8	0.84	0.89	0.89	0.88
Survive rate all other animals	0.97	0.96	0.93	0.96	0.97	0.95	0.97
Fecundity females 5 and up	0.70	0.68	0.75	0.73	0.68	0.68	NA**

**2016 fecundity not reported as not all animals born in 2016 have been recorded as of yet.

Since 2012 there has been over a 90% increase in assignment of naïve rhesus macaques. To meet these growing needs, in 2016 we increased our purchases of NHPs from outside primate facilities. In 2016 we purchased 180 NHPs, 100 more than 2015. These purchases have allowed us to meet the ONPRC's increasing research needs while both maintaining our breeding colony and prioritizing the usage of colony bred animals specifically for NIH funded projects. We made significant strides to lower our non-SPF group of caged rhesus, with the NSPF colony dropping by 16 this year. The remaining non-SPF animals are prioritized to be assigned on project and will be slowly removed from the campus.

Now in its third year of routine use, the Intuitive Biosciences' Colony Surveillance Assay system (multiplex microarray) has enabled simultaneous SPF antibody screening for Simian retrovirus (SRV), *Macacine herpesvirus 1* (Herpes B), Simian Immunodeficiency Virus (SIV), Simian T Lymphotropic Virus (STLV-1) and Measles (Paramyxovirus) of animals across campus. A transition for all testing from current assays to the Intuitive Biosciences' Colony Surveillance Assay is currently being implemented. This change provides greater diagnostic efficiency as well as lowering the need for outsourced confirmatory testing. The SRV 2 & 5 western blot confirmatory testing has been fully employed also reducing the number of samples shipped to outside labs for confirmatory testing. A focus has been placed on screening our non-SPF population to provide up-to-date Herpes B status, important for both colony management and occupational health. Previously validated SRV 1, 2 & 5 SRV qPCR has become a routine screening assay with > 1,600 animals tested in 2016. In addition to our SRV qPCR, we have begun developing and validating a STLV qPCR assay. Four animals within the general population (non-breeding group) tested positive for STLV-1. There have been ongoing efforts to develop a LCV ELISA and a LCV RT-PCR has been considered and gone through its initial validation steps. Working closely with the on-campus information services department has enabled the development of improved search functions to locate animal needing viral surveillance and to display pertinent, accurate and easily accessible animal information. This has greatly increased the ability to communicate clearly between department teams related to animal care. Finally, we have adopted a new testing strategy for all quarantine animals by qPCR and Intuitive Biosciences' Colony Surveillance Assay.

We continue to expand our use of the relatively new Primate Records and Information Management (PRIMe) electronic database for colony management and epidemiology efforts. An automated alert system provides daily updates on disease outbreaks in rooms and groups, behavior disruptions in groups, cage compliance information, pairing status and required viral and tuberculin testing. Morbidity, mortality and reproductive reports can be generated by date and location, allowing us to track and quickly respond to animal health issues. PRIMe information is also used to make objective decisions regarding group formation and animal success within the breeding colony. The expanded electronic data base has greatly improved our ability to retrieve and evaluate retrospective data. For example, we recently developed standard weight curves through the first year of life for healthy male and female infant rhesus in corral and shelter housing. These standards allow early identification and intervention of at-risk infants.

In April 2014, the USDA asked the ONPRC to evaluate alopecia in our NHP colony. DCM immediately established an NHP Alopecia Task Force composed of members from across the scientific, medical and veterinary community, including representation from husbandry, behavior, clinical medicine, pathology, endocrinology, outside consultants and other research investigators. The group is evaluating various factors that may contribute to alopecia, including endocrine, nutritional, behavioral, pathological, seasonal, genetic and housing components. We anticipated no less than a two-year commitment to address this area of interest. We have implemented a center-wide alopecia scoring system to ensure consistency in data collection (i.e., all clinical and behavioral staff score alopecia the same). All animals receive an alopecia score as part of their

physical exams. To date, we have collected alopecia scores from all animal breeding groups in corrals and shelters, as well as all indoor housed animals. We also conducted a focused study on eight sheltered housing units tracking alopecia as well as behavior in these social groups. We found that alopecia in our outdoor housed animals is seasonal, more prevalent in females than males and increases with age. Sunlight exposure was also correlated with alopecia; animals living in units with less sunlight had more alopecia than those living in units with a great deal of sunlight exposure. Interestingly, we also found that social hair pulling, in which animals pulled hair from members of their group, was a significant cause of alopecia in animals living in our sheltered housing units. These findings were presented at the 2016 meeting of the American Society of Primatologists/International Primatological Society and are currently being written up for publication. The Alopecia Task Force now meets on an ad hoc basis, due to budgetary constraints, but will continue to examine alopecia in our colony as time and funding permit.

Finally, we continue to improve our animal housing facilities, aligning ONPRC infrastructure, space, and resources with the maintenance and husbandry requirements of each species we support.

- Received over $750,000 in funding for new cage purchases, cage modifications, cage repairs, manipulanda and associated caging items (tunnels, transfer boxes, lifting stations, forage stations). Our ability to pair caged animals continues to improve. Caging exemptions for singly housed animals due to a lack of ideal caging were eliminated during the last reporting period.

- Numerous modifications and improvements were made to our corrals. These include a new feeding pad in corral 7 to improve sanitation and prevent the pooling of water, a new feed area in corral 1 to prevent water leakage in feed storage areas and a new feed room in corral 2 that improves sanitation, increases perching opportunities, allows for easier animal access, and isolates the feed area from the nearby catch area.

- We improved sanitation in the smaller social housing enclosures by re-sealing and resurfacing the floors in 6 sheltered housing units, and the floors and walls in one colony run.

- We built a new observation tower outside of Corral 7. This corral previously only had one observation tower, limiting our view of the animals. This new tower has significantly increased our field of view, improving behavioral observations and identification of sick or injured animals.

- In order to both better suit the needs of our investigators and improve housing conditions, modifications were made within the buildings that house caged macaques, including a NIH G20 funded remodeling of our existing behavioral suites. The newly remodeled suites allow for greater ease and consistency in cognitive testing, including easily accessible touch screens, sound proof rooms, and a camera system to record and monitor live behavioral testing.

- Additional modifications to our macaque buildings include the construction of a new private surgical suite, replacement of a control panel regulating air flow in our animal biosafety level 3 housing suite and replacement of an exhaust fan in a conventional animal housing room.

- The Colony Annex phase 3 remodel is in the construction stage; this will convert six small laboratory animal housing rooms into four NHP housing rooms able to hold up to 60 macaques. Construction is scheduled to be completed in February, 2016.

- We purchased a new tunnel washer and developed plans for renovations to the associated building. This is currently in the construction phase with completion anticipated in January, 2016.

- We were awarded a P51 Supplement grant that will allow us to build a procedure/examination space in one of our outdoor sheltered housing units. This unit will group house animals assigned to AIDS projects. The space will allow for clinical and research procedures to be performed while the animals remain in their social groups.

- The Animal Services Specific Animal Location expansion was completed, providing us with seven additional animal housing rooms to be used for containment/infectious disease projects, a large diet preparation kitchen and washer/dryer. This area came on line in March, 2016.

- Construction will start in January 2017 on another facility, the Primate Multimodal Imaging Center (PIMC). This building will support the diverse imaging needs of the Cardiometabolic Health Division, and will include areas for ultrasound, PET/SPECT and MRI. The building will connect to the existing Specific Animal Location space to facilitate animal movement from research housing areas.

- We are currently in the programming phase for th Specific Animal Location and DCM/Commons project which will allow for the construction of an animal housing building with the capacity to hold between 300 and 400 nonhuman primates. The DCM Commons project will improve and update administrative space for CMU, BSU and Operations staff. Both projects are scheduled to move into the design phase early in 2017.

Specific Aim 2: Develop improved strategies for the socialization of NHPs.

The ONPRC continues to increase the number of animals socially housed on site. As of January 31, 2016, approximately 84% of our population was socially housed, either in groups or pairs. During the past year, the BSU attempted to pair house approximately 1400 caged monkeys. Over 84% of these attempts were successful (i.e., the animals did not fight or show overt signs of aggression or fear). We also continued to take systematic observations after socialization attempts in an effort to determine whether behaviors between partners following a pairing attempt may predict later success or failure. Technicians conduct focal observations on members of the pair immediately following the attempt, and again one day and one week after the pairing attempt. Since May 2015, technicians have taken over 900 such observations on 312 pairs. While we are currently analyzing these data, we are confident that they will help us to make more compatible pairs

The BSU increased staff dedicated to social housing issues in 2015. In addition to the "Social Housing Coordinator", the BSU also added two additional FTE to assist with socialization. There has been a significant increase in pairing attempts since the addition of these FTE; the BSU attempted to pair house an average of 151 animals/month from Sept-Dec 2015 (after the additional staff), compared to an average of 97 monkeys/month from May- August 2015 (prior to additional staff). On January 31, 2016, 57% of our indoor animals were socially housed (compared to 53% in January 2015). We expect these numbers to increase in the coming year.

Specific Animal Location was a co-Investigator on an ONPRC pilot grant to examine the effects of pairing on menstrual cyclicity in rhesus macaques. There was no difference in menstrual cycle length between the baseline cycle and the 2 cycles following the introductions, or in mean luteal phase progesterone. While based on a small sample size, these results suggest that pair housing introductions might not affect menstrual cyclicity in the majority of rhesus macaques (results were presented at the American Society of Primatologists' meeting in 2016). This information should help to reduce some of the concern about pair housing animals assigned to studies, thus improving socialization.

DCM has also made progress in monitoring group housed animals. Members of the BSU and RFO (now R&L and Operations) work closely together to manage our outdoor groups. The BSU increased the level of monitoring in an effort to ascertain dominance relationships, and were able to do so for 19 sheltered housing groups. Knowing these relationships helps us to make better clinical and colony management decisions. Further, DCM has formed similar oversight teams, consisting of individuals from BSU, R&L, Operations, clinic and scientific staff, to address management issues of groups on research protocols. The increased communication has improved our ability to successfully manage these groups.

Specific Aim 3: Train the next generation of veterinarians dedicated to the advances in the understanding and improvement of NHP models.

Excluded by Requester is head of the recently established Education and Training Unit. This unit was created in November, 2016. As head of the unit, Excluded by Requester serves as the Program Manager for the ONPRC site of the Oregon State Laboratory Animal Medicine Residency Consortium. Under his leadership, CMU Clinical Veterinarian Excluded by Requester completed her residency at the ONPRC in June, 2015 and became an ACLAM Diplomate in July, 2016. Excluded by Requester was hired as an RFO Clinical Veterinarian and also became an ACLAM Diplomate in July, 2016. Excluded by Requester benefited from the strong support program that the ONPRC provides DCM veterinarians with the goal of obtaining ACLAM Diplomate status. Excluded by Requester will complete her 3-year residency in June, 2017 and is expected to become ACLAM board-eligible in 2018. Excluded by Requester became an ONPRC veterinary resident in July, 2016 with an anticipated completion date of June, 2019.

DCM continues to maximize the nonhuman primate resource by providing NHP focused training opportunities for undergraduate, graduate and postdoctoral trainees. As part of the Oregon State Laboratory Animal Medicine Residency Consortium and the ONPRC Veterinary Externship Program, DCM hosted 2 visiting laboratory animal residents and 6 veterinary student externs during the past year. In 2016, DCM provided 30 weeks of training for the externship and residency programs. Given that the average contact time for each trainee is 35 hours per week, DCM provided a total of 1044 hours of nonhuman primate focused training. This training is in addition to the training provided to the full-time ONPRC veterinary residents.

DIVISION OF COMPARATIVE MEDICINE: TRAINING AND PROFESSIONAL DEVELOPMENT

Collectively, DCM provided and participated in a myriad of training and professional development opportunities:

- Excluded by Requester attended the Spring and Fall NPRC Directors Meetings.
- PSU continues to support a one-year pathology fellowship. A second position was added during this reporting period. Excluded by Requester completed her one-year fellowship and was replaced by Excluded by Requester Excluded by Requester
- A monthly training hour is provided for CMU veterinary technicians and support staff consisting of both didactic lectures and wet labs for relevant duties.
- CMU provides an online CE service for technicians specifically designed to address common questions regarding clinical care.
- Excluded by Requester serves as Program Manager for the ONPRC site of the Oregon State Laboratory Animal Medicine Residency Consortium. Excluded by Requester is the current ONPRC veterinary resident for this 3-year ACLAM approved program. Excluded by Requester started her residency with us in July, 2016.
- Residents and veterinary clinicians give lectures at the Oregon State University College of Veterinary Medicine, and to a nationwide audience of laboratory animal veterinarians participating in Virtual Grand Rounds, part of the NPRC Training Consortium.
- Excluded by Requester leads the veterinary student externship program, which provides an in-depth and unique experience working with NHPs in the research environment. Visiting veterinary students (see Table 4) gain a well-rounded perspective on the role of veterinary medicine in NHP-based research by rotating through the Clinical Medicine Unit, Colony Hospital, Surgical Services Unit, Behavioral Services Unit, Small Laboratory Animal Unit and the Pathology Services Unit.

Table 4. Veterinary Externships at ONPRC

Title	School	Start Time	End Time
Excluded by Requester	Oregon State University	1/11/16	1/22/16
	Oregon State University	1/25/16	2/5/16
	University of Georgia	2/29/16	3/11/16
	Washington State University	7/5/16	7/27/16
	Oklahoma State University	8/15/16	9/2/16
	Oregon State University	9/6/16	9/16/16
	Oregon State University	9/19/16	10/14/16

- DCM as a whole conducts training and education for veterinary, husbandry, and research staff preparing for AALAS certification tests, and the veterinarians participate in these educational events by giving didactic lectures on various medical, regulatory and husbandry topics.
- DCM veterinarians attended and presented (as speakers and posters) at continuing education conferences on relevant medical and regulatory subjects (e.g. AALAS, ACLAM Forum, APV, PRIM&R, IACUC training); meetings also allow networking opportunities, cross facility collaboration and information sharing with other NPRC staff and research institutions.
  - Excluded by Requester gave a presentation at the National AALAS meeting in Charlotte, NC in October of 2016.

- Excluded by Requester attended the Association of Primate Veterinarians meeting in Charlotte, NC, October, 2016. Drs. Martin, Sidener and Haertel gave presentations.
- Excluded by Requester attended the Breeding Colony Management Consortium Meeting and combined Breeding Colony Management Consortium/Behavioral Management Consortium Meeting in November, 2016.
- Excluded by Requester attended the Behavioral Management Consortium Meeting and combined Breeding Colony Management Consortium/Behavioral Management Consortium Meeting in November.
- Excluded by Requester completed necessary coursework for her USDA Accreditation.
- Excluded by Requester served as a faculty facilitator for the Oregon Health & Sciences Interprofessional Initiative, as a faculty facilitator for the Washington State University College of Veterinary Medicine's diagnostic challenge, and helped supervise 9 veterinary externs and 3 veterinary residents.
- Two BSU members attended the 2016 joint meeting of the American Society of Primatologist and International Primatological Society.

• Two additional staff spent several days at the Southwest National Primate Research Center and the University of Texas, MD Anderson primate facility, to learn about how they manage their baboons and squirrel monkeys, respectively.

- Excluded by Requester attended the 2016 Annual Meeting of the ACVP and Primate Pathology Workshop held in New Orleans, LA.
- Several DCM technicians attended the National AALAS meeting in Charlotte, NC. Veterinary Technician Excluded by Requester gave a presentation.
- Excluded by Requester attended the 2016 joint meeting of the American Society of Primatologist and International Primatological Society and the Laboratory Animal Medicine & Pathology Seminar, CL Davis Foundation in Madison, WI.
- The SSU technicians attended the following meetings and seminars:
  American College of Veterinary Surgeons, Surgery Summit, Seattle, WA; Dove Lewis Emergency Animal Hospital Annual Conference, Portland, OR; Northwest Veterinary Specialists Winterfest 2016, Portland, OR; Oregon Veterinary Technician and Assistant Association Continuing Education Conference, Albany, OR; Oregon Veterinary Conference, Corvallis, OR
- Excluded by Requester and Several DCM veterinarians attended the Crossing the I's Conference in November, 2016 presented by NWABR Excluded by Requester presented.
- Excluded by Requester attended the combined Public Responsibility in Medicine and Research/Northwest Association for Biomedical Research IACUC Conference in Seattle, WA. Excluded by Requester gave a presentation.
- Excluded by Requester attended the 2016 Charles River Short Course in Providence, RI.

• BSU has a monthly journal club, and staff attend webinars and seminars offered at the ONPRC.

• Excluded by Requester serves as an external advisory committee member for the Caribbean Primate Research Center in Puerto Rico.

- PSU participates in the training of veterinary student clinical medicine externs as part of their comprehensive exposure to NHP medicine. They support the LAM residency program through provision of didactic lectures, rotations through pathology services, and monthly pathology-centered didactic lectures. PSU conducts weekly NHP histopathology rounds and weekly review of the Joint Pathology Center (JPC) Wednesday Slide Conference material open to all veterinarians and trainees.

- All veterinary staff participates in the monthly ONPRC Technician Continuing Education Program coordinated by Excluded by Requester lecturing on various veterinary topics and presenting key case reports to the technical staff.

- All DCM unit veterinarians actively participate in NPRC Consortium efforts, either as Chair, members or project leaders.

- DCM veterinarians, managers and technicians were active in ONPRC outreach efforts, and participated in various programs including Camp Monkey, Saturday Academy, Science Ambassadors, and the PCC Behavior Management of Zoo Animals course. Other activities include serving as information sources for on-site tours (e.g. when ONPRC hosted the NPRC Directors' meeting, and the National Association of Medical Examiners), presenting to school groups of all ages including Lewis and Clark Law School, Portland Community College, and local primary schools, and participating in local middle school science fairs.

- DCM veterinary staff hosted and gave presentations and tours to the visiting veterinarians and staff from Joint Base Lewis-McChord in March, 2016.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

Regulatory Compliance. We anticipate continued USDA scrutiny and look forward to working with the other NPRCs and the USDA Western Regional Director to improve inspection strategies and outcomes.

Training and Personnel Development. Although a primary focus of the Division of Comparative Medicine, funding and workload at times limits the scope and breadth of training opportunities available to veterinary and technical staff.

Animal Rights. Due to the nature of nonhuman primate research, the ONPRC enjoys a high degree of exposure to animal extremist groups and continues to be targeted. The recent increased efforts by activists to ban NHP research worldwide is a significant concern. The OHSU Strategic Communications-ONPRC partnership is crucial to assure adequate security and accuracy of public information. We will continue to assist in outreach efforts to ensure Division participation in this important program.

Infrastructure. Increased demand for space while maintaining nearly maximum capacity harbors potential failure and compromise of existing structures and equipment. ONPRC facilities and infrastructure operating at nearly full capacity are leading to delays in facility maintenance and housing repairs. Improved OHSU funding would mitigate the near-term impact, however long-term optimization of the NHP population will be crucial. Strategic planning around infrastructure will be compromised if federal funding and grant awards allowing infrastructure spending do not improve. Parent institution and outside funding sources will be needed for future progress on this front. Inability to expand particular types of outdoor housing due to local zoning constraints continues to be a roadblock.

Staffing. Personnel shortfalls primarily in the Operations Unit, plus the challenges around increasing salaries to match the skill sets required, have placed heavy burdens on existing staff and respective programs causing increased turnover, especially in entry-level operations positions. The continued growth of scientific programs with the resultant need for sequester and containment housing has maximized holding capacity and increased labor requirements without a commensurate increase in program income to support the need. Additional funding, renovation and new construction of animal holding facilities and administration space are all necessary to avoid staff burnout and reversal of the progress made over the last several years.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5555

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			28,320.00	8,779.00	37,099.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **37,099.00**

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						
9	Unit staff	15.38			76,337.00	23,664.00	100,001.00
9	**Total Number Other Personnel**					**Total Other Personnel**	**100,001.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**137,100.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,475.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,475.00**

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

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	3,910.00
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. Memberships, telecommunications, registration/courses fees, retention program, equipment rental & lease, miscellaneous other expense	4,232.00
Total Other Direct Costs	**8,142.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**147,717.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	147,717.00	41,361.00
		Total Indirect Costs	**41,361.00**

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)	**189,078.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: Justification.pdf

(Only attach one file.)

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Resources, Facilities, and Operations

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Non-human primates are critical animal models for basic and translational biomedical research. Supporting scientists who use NHP's in their research require an integrated program of resource management, breeding, animal husbandry, and facilities oversight. To enhance the scientific utility, health, and well-being of ONPRC's animal resources, Resources, Facilities, and Operations (RFO) coordinates programs of resource allocation and tracking, genetic and disease surveillance, animal husbandry and veterinary care. Working closely with other Department of Comparative Medicine (DCM) units and across the ONPRC campus, RFO manages breeding colonies, animals and animal facilities, oversees animal care, animal assignment and utilization, and coordinates genetic and viral screening to ensure the health and well-being of our research resources.

Our long-term goal is a population of pedigreed, disease-free animals of defined quality which matches current and future research needs. To achieve this, RFO must provide innovative resource management, excellent husbandry and clinical care, relevant genetic and viral screening, and utilize a centralized electronic health record system to document and track all aspects of animal care and management.

The specific aims for accomplishing this are:

Specific Aim 1: To support scientists who use NHP's in their research by providing state-of-the-art, comprehensive management of our animal breeding and acquisition programs and centralized coordination of animal breeding, allocation, assignment, and release.

Specific Aim 2: To operate animal housing and facilities, aligning ONPRC infrastructure, space and resources for maintenance and husbandry of species for which there is a major national demand.

Specific Aim 3: To provide exemplary care to our breeding population of NHP's through an integrated program of animal husbandry, genetic and viral screening, and veterinary clinical and preventative care.

The expected outcome is a physically and psychologically healthy population of NHP's sufficient to support current and future research needs for pedigreed, genotypically and phenotypically defined, disease-free animals.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-RFO_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-RFO_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We have disseminated the results of our findings through poster presentations, presentations at national and international conferences, and currently have 3 publications in preparation on hair pulling and alopecia, general patterns of alopecia at the ONPRC, and the effects of diarrhea on infant growth. We have also authored a chapter on behavioral management in the book Excluded by Requester Excluded by Requester which is currently in press. Finally Excluded by Requester co-presented Managing Group Dynamics, and Developing and Using Common Measures of Relevance to behaviorists and managers to the Breeding Colony Management Consortium (BCMC). A working group has been formed, with the goal of refining these metrics to enhance information sharing across multiple centers.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

DCM will continue to work toward the goals of replacing wash down grates in all cage wash areas, and completing improvement modifications to our inventory of hanging cages (>200) in 2017. The modifications to hanging cages will both increase pairing opportunities as well as improve safety for animals and staff. We will also continue our annual efforts to resurface and repair floors in additional sheltered housing units. In addition, we are working to implement a real-time barcode tracking system for all caging and racks to improve change-out efficiency, provide documentation for specific cage maintenance and repairs, and keep better track of our capital assets.

We are currently in the planning stage of updating the electrical infrastructure in one of our containment housing NHP rooms. We are anticipating an increase in the number of projects in which infants are infected with HIV and placed in containment. Updating the electrical infrastructure will improve the feasibility of housing multiple HIV infected infants in incubators in our containment housing.

To address space limitations, in the short term we plan on completing our remodeling of four rooms in our colony annex and purchasing larger pairing racks, which will open space for approximately 60 caged NHPs. Looking towards the future, we are currently in the design stage of a new animal holding building. In 2016, based on the recommendation of the ONPRC NHP Utilization Task Force, the ONPRC Leadership made the decision to explore the design and construction of a new animal holding building. This proposed building will be able to house between 300 and 400 NHPs in a variety of primary enclosures, from standard social caging to small pens capable of holding groups of animals. This facility will house unassigned animals awaiting or having completed approved projects, resulting in an increase in available space for research assigned animals in other Center facilities. In addition, the Specific Animal Location will provide needed space to hold animals from outdoor groups that were disbanded due to behavioral instability. This new facility will also allow for more efficient acclimation of animals to indoor housing prior to study assignment. The goal is for this project to be completed and the facility Specific Animal Location o receive animals by the end of the 2018 calendar year. The programming phase is currently approaching completion and will y move into design.

Construction will start in January 2017 on another facility, the Specific Animal Location This building will support the diverse imaging needs of the Cardiovascular Division, and will include areas for ultrasound and MRI. The building will connect to the existing o facilitate animal movement from research housing areas.

The increased size of our breeding colony, and the large increase in animal purchases to support current and future research needs has significantly increased the overall veterinary responsibilities that fall under the scope of the R&L unit. We are currently interviewing candidates for a new Assistant Veterinarian position within the R&L unit. The primary duties will include direct liaison with vendors and agents for the sale and purchase of animals, management and veterinary care of domestic and international quarantine, and veterinary care in support of our breeding colony.

In November of 2016, we received a 3-year, 2.8M grant from the Private Source supporting further development of a Campylobacter vaccination. We will vaccinate and follow infants and dams in the sheltered housing areas, then track changes to microbiome, enteric pathogen distribution, herd immunity, infant growth velocity, and infant cognitive function over time. This study continues our previous work with Excluded by Requester to study the underlying mechanisms and clinical outcomes associated with naturally occurring diarrheal disease among outdoor-housed rhesus macaques. The data collected in 2016 suggest that infant rhesus macaques may provide an excellent model of Environmental Enteric Disease (EED), and will enable us to evaluate potential preventative and therapeutic interventions for our NHP population and human infants.

We received $500,000 in support of our U24 eSPF breeding colony. The funds will be used to build a clinical procedure room in one end of our SPF4 Sheltered Housing area. In support of this, and to open 4 sheltered housing spaces for the eSPF breeding colony, we will be consolidating the SPF4 breeding into 28 shelters.

Excluded by Requester continue to refine epidemiologic metrics in support of breeding colony health. With the assistance of Excluded by Requester Excluded by they are expanding the real-time capabilities of the current reports, and adding reporting capacities that will automatically compare current time points with previous year's data.

RESOURCES, FACILITIES, AND OPERATIONS: ACCOMPLISHMENTS

Division Restructure

To enhance responsiveness and streamline reporting, the RFO unit with the DCM division underwent significant restructuring during August. Specifically, the colony health, breeding, and animal utilization piece were separated from the animal husbandry component.

Resources & Logistics (R&L) is now a distinct unit headed by Excluded by Requester and managed by Excluded by Requester Excluded by Requester This unit is responsible for the health and maintenance of the breeding colonies, and oversight of short and long term NHP utilization and planning. This includes medical and clinical care of the breeding colonies, breeding colony maintenance and population management, animal selection and allocation for assignment and breeding, sales and acquisitions, and logistics of animal housing.

Operations is now a distinct unit headed by Excluded by Requester and managed by Excluded by Requester and Excluded by Requester This unit is responsible for all aspects of husbandry for non-human primates housed at ONPRC as well as supporting the research endeavor. This unit also monitors animal facilities and equipment repair, maintenance and operations.

Serology is currently reporting through the existing Pathology Service Unit, headed by Excluded by Requester Our goal is to have all colony healthy metrics managed through R&L, once the new unit is fully staffed.

For the sake of this progress report we will report on all components of the previous RFO (including R&L, Operations, and Serology), as that was the structure of this unit for the majority of the reporting period. Below is an organization chart of the new general structure of the Division of Comparative Medicine, as well as charts for Resources & Logistics, and Operations

Figure 1: Restructured Organization of the Division of Comparative Medicine

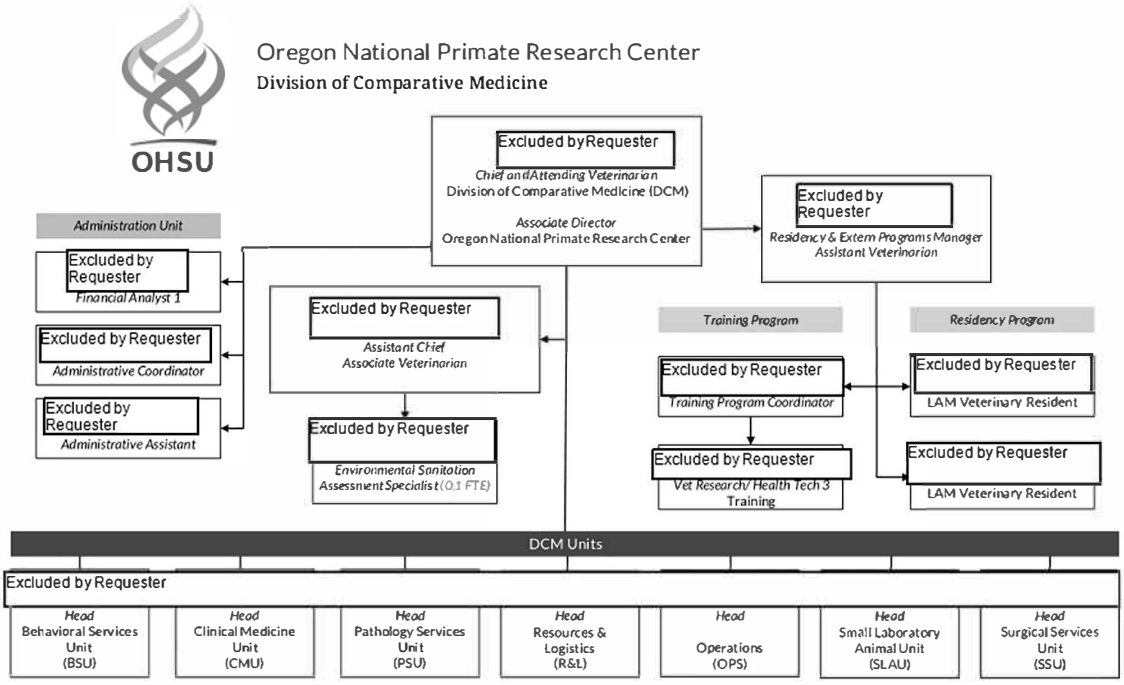


Figure 2: Organization Chart for the Resources & Logistics Unit

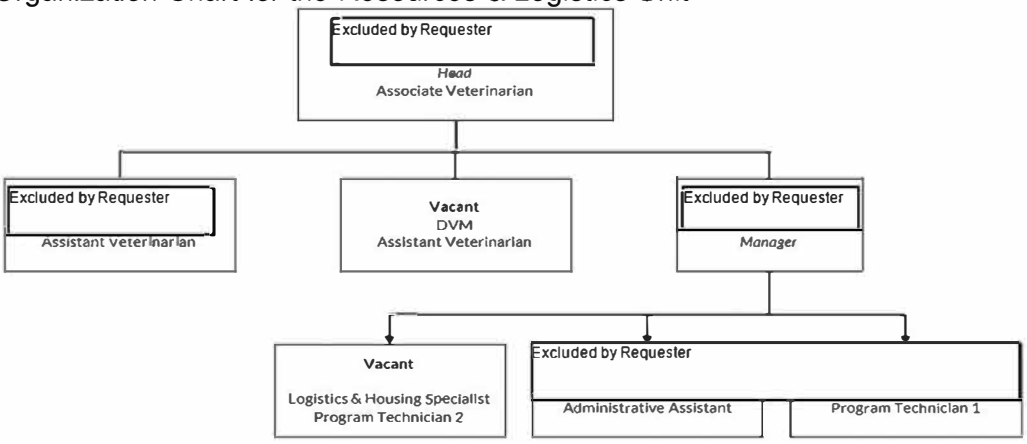
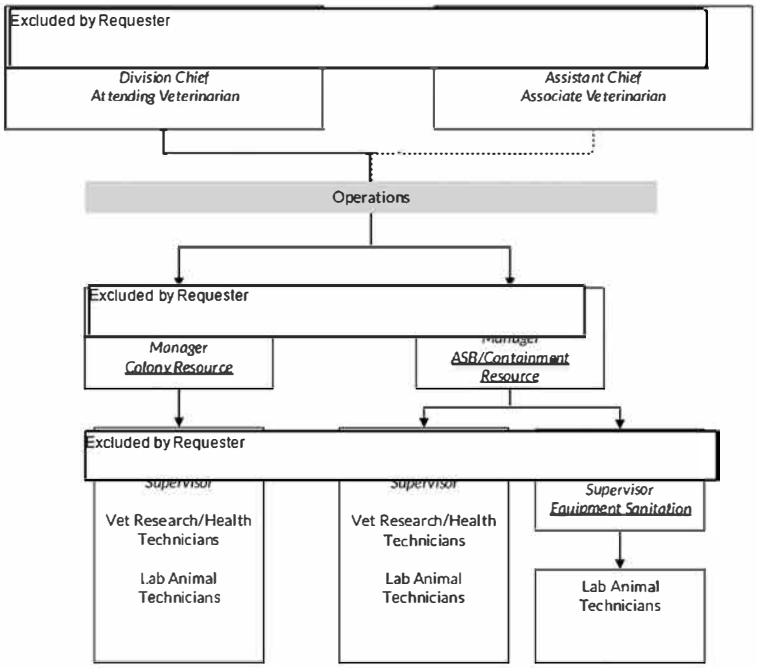


Figure 3: Organization Chart for the Operations Unit



Specific Aim 1:
This aim includes resource planning, breeding, acquisition, and allocation. The unit restructure, separating resource management (R&L) from daily husbandry (Operations), has both formalized and streamlined communication regarding resources within DCM and across ONPRC. Standing meetings are used to address day-to-day planning, communication, and colony management needs. Projection of short and long-term goals for research, refinement of infrastructure, and more nuanced planning such as breeding population size, are managed using stand-alone meetings and task forces.

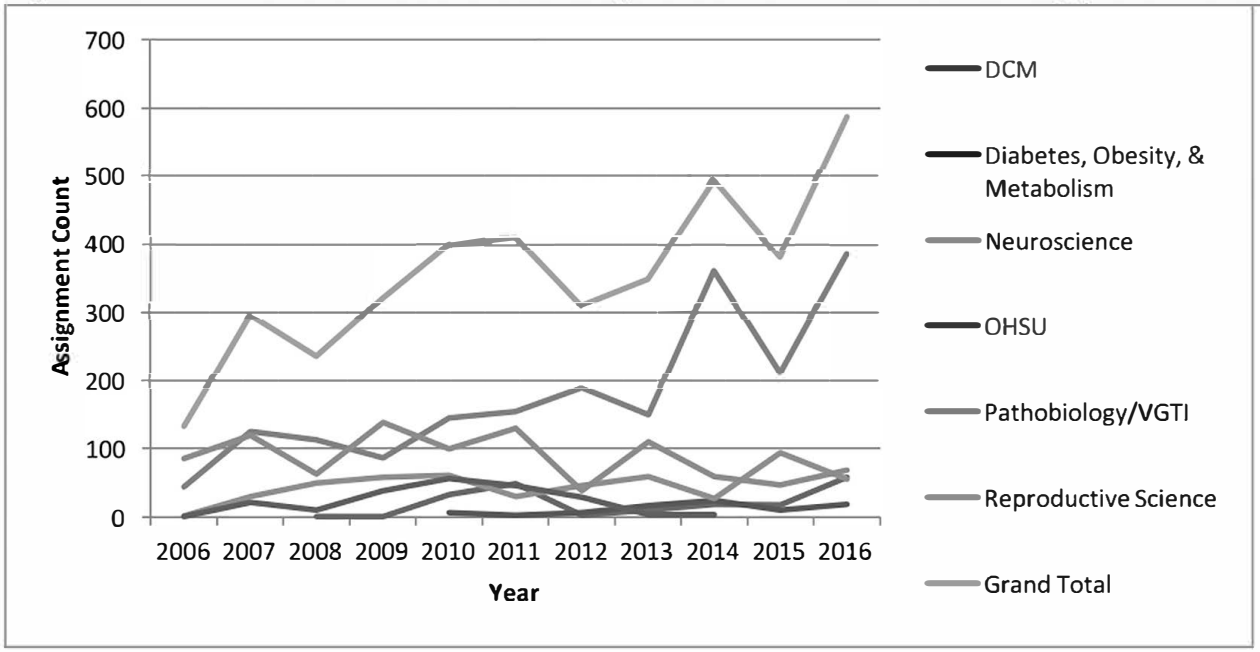
We have further refined our communication with researchers, meeting with individual investigators regularly throughout the grant writing process to identify projected animal, space, and caging needs. These projections are tracked using several electronic communications management tools, including Bridge, projection tools such as Mathematica, and our electronic health record system, PRIMe. Notification of funded grants are received electronically, and trigger a planning meeting with the researcher to ensure space and resources are aligned with project start dates.

A team-based approach is used to manage resources, in particular the NHP breeding colonies. There are weekly Colony Epidemiology Meetings that discuss NHP group dynamics, NHP group stability, potential infectious disease outbreaks, individual clinical cases and other items related to NHP breeding management.

The group consists of: veterinarians, husbandry staff, behaviorists, and colony managers. Additionally, there are monthly Colony Management meetings with veterinarians, geneticists, husbandry managers, cage sanitation, resource managers, behaviorists, and information technology. This group discusses facility repairs and maintenance, animal sales, animal quarantines, new studies, animal harvests, new group formations, etc. There is a monthly Colony Planning Group, which discusses the long-term goals, strategies, and specific timelines of the NHP breeding colonies at the ONPRC. This group makes recommendations to the ONPRC Administration on breeding colony capacity and logistics associated with managing a large colony of macaques. Finally, every month the Animal Utilization Committee reviews all requests for animals produced by the SPF4 Breeding Colony. Priority for use of the animals and space is given to projects funded by NIH extramural grants, followed by NIH intramural funding, nonprofit funding, and then for-profit funding.

Over the last few years there has been a significant increase in animal assignments, particularly for naïve animals (i.e., animals that have not been involved in research that is invasive or alters their physical condition or long term behavior). Figure 4 shows the increase in assignment of naïve animals at the ONPRC division since 2006. Since 2012 there has been over a 90% increase in assignment of naïve rhesus macaques, largely by the pathobiology division. To meet these growing needs, in 2016 we increased our purchases of NHPs from outside primate facilities. In 2016 we purchased 180 NHPs, 100 more than 2015. These purchases have allowed us to meet the ONPRC's increasing research needs while both maintaining our breeding colony, and prioritizing the usage of colony bred animals specifically for NIH funded projects. In order to assure we are maintaining an appropriate sized breeding colony for these increased research needs, we have established an "NHP Utilization Task Force" tasked with the specific goal of maximizing utilization of our unique NHP resource by aligning ONPRC research strategy needs with efficient and effective NHP production and maintenance. This includes developing a short term and long term plan for nonhuman primate utilization that integrates infrastructure carrying capacity, ONPRC strategic planning and NHP breeding and research requirements.

Figure 4: Count of naïve animals that were assigned and not released as naïve by year and division



Resource Management: Table 1 displays NHP population by grant year and species, Table 2 presents NHP (*M. mulatta*) production of animals not assigned to a research project, group formation, and disband rates by grant year (all sp.), and Table 3 depicts the survival rate and fecundity of outdoor socially housed animals by year. Table 4 & 5 depict colony growth over time.

Time Mated Breeding: This program produced 39 feti to seven internal projects and one external project. There are an additional 13 pregnant females whose feti will be used prior to the completion of the grant year. The TMB program has expanded its scope to include three internal projects which aim to confirm fertility of, and provide pregnancies to, investigator assigned animals behaviorally unsuitable for breeding groups. The use of the TMB program continues to be at an all-time high.

Table 1

	Year 51	Year 52	Year 53	Year 54	Year 55	Year 56	Year 57*
Total NHPs	4806	4886	5871	6024	6033	5751	5352
M. mulatta	4348	4437	5259	5335	5436	5175	4853
M. fascicularis	50	87	198	251	172	150	89
M. fuscata	395	352	401	422	416	379	363
Papio anubis	13	10	9	12	9	10	11
Papio hamadryas	0	0	4	4	0	37	30
Saimiri boliviensis	0	0	0	0	0	0	6
Importation	102	71	160	207	123	72	166
Animal Sales	189	23	75	157	249	17	72
Project Assignments	949	1650	1177	1035	1357	1290	1002

Table 2

	Year 51	Year 52	Year 53	Year 54	Year 55	Year 56	Year 57*
Population (snapshot)	2563	2525	2915	3006	3117	2877	3235
Production #	659	712	679	693	668	672	330
New Groups Formed	12	18	11	31	38	26	26
Disbanded Groups	7	35	10	27	34	35	22

*Year 57 numbers are calculated through 12/31/2016, lacking January through April data. These months fall within peak birthing season, and commonly account for 60% of births for the year.

Table 3

	2010	2011	2012	2013	2014	2015	2016
Survival rate up to 1 year old	0.82	0.8	0.8	0.84	0.89	0.89	0.88
Survive rate all other animals	0.97	0.96	0.93	0.96	0.97	0.95	0.97
Fecundity females 5 and up	0.70	0.68	0.75	0.73	0.68	0.68	NA**

**2016 fecundity not reported as not all animals born in 2016 have been recorded as of yet.

Specific Aim 2:

We continue to improve our animal housing facilities, aligning ONPRC infrastructure, space, and resources with the maintenance and husbandry requirements of each species we support.

Facility Improvements:

During the past year, several projects were initiated or completed to improve the cage wash facilities at the ONPRC. A major renovation of the existing tunnel wash building is currently underway to improve the separation of clean and dirty areas, provide a larger clean storage area for equipment, and reinforce the building structure for better temperature and vermin control. Additional improvements to this building will be completed in Phase 2 of this project in the near future. The central chemical storage room was remodeled to enable proper temperature regulation and adequate space for storage of our sanitation chemical inventory. An ongoing project to replace wash down grates in all cage wash areas has focused on those located in Specific Animal Location Specific Animal Location The new grates are made of stainless steel, replacing the short-lasting fiberglass grates, and include design and material improvements to reduce noise created by rolling equipment across open-grated areas. The fabrication of these grates is currently in process, with an anticipated completion date of early 2017.

We received over $750K in funding from OHSU for both the purchase of new NHP housing and associated equipment, and modernization improvements to existing caging and racks. New rolling vertical tunnels were

purchased to both increase paring options and physical therapy opportunities. Additional large pairing racks were purchased to allow for a greater variety of pair-housing options. Newly-designed jump boxes were purchased to provide a more user-friendly and safe method for moving NHPs. Custom wash racks were fabricated to improve sanitation for enrichment manipulanda. Two new three-over-three racks were custom built for the recently-acquired squirrel monkeys to provide appropriate social group housing, perching and climbing opportunities, and olfactory enrichment. Additional Proprietary Info ATP readers were purchased to provide more frequent sanitation monitoring in various animal areas, and additional proportioning dispensers were installed to ensure safe and effective proper dilution of sanitation chemicals.

Numerous modifications were made to our existing inventory of cages, racks, and associated minor equipment, in order to provide safety and animal welfare related improvements. We continued the work to modernize our hanging cages by completing modifications to both Specific Animal Location cages allowing for pair-housing of NHPs in Specific Animal Location buildings. Baboon caging was also modified to provide more usable floor space for the animals. Casters and wheels were replaced on 100 existing racks, allowing for easier movement, quieter transport, and improved braking to help secure caging while in use. Hardware components used to secure slides between cages were updated to provide a secondary safety option to prevent slide removal by animals. Metal feedboxes were modified to facilitate a secure attachment to caging.

A new working group was formed to discuss and implement an environmental sanitation program for equipment and animal housing that is not able to be processed through our existing cage washes. This includes lab equipment, heat-sensitive equipment, indoor/outdoor group housing, hand-sanitized equipment, large play structures, and enrichment devices. During the past year, we have determined and established ATP and RODAC thresholds to be used for testing the efficiency of equipment and environmental sanitation practices. Additionally, we have established consistent testing methods for our animal water supplies, cage washes, dishwashers, and autoclaves, including SOPs and guidelines for proper sanitation and monitoring. Records have been created and updated to show sanitation of additional surfaces.

Numerous modifications were made to our corrals and social group housing in order to improve sanitation and colony management. This includes a new feeding pad in corral 7 to improve sanitation and prevent the pooling of water, a new feed area in corral 1 to prevent water leakage in feed storage areas, and a new feed room in corral 2 that improves sanitation, increases perching opportunities, allows for easier animal access, and isolates the feed area from the nearby catch area. We improved sanitation in the social housing enclosures by re-sealing and resurfacing the floors in 6 sheltered housing units, and the floors and walls in one colony run. Finally, we built a new observation tower outside of Corral 7. This corral previously only had one observation tower, limiting our view of the animals. This new tower has significantly increased or field of view, improving behavioral observations and identification of sick or injured animals.

In order to both better suit the needs of our investigators and improve housing conditions, multiple modifications were made within the buildings that house caged macaques. This includes an NIH G20 funded remodeling of an existing behavioral suite. The newly remodeled suite allows for greater ease and consistency in cognitive testing, including easily accessible touch screens, sound proof rooms, and a camera system to record and monitor live behavioral testing. Additional modifications to our macaque buildings include the construction of a new private surgical suite, replacement of a control panel regulating air flow in our biosafety level 3 housing suite, and replacement of an exhaust fan in a conventional animal housing room.

We are currently remodeling four rooms in our colony annex, allowing for space for approximately 60 caged NHPs. We are purchasing cages such that a portion of these rooms will be able to support either macaque or baboon species, increasing the flexibility and utility of this space.

Resource Improvements:

We added a new NHP resource, Squirrel monkeys (*Saimiri scriureus).* This species was last used at ONPRC in 1986, and since that time there have been significant advancements in caging, husbandry, and enrichment strategies. Prior to the arrival of this species, clinical, research and husbandry staff spent time training with the staff at MD Anderson on handling, care, and management. Special caging, to support species-specific movement opportunities for this arboreal species, was designed by the Behavioral Services Unit (BSU), fabricated, and installed. Facilities and veterinary staff worked together to set an appropriate species-specific

room temperature and humidity, and to install new lighting that does not emit ultrasonic frequency sounds. Additionally, operations team modified existing rhesus macaque caging during quarantine to ensure animals were exposed to appropriate micro-climate temperatures. Finally, wax worms, mealworms, and dry fruits and vegetables were added to the regular rotation of edible enrichment to complement squirrel monkey diets.

We continue our efforts to enhance the heterogeneity of the breeding colony. In late 2015, we purchased 14 genetically valuable SPF4 Indian origin male rhesus macaques. Following conventional quarantine, these males underwent an additional year of viral serology screening to confirm their SPF4 status. We have integrated them into our smaller breeding groups, with the ultimate goal of using them for our corral breeding program.

We made significant strides to lower our non-SPF group of caged rhesus. The colony size has dropped by 16 this year, and we only import SPF macaques. The remaining non-SPF animals are prioritized to be assigned on project and will be slowly removed from the campus.

Specific Aim 3:
We continue to provide exemplary animal care, maintaining an integrated program of animal husbandry, genetic and pathogen screening, and veterinary clinical and preventative care.

Table 5: Colony Medicine Caseload from 1/1/2016 to 12/31/2016.

	Corrals (Total Pop=1931)			Shelters, Runs, Pens (Total Pop=2011)			Jmac (Total Pop=236)			All (Total Pop=4190)		
Master Problem	Unique	Total	%	Unique	Total	%	Unique	Total	%	Unique	Total	%
Behavioral	6	6	0.31	1	1	0.05	0	0	0.00	7	7	0.17
Cardiac	2	2	0.10	0	0	0.00	0	0	0.00	2	2	0.05
Dermatopathy	1	1	0.05	4	5	0.20	3	3	1.21	8	9	0.19
GI-Diarrhea	117	139	6.06	147	209	7.31	5	5	2.02	269	353	6.42
GI-Other	62	64	3.21	52	55	2.59	6	7	2.42	120	126	2.86
Musculoskeletal	22	26	1.14	33	34	1.64	3	4	1.21	58	64	1.38
Neurologic	2	2	0.10	6	6	0.30	4	4	1.61	12	12	0.29
None	4	5	0.21	6	6	0.30	0	0	0.00	10	11	0.24
OBGYN	15	17	0.78	36	38	1.79	2	2	0.81	53	57	1.26
Ophthalmic	4	4	0.21	10	11	0.50	1	1	0.40	15	16	0.36
Other	10	10	0.52	16	16	0.80	0	0	0.00	26	26	0.62
Respiratory	28	29	1.45	22	22	1.09	3	3	1.21	53	54	1.26
Routine/Prevent	115	132	5.96	182	222	9.05	4	4	1.61	301	358	7.18
Urogenital	0	0	0.00	2	2	0.10	0	0	0.00	2	2	0.05
Weight Loss	41	43	2.12	46	49	2.29	9	9	3.63	96	101	2.29
Wound	245	299	12.69	521	756	25.91	25	25	10.08	791	1080	18.88
Total Cases	674	779	34.90	1084	1432	53.90	65	67	27.54	1823	2278	43.51

Refinements to Virology Screening Program:
Over the past three years, the Specific Pathogen Free Laboratory (SPF Lab) has been progressively expanding routine use of [Proprietary Info] SPF4 and SPF9 microarrays for surveillance of our different colonies. Final (i.e. post-confirmatory) SPF surveillance results for our colonies are listed in table 6 below, demonstrating the continued absence of pathogens in our designated SPF and ESPF colonies. The overall

prevalence of SPF agents at our center is very low. Cases of confirmed Herpes B have continued to decrease in our non-SPF colonies, and this year so far there have not been any cases of SRV-positive animals among any of our P51-supported animals, even among non-SPF colonies.

The SPF9 array has been fully adopted for the U24/Expanded-SPF animal colony, and SPF4 microarrays have been increasingly supplementing surveillance of our U42 and P51 supported colonies. Broader surveillance efforts and high microarray sensitivity permitted the recent identification and removal of several STLV-positive animals from the P51 SPF rhesus macaque colony. Since 2014, we have eliminated any residual Herpes B and SRV positive animals from this sub-colony, and all those animals are currently negative for those pathogens. We have also begun screening our non-SPF population with SPF4 microarrays to provide up-to-date Herpes B status, important for both colony management and occupational health. Overall, the modern microarray technology provides us with greater diagnostic efficiency due to multi-pathogen screening and reduces our reliance on less efficient single-agent and legacy assays.

We are continuing to develop in-house expertise in confirmatory and direct virus detection assays, in order to decrease the need for outside confirmatory testing. SRV 2 & 5 Western Blot and SRV 1, 2 & 5 qPCR assays have been fully developed and are in routine use. This has allowed us to adopt a new testing strategy for all quarantine animals by combining qPCR with SPF4 arrays. We have also started using the SRV qPCR assay for silent SRV carrier surveillance (>1,600 animals in 2016). Currently ongoing diagnostic R&D initiatives include an STLV qPCR assay (in development) and LCV RT-qPCR and ELISA assays (in planning).

We have worked closely with our on-campus information services department to build better search functions to locate animals needing viral surveillance and to display pertinent, correct and easily accessible animal information in our electronic records database, PRIMe. This has greatly increased clarity pertinent to animal testing between department teams.

Table 6: SPF Surveillance Summary by Animal (as of October 2016)

P51 Non SPF Non Rhesus (*)	2014	2014		2015	2015		2016	2016
Virus	Negative	Positive		Negative	Positive		Negative	Positive
Macacine herpesvirus 1 (Herpes B)	85	131		91	130		78	21
Simian Betaretrovirus (SRV)	359	0		380	1		212	0
Simian Immunodeficiency Virus (SIV)	212	0		212	0		86	0
Simian T-Cell Lymphotrophic Virus (STLV)	212	0		208	4		83	3
P51 Non SPF Rhesus	2014	2014		2015	2015		2016	2016
Virus	Negative	Positive		Negative	Positive		Negative	Positive
Macacine herpesvirus 1 (Herpes B)	11	3		53	28		30	11
Simian Betaretrovirus (SRV)	150	0		174	0		54	0
Simian Immunodeficiency Virus (SIV)	2	0		64	0		1	0
Simian T-Cell Lymphotrophic Virus (STLV)	0	1		49	15		1	0
P51 SPF Cynomolgus	2014	2014		2015	2015		2016	2016
Virus	Negative	Positive		Negative	Positive		Negative	Positive
Macacine herpesvirus 1 (Herpes B)	34	0		96	0		27	0
Simian Betaretrovirus (SRV)	127	0		107	0		35	0
Simian Immunodeficiency Virus (SIV)	12	0		17	0		27	0
Simian T-Cell Lymphotrophic Virus (STLV)	12	0		17	0		27	0
P51 SPF Rhesus	2014	2014		2015	2015		2016	2016
Virus	Negative	Positive		Negative	Positive		Negative	Positive
Macacine herpesvirus 1 (Herpes B)	2768	2		2734	0		2614	0
Simian Betaretrovirus (SRV)	2852	1		3004	0		2965	0

Simian Immunodeficiency Virus (SIV)	1292	0		966	0	841	0
Simian T-Cell Lymphotrophic Virus (STLV)	1288	4		960	6	840	4
U42 Rhesus	2014	2014		2015	2015	2016	2016
Virus	Negative	Positive		Negative	Positive	Negative	Positive
Macacine herpesvirus 1 (Herpes B)	841	0		695	0	455	0
Simian Betaretrovirus (SRV)	870	0		764	0	469	0
Simian Immunodeficiency Virus (SIV)	197	0		449	0	33	0
Simian T-Cell Lymphotrophic Virus (STLV)	194	3		449	0	33	0
U24 Rhesus	2014	2014		2015	2015	2016	2016
Virus	Negative	Positive		Negative	Positive	Negative	Positive
Lymphocryptovirus (LCV)	13	159		25	155	46	139
Macacine herpesvirus 1 (Herpes B)	172	0		180	0	185	0
Rhesus Cytomegalovirus (CMV)	179	0		186	0	185	0
Rhesus Rhadinovirus (RRV)	179	0		185	1	185	0
Simian Betaretrovirus (SRV)	174	0		184	0	185	0
Simian Foamy Virus (SFV)	179	0		186	0	185	0
Simian Immunodeficiency Virus (SIV)	172	0		180	0	185	0
Simian T-Cell Lymphotrophic Virus (STLV)	172	0		180	0	185	0

*Anubis Baboon, Cynomolgus Macaque, Hamadryas Baboon, Japanese Macaque

Colony Health Program:

We continue to expand our use of the relatively new Primate Records and Information Management (PRIMe) electronic database for colony management and epidemiology efforts. An automated alert system provides daily updates on disease outbreaks in rooms and groups, behavior disruptions in groups, cage compliance information, pairing status, and required viral and tuberculin testing. Morbidity, mortality, and reproductive reports can be generated by date and location, allowing us to track and quickly respond to animal health issues. PRIMe information is also used to make objective decisions regarding group formation and animal success within the breeding colony. The expanded electronic data base has greatly improved our ability to retrieve and evaluate retrospective data. For example, we recently developed standard weight curves through the first year of life for healthy male and female infant rhesus in corral and shelter housing. These standards allow early identification and intervention of at-risk infants.

We continue our efforts to reduce diarrhea associated morbidity and mortality in the breeding colony. Excluded by Requester Excluded by Requester with assistance from Excluded by Requester submitted and received funding for a pilot grant to study the underlying mechanisms and clinical outcomes associated with naturally occurring diarrheal disease among outdoor-housed rhesus macaques. Similar to human infants, infant macaques who develop diarrheal disease during the first year of life experience high rates of diarrhea-associated mortality, high morbidity, poor growth rates, and undernutrition. Our goal is to develop and characterize a NHP model of Environmental Enteric Disease (EED) that would enable us to evaluate potential preventative and therapeutic interventions for our NHP population that can also be used to down-select and de-risk potential preventative and therapeutic interventions for infants. For the 2016 pilot, 40 infants and 40 dams were followed longitudinally. Data collection included anthropromorphic measurements, physical exams, serum chemistry values, and milk. Additionally, the enteric environment of both the dams and the infants was evaluated through rectal fecal culture, xTAG screen for 15 gastrointestinal pathogens, and microbiome analysis. Histologic analysis of the intestinal tract was performed on select individuals. Data from healthy infants was compared both with infants acutely ill with diarrhea and infants who experienced multiple episodes of diarrheal disease. The initial information suggests that infant macaques can be a viable model for EED. At the study conclusion, we were invited to submit a 3-year, 2.8 M grant proposal. The grant was recently funded, and will allow us to continue our previous evaluation of the Campylobacter coli vaccine, in addition to other preventatives.

In April 2014, the USDA asked the ONPRC to evaluate alopecia in our NHP colony. DCM immediately established an NHP alopecia task force composed of members from across the scientific, medical and veterinary community, including representation from husbandry, behavior, clinical medicine, pathology, endocrinology, outside consultants and other research investigators such as Excluded by Requester from the Proprietary Info who has extensively studied alopecia in NHPs. The group is evaluating the endocrine, nutritional, behavioral, pathological, aged, seasonal, genetic, and housing components that may contribute to alopecia in the rhesus macaque. We scored alopecia in our outdoor housed animals over several time points and collected hair samples at the same time for cortisol determination. This data was then compared to housing density, housing type, season, and other parameters. Currently we are working on analyzing, presenting, and publishing these data. To date we have found that alopecia increases with age, males have less alopecia than females, shelters have more alopecia than corrals, shelters with more light have less alopecia, vitamin D levels are not a predictor of alopecia, there is a seasonal pattern to alopecia, there may be a heritability component to alopecia, and alopecia increases with gestational age. Notably, recent analysis of behavioral observations indicated that social hair pulling (animals pulling hair from their cagemates) is a significant contributor to alopecia in our social groups. We are currently considering possible causes of hair pulling and how this may be related to correlations with sunlight exposure and seasonal patterns.

In 2016, we transitioned our Japanese macaque troop to Proprietary Info primate diet. Formulated as a low glycemic diet for weight reduction, the change has decreased the incidence of obesity in this group. In addition to the weight loss and decrease in diarrhea previously noted, we have observed improved mobility and increased social activity with many of the older animals. We continue to evaluate health outcomes.

In October of 2015, we initiated a project with Proprietary Info to evaluate new diet formulations. Currently available diets were formulated in the 1950's, and have changed little since initial formulation. In particular, understanding of fatty acids and probiotics has increased. Recognizing an opportunity to improve the nutritional health of our breeding colony, we partnered with Proprietary Info and added probiotics and updated the balance of essential fatty acids in the standard NHP diet. Throughout 2016, we have fed either enhanced probiotics, rebalanced essential fatty acid, or a combination of the two to our breeding corrals. Metrics include diarrhea rates, infant growth rates, body condition scores, weight, and alopecia. Preliminary analysis suggest the combined diet may lower diarrhea rates. We continue to work with Proprietary Info in the data analysis, and ongoing evaluation of NHP diets.

Utilizing over 3 years of infant weight data from outdoor bred rhesus at the ONPRC, we have created and refined a chart of projected growth of healthy infant rhesus over the first year of life based. The chart clearly demonstrates predicted weights within 2 standard deviations of the mean at any age in the first year of life for both males and females. The chart is a particularly helpful tool as we check growth of infant rhesus that present to the hospital for illness. Target weights for certain age-sex rhesus infants can be obtained easily, and decisions on failure to thrive infants are made in part information obtained from the chart when weights fall below 2 standard deviations.

RESOURCES, FACILITIES, AND OPERATIONS: TRAINING

Training: Excluded by Requester provided training to 3 post-doctoral fellows, 4 regional ACLAM residents and a visiting ACLAM resident, 7 veterinary student externs, and 2 veterinary student summer interns. Additionally, Excluded by Requester served as a faculty facilitator for 12 veterinary students and 12 OHSU School of Medicine and School of Nursing students.

Professional Development: During the period, Excluded by Requester attended the 44th Association of Primate Veterinarians conference in October. At this conference Excluded by Requester co-authored an original research poster. "Infant Diarrhea Reduces Growth and Survival Rates of Rhesus Macaques," and Excluded by Requester co-authored a case report poster "Combination of Internal and External Bone Fixation for a Comminuted Fracture in a Rhesus Macaque." Excluded by Requester attended the Breeding Colony Management Consortium Meeting in November, and presented on the Campylobacter vaccine development program. Excluded by Requester attended the Joint Meeting of the International Primatological Society and the American Society of Primatologists, where he co-authored a talk along with Excluded by Requester Excluded by Requester and others titled "The effects of probiotic supplementation on alopecia and behavior in socially housed rhesus macaques (*Macaca mulatta*)". In addition Excluded by Requester co-authored a chapter on behavioral management in the book Excluded by Requester entitled Excluded by Requester

During this reporting period, Excluded by Requester re-credentialed as a Diplomate of the American Board of Veterinary Practioners, certified through 2026. She completed 18 hours of continuing education at the 2016 Association of Primate Veterinarians conference, and attended the Oregon Veterinary Emergency Response Team training on avian influenza in February. She served as a faculty facilitator for the Oregon Health & Sciences Interprofessional Initiative, as a faculty facilitator for the Washington State University College of Veterinary School's diagnostic challenge, and supervised 9 veterinary externs and 3 veterinary residents. She presented didactic and clinical instruction to 4 veterinary residents in the Oregon State Laboratory Animal Medicine Consortium. She also reviewed resident credentialing packages and quarterly progress reports for the American Board of Veterinary Practitioners, and served as a reviewer for the American Journal of Primatology, Journal of Medical Primatology, and Brain Research.

Excluded by Requester professional accomplishments during this period include passing the ACLAM board examination, and certification as a Diplomate of the American College of Laboratory Animal Medicine. He served as a lecturer for the Oregon State Laboratory Animal Medicine Residency Consortium. He provided supervision for 3 veterinary students and 4 veterinary residents. He completed 15 hours of continuing education at the 2016 Workshop in Laboratory Animal Medicine in Raleigh, NC; and 15 hours of continuing education at the 2016 Association of Primate Veterinarians (APV) Workshop in Charlotte, NC. At APV, he presented a case report on Respiratory syncytial virus.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

The RFO Unit continues to have funding shortfalls with targeted goals for caging purchases, maintenance, and upgrades, as well as equipment upgrades and facility improvements. RFO meets with the DCM Chief and the Business Office and Administration leadership on a regularly scheduled basis to discuss hurdles blocking achievement of these goals and to seek solutions as to how to address these issues. The RFO Unit is encouraged that leadership fully understands the needs of both the Unit and Division.

ONPRC facilities and infrastructure are operating at full capacity. This is due in part to a significant increase in animal utilization for research projects. Trending shows a rise in NHPs at the ONPRC and in naïve animal assignments since 2011. This growing need for research animals has led to both a general increase in the number of animals housed at the ONPRC, as well as a decrease in "flex" space. As research assignments increase, "flex" space (e.g., space for animals awaiting projects, recently off project, staging for new social group, recently removed from social group, etc.) has slowly been transformed into space exclusively for research animals. The lack of "flex" space has negatively impacted colony management efficiency, led to delays in facility maintenance, project start dates, and group formations, and increased the need for cage repairs. The Resources & Logistics unit has presented and will continue to emphasize these difficulties at regular meetings of the Animal Utilization Committee (AUC), Executive Leadership Committee, and the IACUC. To develop solutions and long term strategies, we have established an "NHP Utilization Task Force". The initial goal of this task force was to determine the optimal colony size given both current research needs as well as current infrastructure. Once it was clear our current infrastructure was not sufficient to meet our optimal colony size, this task force identified the need to design and construct a new animal holding building capable of housing between 300 and 400 NHPs. The need for this building has been fully supported by ONPRC leadership. This project is currently in the design phase, and we are anticipating the building to be complete and ready for animals in 2018. Beyond the identification of the need for this animal holding building, the NHP Utilization Task Force still regularly meets with the additional goal of identifying ideal demographics for our breeding colony and pool of available research animals, and strategies to maintain this ideal population.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5556

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			13,185.00	5,142.00	18,327.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **18,327.00**

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						
78	Unit staff	127.06			464,585.00	176,451.00	641,036.00
78	**Total Number Other Personnel**					**Total Other Personnel**	**641,036.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**659,363.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	1,540.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**1,540.00**

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

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	377,699.00
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. Shipping, equipment maint contract, Genetic services, laboratory services, hazardous waste disposal, memberships, maintenance & repair, bioengineering services, miscellaneous other expenses	67,690.00
Total Other Direct Costs	**445,389.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**1,106,292.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	1,106,292.00	309,762.00
		Total Indirect Costs	**309,762.00**

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)	**1,416,054.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: Justification.pdf

(Only attach one file.)

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Pathology Services

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

PATHOLOGY SERVICES UNIT
Anatomic and clinical pathology expertise and services are key elements of ONPRC's veterinary care program dedicated to the maintenance of self-sustaining populations of genetically characterized, disease-free NHPs for research. They are also essential for meeting the objectives of our research programs. The primary goals of the Pathology Services Unit (PSU) are to provide disease diagnostic and surveillance services that promote the health and safety of ONPRC's animal resources and provide research support services that strengthen the research infrastructure and contribute directly to the mission of ONPRC through participation in multidisciplinary research programs.

The specific aims for accomplishing this:

Specific Aim 1: To provide disease diagnosis and surveillance for ONPRC's animal resource through diagnostic necropsies, biopsies, clinical pathology and maintenance of databases for epidemiologic queries.

Specific Aim 2: To participate in the research mission of ONPRC by providing pathology support for research projects through necropsies, tissue distribution, clinical laboratory services and participation in study design; and through characterization of spontaneous NHP diseases potentially useful as models for human diseases.

Specific Aim 3: To act as a national resource for NHP pathology through maintenance of archived tissues, slides and blocks, databases of biological data and images.

Specific Aim 4: To serve as a resource for educating veterinarians, laboratory animal professionals and investigators, about primate pathology by participation in publication, teaching and presentation in local, national and international settings.

The expected outcome is a highly productive resource for the support of the research mission and the NHP population through centralized provision of pathology services and expertise.

TISSUE DISTRIBUTION PROGRAM SPECIFIC AIMS
The nonhuman primate (NHP) is, and will always remain, a limited and valuable research resource. Continued efforts to maximize distribution of NHP tissues to biomedical investigators will ensure the best possible use of this resource. Centralized coordination of tissue requests with scheduled necropsies permits support for increased numbers of biomedical research efforts with less impact on the primate resource.

Specific Aim 1: Ensure maximum and efficient utilization of the unique primate resource through continued and expanded promotion of the Tissue Distribution Program (TDP)

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-Patho_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-Patho_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will continue to provide timely and valuable pathology support both to our colony resource and the ONPRC research mission. Much of the ongoing review of archival material for inclusion in the PPID, and as a basis for case series publications, will also serve as the foundation for advanced work in the identification and characterization of disease phenotypes for use as models of human disease.

PATHOLOGY SERVICES: ACCOMPLISHMENTS

PSU continues to provide pathology support for the animal resource and research mission through necropsies, tissue distribution and clinical pathology laboratory services. During the reporting period, the histology laboratory generated 19,090 H&E stained slides, 3823 slides for recuts and special stains, 154 slides for immunohistochemistry, and 138 slides for evaluation of surgical biopsies. Our capabilities for in house immunohistochemistry have been expanded to include antibodies directed against chromogranin, herpes simplex virus, thyroid stimulating hormone, neuron-specific enolase (NSE), S100, Helicobacter pylori and EBNA-2 for Epstein Barr virus.

The Clinical Pathology Laboratory performed 19,186 tests during the reporting period. In-house tests included 9,538 complete blood cell counts, 492 white blood cell differential counts, 3,826 serum biochemistry profiles, 575 high and low density lipoprotein levels, 740 amylase, 1,394 fecal microbiology cultures, 736 general cultures, 209 anaerobic cultures, 268 Yersinia cultures, 265 antibiotic sensitivity profiles, 644 assessments for fecal occult blood, and 146 urinalyses. An additional 353 miscellaneous tests were performed both in-house and through external laboratories including hematocrit, erythrocyte morphology, reticulocyte count, glycosylated hemoglobin, lipid panel, dermatophyte culture, C-reactive protein, cerebrospinal fluid analysis, fecal parasite screens, clotting profiles, serum profiles and others.

The Tissue Distribution Program (TDP) is administered by the Pathology Services Unit to maximize the availability and use of NHP tissues and minimize the number of NHPs required for research. As part of the NHP TDP, 37 ONPRC/OHSU investigators received 6,199 tissue specimens and 15 non-OHSU investigators received 296 specimens prepared according to their specifications. An additional 1210 tissues were distributed for use in tissue banks administered at ONPRC. Of 6,495 total tissue samples distributed, 4,458 tissues were received by investigators from animals assigned to them as part of terminal research protocols.

A major way in which ONPRC serves as a national resource for NHP pathology is through participation in the Primate Pathology Image Database. During the 2016-17 reporting period, the number of registered academic users rose from 291 to 427 and now represents more than 107 institutions. Regular email communications highlighting a selected image or case with questions to guide trainees were continued throughout this year.

PSU served as a resource for educating veterinarians, laboratory animal professionals and investigators, about primate pathology through the education of externs, visiting pathologists and residents, and through publications. Currently, PSU faculty are coauthors on three publications in review and three accepted abstracts. Excluded by Requester serves as a member of the Certifying Examination Board for the American College of Veterinary Pathologists (ACVP) and is chair of the 2017 Phase II Certifying Examination held in Ames, IA. Dr. Excluded by Requester was an invited speaker on the histology of juvenile nonhuman primates at the 2016 ACVP Annual Meeting in New Orleans, LA. Excluded by Requester presented at the 2016 Primate Pathology Workshop held in conjunction with the ACVP Annual Meeting. Excluded by Requester each prepared and presented cases for the August 2016 Pathology Working Group Virtual Slide Conference. Two cases were submitted to the Joint Pathology Center Wednesday Slide Conference in June 2016 as part of our participation in that important teaching resource.

PATHOLOGY SERVICES: TRAINIING AND PROFESSIONAL DEVELOPMENT

The Pathology Services Unit (PSU) supports a one year training fellowship in NHP Pathology. During the current reporting period, Excluded by Requester completed her one year fellowship and has begun a residency in veterinary anatomic pathology at University of Connecticut. Two trainees, Excluded by Requester Excluded by Requester were recruited for 2016-17. Excluded by Requester has been accepted to a residency in veterinary anatomic pathology at the North Carolina State University College of Veterinary Medicine to begin in July 2017 at the end of her one year fellowship. We are currently recruiting for the next year's fellow.

PSU participates in the training of veterinary student clinical medicine externs as part of their comprehensive exposure to NHP medicine. In addition to students with interest in clinical laboratory animal medicine, Excluded by Requester Excluded by Requester a 4th year veterinary student from Washington State University College of Veterinary Medicine, spent four weeks in a pathology-specific externship in July 2016. We support the Laboratory Animal Medicine (LAM) residency program through provision of didactic lectures, rotations through pathology services, and monthly pathology-centered lectures. Excluded by Requester has extensively revised the pathology content of the LAM residency by organizing and providing a majority of the species-specific pathology lectures and conducting wet labs on rodent necropsy techniques. PSU veterinarians also provide lectures to the ONPRC Technician CE lecture series coordinated by Excluded by Requester Additionally, we conduct weekly NHP histopathology rounds and weekly review of the Joint Pathology Center (JPC) Wednesday Slide Conference material open to all veterinarians and trainees.

Excluded by Requester attended the 2016 Annual Meeting of the ACVP and Primate Pathology Workshop held in New Orleans, LA.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5557

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Project Lead	Institutional Base Salary	EFFORT			14,009.00	4,763.00	18,772.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **18,772.00**

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						
17	Unit staff	17.55			83,763.00	28,933.00	112,696.00
17	**Total Number Other Personnel**					**Total Other Personnel**	**112,696.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**131,468.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	540.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**540.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	13,256.00
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. Laboratory services, shipping, miscellaneous other expense	3,709.00
Total Other Direct Costs	**16,965.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**148,973.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	148,973.00	41,712.00
		Total Indirect Costs	**41,712.00**

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)	**190,685.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Surgical Services Unit

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Surgical Services Unit is a specialized, unified team delivering centralized, reliable, and consistent surgical services in a state-of-the-art surgical facility. Complete surgical service and expertise that includes procedural planning and development, anesthesia, analgesia, and post-operative animal care. All are essential for meeting the objectives of the research programs at ONPRC, as well as supporting a comprehensive clinical care program. The primary goal of SSU is to provide superior surgical expertise while ensuring compassionate care for animal patients and the scientific integrity of research objectives. The specific aims in support of this goal are:

Specific Aim 1. To provide surgical support for research projects through comprehensive surgical, anesthetic, analgesic and post-operative care. Research support includes collaboration with investigators to refine surgical procedures through careful planning, proper training, and optimal instrumentation to minimize invasiveness and discomfort to the animal subjects. We will continue to provide and refine anesthesia and analgesia modalities tailoring them for specific surgical procedures, subject size, age, and species while also accommodating for physiologic factors that may compromise anesthesia, such as obesity. We will continue to find ways of providing these services while maximizing efficiency through work flow analysis and computational automation.

Specific Aim 2. To support colony health maintenance by providing diagnostic, therapeutic, and emergency surgical services for spontaneous or experimentally induced diseases or conditions. SSU provides support for colony health maintenance through the provision of aseptic surgical suites equipped with quality anesthesia machines, instrumentation, endoscopic equipment, and experienced surgical veterinarians available for referral procedures or consult. Specific examples of routine colony health support we will continue to provide include intestinal resection and anastomosis for intestinal neoplasia, emergency Caesarian section, orthopedic fracture repair, diagnostic endoscopy and laparoscopy, and critical care.

Specific Aim 3. To serve as a resource for training veterinary students, residents, technicians, and veterinarians as well as investigative staff in all aspects of nonhuman primate surgical techniques, anesthesia, and analgesia practices. A significant part of this training is continued proficiency evaluation of personnel performing surgeries on animals. We are working with other units to develop an interactive, software-based means of training and competency evaluation to compliment the traditional hands-on training and observational modalities currently in use. Intraoperative imaging will continue to be a primary component of the preparatory materials personnel must review prior to hands-on training, as well as a key aspect of continued proficiency assessment after initial certification.

Specific Aim 4. To expand collaborative and independent research with the goal of refining practices to minimize adverse physiological sequelae that may result from experimental interventions for the betterment of animal welfare and science. SSU will explore long-acting analgesic modalities to reduce subject distress associated with frequent post-operative injections. Current collaborations to determine the physiological effects of various anesthesia modalities on neonatal and pregnant rhesus macaques will continue. Finally, we are developing a novel medical device that quickly, accurately, and inexpensively measures the total blood volume of rhesus macaques and other species.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-SSU_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-SSU_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

THE FOLLOWING ORAL PRESENTATIONS WERE GIVEN:

Excluded by Requester Research Design and Protocol Development" Lab Animal Medicine & Pathology Seminar. CL Davis Foundation. Madison, WI.

Excluded by Requester "Anesthetic and Surgical Considerations for the Geriatric or Obese Patient" Lab Animal Medicine & Pathology Seminar. CL Davis Foundation. Madison, WI.

Excluded by Requester "Innovations in Blood Volume Assessment" Lab Animal Medicine & Pathology Seminar. CL Davis Foundation. Madison, WI.

Excluded by Requester Blood Volume Determination Via Catheterized Optical Fiber." Portland State University School of Business Administration, Capstone Project. Portland, OR.

Excluded by Requester "Blood volume determination device." Featured presentation, 2016 MedTech Alliance Showcase. Portland, OR.

Excluded by Requester "Anesthesia & Critical Care Techniques in Neonatal Macaques." Association of Primate Veterinarians 44th Annual Workshop. Charlotte, NC.

Excluded by Requester "Neonatal Nonhuman Primates in Biomedical Research." American Association for Laboratory Animal Science 67th National Meeting. Charlotte, NC.

Excluded by Requester "Anesthesia & Critical Care Techniques in Neonatal Macaques." American Association for Laboratory Animal Science 67th National Meeting. Charlotte, NC.

THE FOLLOWING POSTERS WERE PRESENTED:

Excluded by Requester. "Quantiport: We bring objective blood volume measurement to clinical practice" MedTech Alliance Showcase. Portland, OR.

Excluded by Requester "The Combination of Internal and External Bone Fixation for a Comminuted Fracture in a Rhesus Macaque (Macaca mulatta)" Association of Primate Veterinarians Annual Workshop. Charlotte, NC.

ADDITIONAL ACTIVITIES:

Excluded by Requester Appointed to the Oregon Veterinary Exam Board 2016-2019

Excluded by Requester Animal health technician for National Disaster Medical System under Department Health and Human Services. Deployments: Republican National Convention, Cleveland, Ohio; Hurricane Matthew, South Carolina; Presidential Inauguration, Washington D.C.

CONSORTIUM ACTIVITIES:

Excluded by Requester continues to chair the Clinical and Surgical Techniques Working Group. This group, part of the NPRC Consortium, has met once monthly via webinar since 2012. The goals of this group are to improve procedural competency and repertoire as well as improve workflow efficiencies associated with procedures that are commonly performed among the NPRCs. A website is maintained that serves as a reference library of past presentations. All of the NPRCs are represented at the monthly meetings which consist of approximately 65 veterinarians and veterinary technicians.

LECTURES GIVEN TO THE OREGON LABORATORY ANIMAL MEDICINE RESIDENCY CONSORTIUM:
NHP Taxonomy, Biology, and Use in Research Excluded by
NHP Anesthesia and Analgesia Excluded by
Large Animal Surgical Models in Biomedical Research Excluded by Requester
Biomedical Ethics in NHP Research Excluded by Requester

VETERINARY TECHNICIAN CONTINUING EDUCATION PROGRAM LECTURES GIVEN:
Obesity in NHPs, tips to keep anesthesia boring Excluded by Requester
NHP Models of Ebolavirus Excluded by

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

SSU will continue to provide comprehensive anesthesia, analgesia, and surgical services in support of the research activities on campus. New techniques and refinements will be adopted as they are developed. A neonatal MCA occlusion model is being anticipated, as well as the development of a macaque surgical preeclampsia model. Independent research will continue to be a focus with the development and expansion of research projects the SSU veterinarians have initiated. Longitudinal studies of blood volume changes throughout pregnancy, as well as a cross-sectional study of blood volume as function of age are planned. Additionally, a study assessing neuroapoptosis caused by midazolam and caffeine in fetal macaques is planned as well as further studies with nitrous oxide/isoflurane and xenon/isoflurane in neonatal macaques. Continued development of the guinea pig and baboon contraceptive delivery and testing models will be completed. Additional resources will be put towards evaluation of sustained release analgesia formulations to improve compliance and animal welfare in the NHPs.

SURGICAL SERVICES UNIT: ACCOMPLISHMENTS

Specific Aim 1: The Surgical Services Unit (SSU) is projected to complete approximately 7,000 surgical cases by the end of this reporting period. This represents a decrease from the previous reporting period. This off-year is due to the completion of several Pathobiology projects. Additional effort was necessary in model development for new CPAP and NICU procedures as well as neuromuscular blocking agent use during MR imaging. Additional new projects are funded and underway and we anticipate an increase in surgical case load next fiscal year. We continue to utilize novel computational tools that automate many SSU processes. These technological advancements and the transition to PRIMe have freed our staff to spend less time doing data entry tasks and more time providing excellent animal care. Several new surgical procedures have been developed during this reporting period in support of approved experimental protocols. New procedures include cardiac transducer placement, epididymal aspirations, oviduct catheterization with drug administration, and neonatal PICC line placement.

Specific Aim 2: Approximately 80 procedures were performed over this reporting period in support of colony health maintenance and not as part of any experimental protocol. These procedures included 10 exploratory laparotomies that resulted in intestinal resection and anastomosis as treatment for GI adenocarcinoma, a common neoplasia of older rhesus macaques; 10 wound repairs; and 9 emergency cesarean sections. Miscellaneous other procedures performed included bone fracture repairs, tail amputations, herniorrhaphies, orchidectomies, and diagnostic endoscopies.

Specific Aim 3: Surgical training has been provided to 6 veterinarians; 3 veterinary residents; 10 veterinary student externs; 16 veterinary technicians; and 60 members of investigative staff. Surgical training is typically multimodal and includes a written SOP, guideline, and/or surgical narrative, PowerPoint presentation, observation, hands-on training, and follow-up proficiency assessments. A list of surgical task certification by employee is maintained in PRIMe. SSU staff also collaborates with other units within DCM to standardize and centralize training. A result of this collaboration is a formalized training program for investigative staff in the use of inhalant anesthesia.

Specific Aim 4: During this reporting period, considerable independent research was conducted by the SSU veterinary staff Excluded by Requester completed and published Excluded by Requester Excluded by Requester which compared two methods of measuring blood volume and provides practical equations for accurately estimating blood volume given body weight and body condition. Additionally Excluded by Requester was awarded the Biomedical Innovation Pilot Grant from the Oregon Clinical and Translational Research Institute to develop and test a novel device to measure blood volume using fiber optic technology. The project was successful and a provisional patent was obtained. Additional animal studies are planned to evaluate the precision and accuracy of the device for translation and marketing to human medicine and surgery. Excluded by Requester continues to work closely with a multi-institutional research group evaluating the neuroapoptotic effects of various anesthetics on fetal and neonatal brain development. She was a co-author on two manuscripts accepted for publication this year Excluded by Requester Excluded by Requester Excluded by Requester Additionally, initial studies assessing the effect of dexmedetomidine/isoflurane and nitrous oxide/isoflurane anesthesia protocols on neural development and intraoperative physiologic values in neonatal macaques have been completed. Excluded by Requester has also collaborated with the Oregon Permanent Contraceptive Core (OPERM) to help with NHP model development and participated in their annual Scientific Advisory Board meeting in Washington DC in the fall. Along with Excluded by Requester is the co-principal investigator on a grant funded by OPERM to develop a small mammal model for contraceptive testing prior to transitioning contraceptives into the established baboon model. This grant resulted in development of a transcervical cannulation model for contraceptive administration with fluoroscopic imaging in the guinea pig. Finally, work has begun looking at the feasibility of utilizing sustained release analgesia preparations at the ONPRC through initial evaluations in rodent models using BuprenorphineSR in a splenic injection model.

SURGICAL SERVICES: TRAINING AND PROFESSIONAL DEVELOPMENT

The SSU veterinarians attended the following meetings and seminars:

- Joint meeting of the International Primatology Society and the American Society of Primatologists, Chicago, IL
- Association of Primate Veterinarians Annual Workshop, Charlotte, NC
- American Association for Laboratory Animal Science 67th National Meeting, Charlotte, NC
- Lab Animal Medicine & Pathology Seminar. CL Davis Foundation. Madison, WI.

The SSU technicians attended the following meetings and seminars:

- American College of Veterinary Surgeons, Surgery Summit, Seattle, WA
- Dove Lewis Emergency Animal Hospital Annual Conference, Portland, OR
- Northwest Veterinary Specialists Winterfest 2016, Portland, OR
- Oregon Veterinary Technician and Assistant Association Continuing Education Conference, Albany, OR
- Oregon Veterinary Conference, Corvallis, OR

The following professional certifications were achieved:

- FEMA: “National Response Framework, An Introduction”
- FEMA: “Active Shooter: What can you do?”

The following awards were received:

2016 Biomedical Innovation Program Award (TH)

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5558

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			14,194.00	4,542.00	18,736.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **18,736.00**

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						
8	Unit staff	8.64			48,567.00	15,541.00	64,108.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**64,108.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**82,844.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	300.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**300.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	15,825.00
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. Equipment maint & repair, hazardous waste disposal, laboratory services, shipping	3,732.00
Total Other Direct Costs	**19,557.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**102,701.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	102,701.00	28,756.00
		Total Indirect Costs	**28,756.00**

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)	**131,457.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Behavioral Services Unit

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Behavioral Services Unit (BSU) is a service unit in the Division of Comparative Medicine. The BSU is responsible for overseeing behavioral management of nonhuman primates (NHPs) at the ONPRC. As such, the BSU plays a major role in ensuring that the ONPRC is compliant with both the Animal Welfare Act and the Guide for the Care and Use of Laboratory Animals. The primary objectives of this unit are to provide social opportunities and environmental enrichment promoting species-typical behaviors for the monkeys, to assess and attempt to decrease abnormal behaviors and promote animal well-being by using and developing techniques, devices and procedures that contribute to their psychological health. Pursuant to these objectives, the specific aims of this unit are:

Specific Aim 1. Reduce the number of single housed animals. A major goal of the ONPRC is to further reduce the number of single housed animals. Social housing increases the opportunity for animals to engage in many species typical behaviors, including play, feeding, and grooming, and is considered one of the best ways to promote their psychological well-being. We will continue to explore and further define the factors that positively influence pair or group success.

Specific Aim 2. Improve and expand upon our NHP training program. Training animals to cooperate with procedures such as injections or blood draws reduces the stress associated with these procedures. In addition, by reducing the stress associated with husbandry and handling procedures, inter-individual variation in stress response may also be reduced, enhancing the use of NHPs as research subjects. Training can also allow experimental animals to be housed in social groups as opposed to cages. Therefore, a major objective of our program is to expand upon our Positive Reinforcement Training, including training group housed monkeys to come to the front of their pen for injection or blood draw. We are currently undertaking studies geared at increasing training success, and will continue to investigate ways to improve and expand these efforts.

Specific Aim 3. Improve well-being and decrease abnormal behavior in NHPs. Abnormal behaviors, including self-injurious behavior and stereotypical behavior, can be indicators of compromised well-being in captive NHPs. Therefore, a major goal of the BSU is to reduce the occurrence of abnormal behaviors in our NHPs by improving conditions that promote well-being and decreasing situations known to compromise well-being (such as nursery rearing). To achieve this aim, we plan to: 1) Improve early rearing for orphaned infants by providing opportunities for them to be with foster females (i.e., non-lactating females trained to allow infants to feed from a bottle); 2) Provide a wider variety of enrichment options to NHPs, particularly for singly housed monkeys; and 3) Work with the Clinical Medicine Unit, the Behavioral Management Consortium and others to develop novel treatments for these behavioral problems.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-BSU_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-BSU_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

In 2016 Excluded by Requester co-chaired a symposium on Laboratory Primate Welfare at the ASP/IPS meeting, in which she gave a talk. She was invited to participate as an instructor in the "Primate Behavioral Management Conference", and was invited to give a seminar as well as participate as an instructor in a workshop entitled "Teaching monkeys to cooperate with restraint: Using positive reinforcement training and temperament testing methods" at AALAS. She also helped organize and teach in the "Workshop on Pair Housing Macaques" offered at Yerkes NPRC. In 2016, the BSU mentored 17 interns, including one undergraduate student, and one student from the PCC Behavior Management of Zoo Animal (BMZA). Members of the BSU were active in outreach (over 110 hours), and participated in various programs including the Camp Monkey, Saturday Academy, Science Ambassadors, and PCC BMZA, as well as various ONPRC tours. Excluded by Requester serves on the Dissertation committee for one PhD student (University of Puerto Rico) and was the Ad Hoc committee member for a second PhD student (OHSU).

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In the coming year, we plan to continue to work on our specific aims.
1.We will continue to reduce the number of singly housed animals, and to avoid breaking established pairs. We are investigating whether variables such as temperament can affect pairing success. Further, we have started to organize and plan to submit an R24 grant to further examine the effects of pairing on a wide variety of research outcomes. This grant is to be a collaborative effort with scientists from each Division within the ONPRC.
2.We will continue to utilize positive reinforcement techniques to train animals to more willingly cooperate with procedures. We hope to have more operations technicians involved with this process.

3.We will continue to examine ways to help reduce abnormal behavior. In particular, we plan to evaluate our use of extra enrichment for single housed animals. In addition, we plan to provide additional enrichment to our outdoor housed animals.

BEHAVIORAL SERVICES: ACCOMPLISHMENTS

Specific Aim 1: Our specific objective in this aim was to increase the number of animals socially housed at the ONPRC. Results: 1) Pair housing was a focus of the BSU in the past year. In 2016, the BSU attempted to socialize (full contact pairs or small groups) approximately 1600 caged monkeys (approximately 1000 from May 1-Dec 31, 2016). This number represents an increase over last year, due, at least in part, to the 2 additional FTE we added to BSU in 2015. Over 80% of these attempts were successful. We also continued to take systematic observations after socialization attempts in an effort to determine whether behaviors between partners following a pair attempt may predict later success or failure. Technicians conduct focal observations on members of the pair immediately following the attempt, and again one day and one week after the pair attempt. Since May 2016, technicians have taken over 1000 such observations on 356 pairs. While we continue to analyze these data, we are confident that they will help us to make more compatible pairs. For example, we found that pairs in which animals engage in bidirectional grooming within the first two days are more likely to be successful (i.e., live together for at least 1 month without aggression) than those that do not engage in that behavior. 2) In the past year, the BSU worked closely with other DCM units to identify obstacles to pairing. As a result, no animals have been single housed due to caging issues since May 2016. We continue to record the reasons animals are singly housed on a monthly basis. 3) In 2015, we were awarded an ONPRC pilot grant to examine the effects of pairing on menstrual cyclicity in rhesus macaques (along with Dr. Excluded by Requester Reproductive and Developmental Sciences Division). We continued to collect data for this project in 2016, and found that pair attempts, regardless of the outcome (i.e., successful or unsuccessful), did not alter patterns of menstrual cyclicity for most female rhesus macaques. 4) We have also continued to work with other DCM units to oversee our outdoor groups. We increased our level of monitoring in an effort to ascertain dominance relationships, and were able to do so for 10 sheltered housing groups (bringing the total up to 26). Knowing these relationships help us to make better management decisions. We helped establish approximately 23 social groups since May 2016. Outcomes: In 2016, the BSU added a PhD-level position of "Social Housing Coordinator". This position, filled by Excluded by Requester who was a postdoctoral fellow with the BSU, improved our ability to establish and monitor both pair and group socialization attempts. Dr. Excluded by Requester has analyzed data from pair observations and will present those results at the 2017 American Society of Primatologists meeting. She is working on developing more efficient tools for monitoring group dynamics, in an effort to identify factors that could influence group stability. On January 4, 2017, 62% of our indoor animals were socially housed (compared to 56% in January 2016). We expect these numbers to increase in the coming year. The majority of our single housed animals have IACUC exemptions or clinical reasons necessitating temporary single housing. Results from our pilot grant were presented at the 2016 joint meeting of the American Society of Primatologists (ASP) and the International Primatological Society (IPS).

Specific Aim 2: Our objective was to expand our training program. Results: In 2016, we used positive reinforcement techniques to train over 300 monkeys to voluntarily cooperate with noninvasive procedures including remaining stationary for vaginal swabbing and presenting a body part for venipuncture (this number was 120 in 2015). Many of these monkeys were assigned to research projects. We worked closely with DCM and PI staff to improve the method by which "Pole and Collar" training (moving animals from their home cage to a primate chair for procedures) is performed. We also continued to examine factors that might influence trainability, including temperament and fear towards caretakers. We worked with ITG to add a module to PRIMe to allow training data to be tracked. Outcomes: Results from these studies were presented at an AALAS (American Association for Laboratory Animal Science) workshop entitled ""Teaching monkeys to cooperate with restraint: Using positive reinforcement training and temperament testing methods" and are currently being written and submitted for publication.

Specific Aim 3: Our specific objective was to decrease the incidence of abnormal behavior in our population. The focus of this aim has been to prevent abnormal behaviors by improving conditions that promote well-being and decreasing situations known to compromise well-being. Results: 1) We have continued to modify and improve upon our "Foster program", in which abandoned or orphaned infants are reared by a non-lactating female trained to allow the infant to drink from a bottle. We reared four infants in this fashion in the past year. As a result of this program, we have significantly reduced the need for nursery rearing; no infant was nursery reared for husbandry (as opposed to scientific) reasons in 2016. 2) We improved upon our enrichment strategies in 2016. Because cognitive enrichment is known to be of value to captive primates, we purchased several Kindle Fire tablets and iPads, and evaluated their use. We worked with members of the Obese

Resource to test monkeys' preference for various apps. We also modified and expanded our "Human Interaction program" for caged animals, in which technicians spent time doing activities such as blowing bubbles or giving extra treats to the animals in their areas. This program has reduced fear towards caretakers and reduced anxiety behaviors in some animals. In the coming year, we will continue to evaluate and refine the use of this enrichment. We also started to provide additional enrichment to singly housed animals, something we are still evaluating. 3) The ONPRC 'Alopecia Working Group", comprised of members from BSU, the Pathology Services Unit, Operations, and scientific staff, made huge advances in our goal of identifying factors underlying alopecia. We had previously found that factors such as sunlight, time of year, pregnancy and social status all have a role in alopecia in our colony. This past year, we examined behavioral concomitants associated with alopecia in 8 sheltered housing units, and measured the effect probiotics had on hair loss. We found that social hair pulling, in which animals pull hair from other members of their group, was relatively common in the sheltered housing units. We also found that the probiotics helped to reduce this behavior, at least in the short term. Further, the BSU worked with the veterinary and clinical staff to ensure that we are all scoring alopecia in the same manner. These alopecia assessments have become a part of the annual or semi-annual physical exams on all monkeys at the ONPRC, allowing us to better track alopecia in our colony. Members of BSU also worked with other NPRCs, to help establish a cross-facility method for assessing alopecia (as part of the Behavioral Management Consortium). 4) We have increased behavioral assessments on our indoor-housed population. Previously, we were assessing these animals annually. We will now perform these assessments quarterly on most animals in our indoor colony. During assessments, BSU technicians observe the animals, and record instances of abnormal behavior. These assessments will better enable us to determine the efficacy of our efforts for reducing abnormal behaviors. Outcomes: The number of animals with behavioral problems decreased in 2016 (259 animals in 2016, 340 in 2015), likely as a result of increased socialization and enrichment. We presented results from our foster program at the 2016 joint meeting of ASP and IPS. We also presented results from our collaborative study on the use of the tablet enrichment as well as results from our alopecia study at that meeting. Papers on Excluded by Requester Excluded by Requester are currently being written and will be submitted in early 2017.

BEHAVIORAL SERVICES: TRAINING

Two BSU members took and passed their AALAS Laboratory Animal Technologists (LATg) certifications in 2016. Two BSU members attended the 2016 joint meeting of the American Society of Primatologist and International Primatological Society. Two additional staff spent several days at the Proprietary Info Proprietary Info primate facility, to learn about how they manage their baboons and squirrel monkeys. In addition, the BSU has a monthly journal club, and staff attend webinars and seminars offered at the ONPRC.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

We intend to increase the amount of NHP enrichment, including positive reinforcement. In order to achieve this goal, we will need involvement from staff in other units.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5559

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Project Lead	Institutional Base Salary	EFFORT			15,837.00	6,335.00	22,172.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **22,172.00**

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						
10	Unit staff	19.26			70,499.00	23,065.00	93,564.00
10	**Total Number Other Personnel**					**Total Other Personnel**	**93,564.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**115,736.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	510.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**510.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	3,263.00
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, miscellaneous other expense	430.00
Total Other Direct Costs	**3,693.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**119,939.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	119,939.00	33,583.00
		Total Indirect Costs	**33,583.00**

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)	**153,522.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Clinical Medicine Unit

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Non-human primates are critical animal models for basic and translational biomedical research. Enhancing the scientific utility, health, and well-being of these populations requires an integrated program of clinical care, animal husbandry, genetics, and psychological health. Working closely with other DCM units, the Clinical Medicine Unit (CMU) maintains animal health through preventative and clinical care, ensuring the health and well-being of ONPRC NHP research resources while supporting breeding populations of genetically characterized, disease-free NHPs.

CMU's long term goal is efficient and humane management of ONPRC's NHP colonies using innovative techniques and procedures to identify, treat, and manage disease and abnormalities. To achieve this, the CMU must provide disease surveillance, diagnosis and treatment, work with ONPRC investigators to ensure experiments are well-planned and have clear scientific and humane endpoints, provide veterinary emergency care both during working hours and afterhours, and utilize a state-of-the art electronic health record system for documenting and managing animal care.

The specific aims for accomplishing this are:

Specific Aim 1. To provide preventative and clinical care to ONPRC's NHPs through annual physical examinations, reproductive health monitoring, geriatric wellness programs, and weight management programs; and to provide rapid diagnosis and treatment of disease, illness, and injury.

Specific Aim 2. To provide clinical veterinary support for NHP related research, including technical assistance with protocol development, protocol review, animal model development, veterinary medical research, and resource management to optimize the NHP resource for current and future research use.

Specific Aim 3. To serve as a resource for educating pre- and post-graduate veterinarians, researchers, and technicians about clinical veterinary care and veterinary support of NHP research, including teaching, mentoring, collaborating, and presenting in local, national and international settings.

The expected outcomes are physically and psychologically healthy animals for support of biomedical research, and a population of disease free, genetically characterized NHP's sufficient to support current and future research needs. These outcomes support scientists who use NHPs, while ensuring the highest level of veterinary care for all NHP species at the ONPRC.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-CMU_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

CMU veterinarians provide formal monthly continuing education opportunities on campus for certified veterinary technicians. We also disseminate updated practices or medical information to researchers using a variety of modalities, including presentation at "Work in Progress" lectures, discussions at scientific division meetings, and participation in All Hands and All Campus meetings. All CMU veterinarians participate in the rotation of lectures on various subjects for the OHSU residency consortium.

This year, all CMU veterinarians provided an update for the campus regarding DVM led research and projects entitled "What, my vet does research? Current updates on DVM led projects." These presentations included summaries of research both currently in process (such as the retrospective evaluation of treatment success of reactive arthritis cases by Excluded by Requester and from recently published manuscripts, such as that authored by Excluded by Requester Excluded by Requester Excluded by Requester

Multiple CMU veterinarians participated in Camp Monkey activities for middle schoolers, a day long science camp that focused on introducing almost 100 kids to the basic concepts and structure of science via interactive, engaging activities led by scientists and lab animal vets. We also participated in outreach by participating in speaking panels and tours of the outdoor animals for a wide variety of groups, including a middle school Lego Robotics team, a local specialty veterinary clinic, the ONPRC public tour and the OHSU employee tour, the OSU Pre-Veterinary Club, the Military Veterinarians' tour from Joint Base Lewis McCord, the Lewis and Clark Animal Law class, and a high school group undergoing the "Biomedical Research Immersion Experience". The Military Veterinarians' tour included an interactive component where CMU veterinarians demonstrated practical techniques including physical examination and

ultrasound of NHPs, and a detailed tour of our surgical and pathology facilities. CMU veterinarians and technicians went into school classrooms and to science fairs for elementary, middle, and high school students with interactive activities and presentations that discussed scientific concepts and animal research at a level accessible for those ages.

Excluded by Requester presented at the 2016 Association of Primate Veterinarians conference, including both a case presentation and as part of a panel presentation about infant care, where she outlined ONPRC's processes for fostering infants (a process that is an integral part of avoiding nursery rearing and contributes to the physical and mental health of the colony).CMU veterinary technician Excluded by Requester and Excluded by Requester provided an update regarding the Center's computer based weight management system at the 2016 National AALAS meeting. Excluded by Requester (the current ONPRC first year resident) presented an update about the diagnosis and treatment of Interstitial Cystitis as a part of the Primate Center Virtual Grand Rounds.

Excluded by Requester contributed to a publication authored by a former ONPRC resident extern regarding a cardiac case she encountered during her time at the ONPRC. Excluded by Requester additionally contributed to two publications from the labs he supports. Excluded by Requester has one manuscript in preparation and another in review, both collaborative efforts with ONPRC scientists. Excluded by Requester contributed to two manuscripts published in 2016, and a third as the first author, published in Comparative Medicine. Excluded by Requester has two manuscripts in review and another in preparation, all three for which she is the first author, and another accepted for publication to which she contributed. Excluded by Requester has a first author manuscript in preparation in collaboration with several primate center pathologists. Excluded by Requester has a first author manuscript that has been accepted for publication.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Conducting veterinary-focused NHP research using data collected from the electronic health records system or through pilot grant funds, in addition to projects coordinated with scientific staff where possible, will help us fulfill our goal of expanding basic knowledge of our important animal models. It is anticipated that the in- process manuscripts will be published, and that other projects and manuscripts will be initiated and concluded during the five-year time frame of the base grant. Projects currently underway include two by Excluded by Requester a retrospective review of both cystitis and reactive arthritis cases over the past 10 years with the goal of evaluating the most effective treatments and diagnostics. Partnering with ONPRC investigators to produce publishable data that specifically contributes to the basic knowledge and understanding of NHP medicine and husbandry, and authored by the veterinarians, continues to be a primary CMU goal.

The competency-based training program for DCM and research staff will continue to expand and become more formalized and better documented over the next several years. This process will help ensure consistent skill levels for those performing procedures, and also validate the parameters for "trained individuals" at each skill level. There will be significant expansion of the hands on segments of the core skills training within 2017, and each didactic lecture will be reviewed and updated to ensure best practices and current information.

We plan to continue to refine our dental care program over the next year, evaluating methods of tracking animals likely to need ongoing care and ensuring appropriate prioritization of all cases based on multiple factors.

We will continue to use IT technology to help decrease time needed for reviewing information and data entry. Our current focus is developing Proprietary Info software to review weights of animals under 1 year of age to track growth curves and produce alerts if animals do not closely follow the expected curve. This will allow earlier and more reliably detection of subclinical illness in this vulnerable population allowing more effective care and facilitating appropriate colony management decisions. This project is well underway and expected to be finalized and in production within the next year. Increasing the use of PRIMe for reporting purposes to evaluate treatment modalities and addressing other key questions is a goal for the upcoming year as well, although one that is dependent upon resources in departments outside CMU as well. In addition Excluded by Requester has recently begun regular meetings with the IT department to represent the CMU's interests with regard to updates made to the electronic medical records system.

We will work to more regularly bring information regarding scientific projects to the DCM staff by partnering with the researchers to create short, layperson targeted presentations about the important research occurring at the Center. We strongly believe this link will improve staff loyalty and job satisfaction. We continue to aim for least one presentation per quarter, and to have presentations coincide with project initiation so that those caring for the animals understand the value of the research and have the opportunity to identify potential challenges prior to project initiation so they may be addresses in a proactive manner.

CLINICAL MEDICINE UNIT: ACCOMPLISHMENTS

Aim 1:
We have begun routinely utilizing a non-invasive method to evaluate NHP blood pressure (a cuff system designed for use in domestic pets, validated by comparison to established techniques currently utilized peri-operatively). The use of this portable, digital diagnostic has been an important investment that has been in regular use since purchase and has provided significant improvement in case management of hypertensive animals. Atherosclerosis and essential hypertension are not uncommon in aged macaques, and focusing on better diagnostic evaluation of medical treatment has led to refinement in our clinical treatment regimens to allow a high quality of life and maintenance of animals with this common disease of aging. In addition, it's been added as a component of a protocol evaluating the effect of CPAP on premature infants, and is currently being evaluated as a method for refinement of other existing protocols and standard procedures on campus.

We increased the use of our ultrasound machine and refined practices by training additional personnel to utilize the ultrasound, and provided additional advanced training to those already utilizing this modality. Use of the portable ultrasound by clinical veterinarians continues to increase, and we have begun renting the machine to research groups to improve their diagnostic capabilities (typically with regard to pregnancy diagnosis and delivery estimation). CMU and research staff have worked cooperatively to increase skill levels across departments, improving the capabilities associated with this important diagnostic tool. Recently, ONPRC recruited a cardiologist to lead the Division of Cardiometabolic Health, who has performed echocardiograms on our patients in the past, again increasing the level of CMU's diagnostic capabilities and further refining treatment options for patients with cardiac compromise.

Over the past year, the CMU was able to become fully staffed. Maintaining a stable unit with all staff well trained in their tasks further supports our goal of uninterrupted, high quality NHP care. We've begun to train our medication technicians to perform a number of entry level tasks, including phlebotomy, therapeutic baths, weight updates, and basic records entry, which frees the certified veterinary technicians and veterinary staff to focus on complex tasks. The ability to have a small number of experienced personnel administer daily medications results in the veterinary staff being quickly alerted to subtle changes in animal presentation and behavior.

One of the residents Excluded by Requester has helped significantly with improving the routine dental care of the colony over the past year.

The husbandry and clinical care for our new troop of Hamadryas baboons continues to develop. Standard husbandry processes have been refined to preserve group cohesion, updated enclosure facilities ensure a safe and secure environment for these powerful animals, and enrichment possibilities have been evaluated to refine the options provided. The surgical, clinical, research and pathology groups are coordinating an investigation of non-clinical gastritis seen in some animals from this colony at necropsy, and hope to determine an etiology, appropriate care regimens, and a better understanding of the impact of this diagnosis on animal health and wellbeing.

The software based weight management system has been further refined, and in addition to being included in an AALAS platform session in 2015, a senior ONPRC veterinary technician Excluded by Requester presented an update on the system at the AALAS conference in 2016. The same staff involved with the weight management project Excluded by Requester began development of a software based approach to reviewing growth rates for infant monkeys using a similar system to alert veterinary staff when infants do not grow at expected rates. This systematic approach is expected to result in early detection of potential issues and improved animal health and welfare accordingly. The veterinarian Excluded by Requester responsible for the clinical care of both the Time Mated Breeder (TMB) resource and the aging population has made heavy use of the weight management monitoring system to closely manage the health of these two populations. This system also helped evaluate and refine the feeding amounts of animals receiving protocol-approved novel diets, and supported the routine evaluation of study animals using a Body Condition Score, which represents a refinement of health assessment over simple weight evaluations, which can be misleading, particularly in growing animals.

Excluded by Requester serves as the primary veterinarian overseeing clinical care in the NHP nursery, working with husbandry staff to continually refine and update processes to improve outcomes of this vulnerable population. In a collaborative effort with the Behavioral Services Unit and the research groups working with infant primates, we have established new protocols to improve the welfare of infants by altering grouping processes and cage set-up (including use of surrogates). Excluded by Requester provides hands on infant care and handling training for researchers working with infant macaques. She assisted one of the husbandry supervisors, Excluded by Requester in a review and finally implementation of a refinement to nursery incubator cleaning processes. These changes are expected to reduce potential exposure of our infant monkeys to harsh chemicals and improve efficiency with regard to the intensive labor associated with cleaning these non-standard housing options, without sacrificing appropriate levels of sanitation.

In the last year, we refined routine screening of our aged population for the most common neoplasm in macaques (GI adenocarcinoma). All animals over the age of 18 are tested twice yearly for fecal occult blood (a common positive diagnostic for animals with these tumors) and so far, we have identified and resected two tumors in animals using this screening mechanism that would have potentially been missed using previous screening practices. Early identification of these neoplasms is expected to prolong life expectancy and provide a higher quality of life than those with larger tumors or those which have evidence of metastasis. In this way, use of a noninvasive, inexpensive screening tool has improved the welfare for this important and vulnerable population. In addition, aging colony animals are reviewed for husbandry and diagnostic needs prior to physical exams in order to coordinate procedures and reduce the need for sedation. For example, aged animals will commonly have Tb testing, routine dental care, and recheck diagnostics such as blood pressure or ultrasound performed within a single sedation coincident with their physical examination. We find that this increased level of pre-sedation organization and coordination improves the health and quality of life for this highly desirable research population. Similarly, organization and coordination of necessary procedures for females participating in our TMB program has significantly reduced the number of times these animals require sedation for care, while simultaneously improving their overall health status and quality of life.

Aim 2:
Grant pre-planning and pre-project meetings have continued and evolved over the past year, with DCM stakeholders taking an active role in ensuring that projects are clearly understood and appropriate planning is undertaken, particularly as the complexity of the projects at the ONPRC continues to increase. This process has had unexpected downstream positive impacts with scientists more readily initiating modifications to established protocols to improve processes and animal care. A good example of the success of this system has been our participation in the current Zika research, something ONPRC is uniquely capable of performing with our imaging, reproductive and virology resources. Excluded by Requester is part of a multidisciplinary team developing a nonhuman primate Zika virus model, and has played an essential role in advising the scientists regarding best practices for care of this important research model.

CMU veterinarians (primarily Excluded by Requester continue to actively collaborate with Excluded by Requester Excluded by Requester in the development of an allogeneic hematopoietic stem cell transplantation (HSCT) model in Mauritian origin Cynomolgus macaques. Veterinary staff are assisting in the development of the clinical supportive care of animals undergoing stem cell transplantation and work closely with members of the Infectious Disease Resource, who are also intimately involved in model development, to provide research support for the project. The HSCT model also involves support from human bone marrow transplant specialists Excluded by Requester Excluded by Requester from the OHSU hospital who provide guidance on appropriate clinical management of animals undergoing bone marrow transplantation based on their experience in humans. The contribution of CMU has been solidified as Excluded by Requester has been listed as key personnel on Excluded by Requester recently funded RO1 which supports the HSCT project.

Excluded by Requester in conjunction with the Behavioral Services Unit and the Division of Pathobiology and Immunology is evaluating and updating the process of acclimation of NHPs at ONPRC. Currently, the team is specifically focused on the effect of acclimation between groups of animals receiving antiretroviral therapy (ART) via daily subcutaneous dosing often for periods exceeding one year. Other areas of focus include evaluating the behavior and physiological effects of varying acclimation times for animals moved from outdoor groups to the indoor environment prior to project start. This project evaluates the use of temperament testing as a potential additional screening measure for animals placed on studies requiring daily ART injections.

As a method to improve the screening of animals intended for studies in the Pathobiology division, a new database was developed that allows pre-review of animals prior to hands on examination. This process continues to be refined and is intended to streamline current practices to ensure that appropriate animals are assigned to these important projects with maximum of efficiency.

Several CMU veterinarians have collaborated with dermatologists from the main campus of OHSU to initiate the use of complex diagnostics such as allergy patch testing to evaluate dermatitis cases.

Our clinical staff continues to provide technical research support to scientists by performing complex [Excluded by Requester] procedures where the health of the animal could potentially be impacted (e.g. bronchoaveolar lavages, lymph [Excluded by Requester] biopsies, bone marrow aspirates and CT scan support), primarily for projects occurring in the ABSL-3 suites.

The [Excluded by Requester] lab expanded the research aims of the Division of Neurosciences to include brain mapping of in the visual and somatosensory cortex. This research area has brought new procedures and techniques to the ONPRC requiring prolonged anesthesia with craniotomies, cortical surface imaging and head post implant maintenance and monitoring. [Excluded by Requester] in coordination with the research group and the surgical veterinarians has refined animal care during these procedures by instituting metabolic and direct blood pressure monitoring during procedures. This group also brought squirrel monkeys (*Saimiri sciureus boliviensis*) to the ONPRC, a species new to campus. DCM sent husbandry, behavior and clinical unit staff to [Proprietary Info] to learn about this species prior to their arrival on campus, and [Excluded by Requester] played an essential role in developing SOPs and processes for their care. With the aid of our BSU department, all squirrel monkeys have been successfully group housed and often are able to be maintained in at least pair housing during the post-operative period if recovering well from protocol procedures. Caging for this species was specifically designed for their needs and includes individual housing that can be transformed to group housing of 2-6 animals with vertical climbing space. There is also a large play cage with perches, swings and other enrichment devices that squirrel monkeys have full access to at all times except during the post-operative period.

The ESPF (Expanded SPF) working group evolved and took on new challenges over the past year to improve the welfare of these valuable animals. A fostering program specific to this closed group was developed and communicated to improve our ability to preserve the viral status of infants needing additional care. Animals are expected to begin utilizing a newly remodeled outdoor enclosure in the spring, and this space will include a clinical care area that will allow treatment of animals within the outdoor group without the need to transport them to areas that could potentially compromise their viral status. [Excluded by Requester] has been an essential member of this group, providing clinical information and guidance about animal selection and utilization.

[Excluded by Requester] continues to provide clinical care for the Japanese macaques diagnosed with lipofuscinosis and to contribute to the development of a formal model for research purposes. In addition, he's continued to work with the investigators studying ONPRC's Multiple Sclerosis model (Japanese Macaque encephalomyelitis) to update, refine, and formalize the guidelines for diagnosis and care of these animals. As a part of his work providing veterinary support for ONPRC's newest scientific division, the Division of Cardiometabolic Health, Dr. [Excluded by Requester] has assisted the research group in the process of transferring their maternal obesity models from Japanese Macaques to Rhesus as well as in refining and improving the clinical monitoring of animals receiving infusions of ferumoxytol, an iron containing MRI contrast agent with potential safety concerns. [Excluded by Requester] collaborates with this research group to develop clinical plans for the induction and monitoring of both type 2 and type 1 diabetic animals (the latter using streptozoocin, a process that will be new to ONPRC) and assisted in the development of standard procedures for IV Glucose Tolerance Tests and for other important refinements including best practices for positioning of pregnant animals during extended MRI imaging to improve dam and fetal safety, and clinical monitoring of fetal effects of maternal low protein diets.

[Excluded by Requester] continued to provide guidance to multiple labs in the planning (both pre-grant submission and during the IACUC protocol development) stages of projects as both a member of the DCM team that meets with researchers and as a subject matter expert and a regular attendee of the West Campus IACUC. She regularly attends Main Campus IACUC meetings as the alternate for [Excluded by Requester] and reviews all protocols

during the initial and modification stages. She continues to provide veterinary oversight and guidance for most of the active reproductive protocols, including several challenging projects such as the Polycystic Ovarian Syndrome project which has recently entered the fertility phase of the project.

In the last year, Excluded by Requester was added to the OHSU Institutional Biosafety Committee to review studies that involve nonhuman primates.

During this grant year, CMU veterinarians reviewed 291 protocols (new protocols, 3-year renewals, and modifications to existing protocols) prior to IACUC approval. Through this process, CMU veterinarians ensured the best possible animal welfare, health and safety. This represents a significant increase since last year (90 more than in 2015) and may be in part attributable to the implementation of the Veterinary Verification and Consultation system which allows researchers to more readily make needed revisions to existing protocols within a short turnaround time.

Aim 3: See training and development section B.4.

DIVISION OF COMPARATIVE MEDICINE: TRAINING AND PROFESSIONAL DEVELOPMENT

Collectively, DCM provided and participated in a myriad of training and professional development opportunities:

- Excluded by Requester attended the Spring and Fall NPRC Directors Meetings.
- PSU continues to support a one-year pathology fellowship. A second position was added during this reporting period. Excluded by Requester completed her one-year fellowship and was replaced by Excluded by Requester Excluded by Requester
- A monthly training hour is provided for CMU veterinary technicians and support staff consisting of both didactic lectures and wet labs for relevant duties.
- CMU provides an online CE service for technicians specifically designed to address common questions regarding clinical care.
- Excluded by Requester erves as Program Manager for the ONPRC site of the Oregon State Laboratory Animal Medicine Residency Consortium. Excluded by Requester is the current ONPRC veterinary resident for this 3-year ACLAM approved program. Excluded by Requester started her residency with us in July, 2016.
- Residents and veterinary clinicians give lectures at the Oregon State University College of Veterinary Medicine, and to a nationwide audience of laboratory animal veterinarians participating in Virtual Grand Rounds, part of the NPRC Training Consortium.
- Excluded by Requester leads the veterinary student externship program, which provides an in-depth and unique experience working with NHPs in the research environment. Visiting veterinary students (see Table 4) gain a well-rounded perspective on the role of veterinary medicine in NHP-based research by rotating through the Clinical Medicine Unit, Colony Hospital, Surgical Services Unit, Behavioral Services Unit, Small Laboratory Animal Unit and the Pathology Services Unit.

Table 4. Veterinary Externships at ONPRC

Title	School	Start Time	End Time
Excluded by Requester	Oregon State University	1/11/16	1/22/16
	Oregon State University	1/25/16	2/5/16
	University of Georgia	2/29/16	3/11/16
	Washington State University	7/5/16	7/27/16
	Oklahoma State University	8/15/16	9/2/16
	Oregon State University	9/6/16	9/16/16
	Oregon State University	9/19/16	10/14/16

- DCM as a whole conducts training and education for veterinary, husbandry, and research staff preparing for AALAS certification tests, and the veterinarians participate in these educational events by giving didactic lectures on various medical, regulatory and husbandry topics.
- DCM veterinarians attended and presented (as speakers and posters) at continuing education conferences on relevant medical and regulatory subjects (e.g. AALAS, ACLAM Forum, APV, PRIM&R, IACUC training); meetings also allow networking opportunities, cross facility collaboration and information sharing with other NPRC staff and research institutions.
  - Excluded by Requester gave a presentation at the National AALAS meeting in Charlotte, NC in October of 2016.

- Excluded by Requester Excluded by Requester attended the Association of Primate Veterinarians meeting in Charlotte, NC, October, 2016. Excluded by Requester Excluded by Requester gave presentations.
- Excluded by Requester and Excluded by Requester attended the Breeding Colony Management Consortium Meeting and combined Breeding Colony Management Consortium/Behavioral Management Consortium Meeting in November, 2016.
- Excluded by Requester attended the Behavioral Management Consortium Meeting and combined Breeding Colony Management Consortium/Behavioral Management Consortium Meeting in November.
- Excluded by Requester completed necessary coursework for her USDA Accreditation.
- Excluded by Requester served as a faculty facilitator for the Oregon Health & Sciences Interprofessional Initiative, as a faculty facilitator for the Proprietary Info Proprietary Info diagnostic challenge, and helped supervise 9 veterinary externs and 3 veterinary residents.
- Two BSU members attended the 2016 joint meeting of the American Society of Primatologist and International Primatological Society.

- Two additional staff spent several days at the Proprietary Info and the Proprietary Info primate facility, to learn about how they manage their baboons and squirrel monkeys, respectively.
  - Excluded by Requester attended the 2016 Annual Meeting of the ACVP and Primate Pathology Workshop held in New Orleans, LA.
  - Several DCM technicians attended the National AALAS meeting in Charlotte, NC. Veterinary Technician Excluded by Requester gave a presentation.
  - Excluded by Requester attended the 2016 joint meeting of the American Society of Primatologist and International Primatological Society and the Laboratory Animal Medicine & Pathology Seminar, CL Davis Foundation in Madison, WI.
  - The SSU technicians attended the following meetings and seminars:
    American College of Veterinary Surgeons, Surgery Summit, Seattle, WA; Dove Lewis Emergency Animal Hospital Annual Conference, Portland, OR; Northwest Veterinary Specialists Winterfest 2016, Portland, OR; Oregon Veterinary Technician and Assistant Association Continuing Education Conference, Albany, OR; Oregon Veterinary Conference, Corvallis, OR
  - Excluded by Requester and Several DCM veterinarians attended the Crossing the I's Conference in November, 2016 presented by NWABR. Excluded by Requester presented.
  - Sidener attended the combined Public Responsibility in Medicine and Research/Northwest Association for Biomedical Research IACUC Conference in Seattle, WA. Excluded by Requester gave a presentation.
  - Excluded by Requester attended the 2016 Charles River Short Course in Providence, RI.
- BSU has a monthly journal club, and staff attend webinars and seminars offered at the ONPRC.
- Excluded by Requester erves as an external advisory committee member for the Caribbean Primate Research Center in Puerto Rico.

- PSU participates in the training of veterinary student clinical medicine externs as part of their comprehensive exposure to NHP medicine. They support the LAM residency program through provision of didactic lectures, rotations through pathology services, and monthly pathology-centered didactic lectures. PSU conducts weekly NHP histopathology rounds and weekly review of the Joint Pathology Center (JPC) Wednesday Slide Conference material open to all veterinarians and trainees.

- All veterinary staff participates in the monthly ONPRC Technician Continuing Education Program coordinated by Excluded by Requester lecturing on various veterinary topics and presenting key case reports to the technical staff.

- All DCM unit veterinarians actively participate in NPRC Consortium efforts, either as Chair, members or project leaders.

- DCM veterinarians, managers and technicians were active in ONPRC outreach efforts, and participated in various programs including Camp Monkey, Saturday Academy, Science Ambassadors, and the PCC Behavior Management of Zoo Animals course. Other activities include serving as information sources for on-site tours (e.g. when ONPRC hosted the NPRC Directors' meeting, and the National Association of Medical Examiners), presenting to school groups of all ages including Lewis and Clark Law School, Portland Community College, and local primary schools, and participating in local middle school science fairs.

- DCM veterinary staff hosted and gave presentations and tours to the visiting veterinarians and staff from Joint Base Lewis-McChord in March, 2016.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5560

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			18,932.00	7,005.00	25,937.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **25,937.00**

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						
22	Unit staff	43.51			204,411.00	75,632.00	280,043.00
22	**Total Number Other Personnel**					**Total Other Personnel**	**280,043.00**
					Total Salary, Wages and Fringe Benefits (A+B)		**305,980.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	816.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**816.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	11,452.00
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. Vet licenses, laboratory services, equipment maint contract, shipping bioengineering servicesw	5,860.00
Total Other Direct Costs	**17,312.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**324,108.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	324,108.00	90,750.00
		Total Indirect Costs	**90,750.00**

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)	**414,858.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Obese NHP Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Obese NHP Resource is closely linked with the Division of Cardiometabolic Health (formally Diabetes, Obesity, and Metabolism) and the Division of Comparative Medicine, and exploits the macaque model of diet-induced obesity (DIO) developed at ONPRC. This Resource was established to provide qualified internal and external investigators access to metabolically characterized animals and clinical samples for a variety of studies in metabolism, obesity, pre-diabetes, and other co-morbidities. Through provision of the services and expertise supported by this Resource, it fulfills the mandate of the ONPRC to serve as a national resource for valuable NHP models. In furtherance of this goal, the Resource will pursue the following Specific Aims:

Specific Aim 1. Maintain a healthy and well-characterized DIO macaque colony. Since diet-induced obesity is a serious disease state, the animals become more susceptible to health complications when maintained on the Western-style diet used to produce weight gain. Therefore, the progression of disease state is accomplished through the quarterly measurement of body weight, adiposity (by DEXA), insulin resistance and glucose tolerance (through intravenous glucose tolerance tests).

Specific Aim 2. Expansion of animal availability. There is an ever-expanding demand, both locally and nationally, for the macaque DIO model. Resource constraints will be addressed by targeting short-term studies supported by industry to maintain animals during phenotype development and the establishment of a cynomolgus DIO model.

Specific Aim 3. Increased collaboration with the ONPRC Aging NHP Resource. Most current ongoing studies using the Obese NHP Resource focus on early developmental programming or the young adult. However, one of the major challenges that clinicians will face in the future is the management of aging, obese patients. To address this issue, Obese NHP Resource staff will cooperate with Aging NHP Resource personnel to evaluate the metabolic status of aged animals as well as making older Obese NHP Resource animals available for studies as they reach the appropriate age.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-ObeseResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-ObeseResource_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We have started presenting the work of the Obese NHP Resource throughout division at ONPRC as well as OHSU. Currently scheduled presentations are with the Knight Cardiovascular Institute and Physiology and Pharmacology. Research using animals from the Obese Resource or tissues as received from our tissue bank has been presented at national meetings or published in scientific journals.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The next reporting period will focus on further developing the group-housed Rhesus macaque groups to provide animals that can address the health issues affiliated with maternal obesity. We are also focused on expanding our characterizations of the animal models using computer modeling to investigate insulin resistance in more detail, as well as collecting information on genetics, epigenetics, microbiome and the metabolome where possible by making obtained results public. This year we will also initiate the generation of a new web-based database that will allow us to integrate the obtained data with the anthropomorphic data maintained in the general animal database, PRIME.

OBESE NHP RESOURCE: ACCOMPLISHMENTS

We have continued with our extensive monitoring program, which has resulted in identifying several animals that were progressing from diet-induced obese and insulin resistant towards a more diabetic state. Animals that were identified earlier as type 2 diabetic animals are successfully maintained for an upcoming NIH funded study investigating retinopathy.

The cohort of cynomolgus macaques have been very useful and are demonstrating to be a similar model to the Rhesus macaque. These animals were utilized in studies investigating the potential treatments for fatty liver disease with collaborators at an external university.

We will have the first of several aged obese animals that have reached the age of 20+ years. These animals are made available to the Aging resource and we will be performing our first collaborative scans with MRI during the 2017 calendar year.

OBESE NHP RESOURCE: TRAINING AND PROFESSIONAL DEVELOPMENT

The Obese NHP Resource continuous to provide both technical assistance, as well as training for investigators that are interested in measuring metabolic changes in their studies. We have trained research staff from several investigators to perform their own metabolic analyses and are active participants in several funded projects within ONPRC.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Research Material	The Obese NHP Resource provides NHP samples to internal and external users based upon published rates. Reagents and other resources developed through NIH-funded studies are shared according to NIH guidelines

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Limited. As part of the distribution program, we have provided samples from obese animals to pharmaceutical industry, as well as academic partners at different universities.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5561

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			33,652.00	12,788.00	46,440.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **46,440.00**

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						
6	Unit staff	40.2			120,690.00	42,775.00	163,465.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**163,465.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**209,905.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	63,414.00
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. per diem, maint & repair, morphology fees, lab fees, hazardous waste disposal, miscellaneous other expense	124,681.00
Total Other Direct Costs	**188,095.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**400,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	400,000.00	112,000.00
		Total Indirect Costs	**112,000.00**

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)	**512,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Primate Aging Resource
Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Primate Aging Resource (PAR) has been in existence since 1999 and incorporates the Primate Aging Study (PAS) colony, which is a NIA-supported NHP resource at ONPRC. The NIA funding is supplemented by P51 support. The PAS colony serves the research community by identifying, maintaining, and supplying projects with aged Indian-origin rhesus macaques. To further facilitate this process and strengthen the resource for the future, we propose the following specific aims:

Specific Aim 1. Formalization of organizational ties with the Division of Comparative Medicine (DCM). To integrate the goals of the PAR with DCM operations, strong and direct connections of PAR with senior management in animal resources, facilities, research, clinic, surgery and pathology departments will be necessary for smooth PAR operations.

Specific Aim 2. Leveraging of Information Services (IS) and other computational resources. The Aging Resource will continue to work with ONPRC information services in the development of management tools for tracking animals in the aging resource and for searching for replacement animals. Background information from the electronic health records are used for project assignment.

Specific Aim 3. Enhancement of husbandry practices. Physical exams (PE) of old animals are now more frequent (biannual) and allows for earlier intervention for serious disease prevention.

Specific Aim 4. New model development. Areas of scientific development using aging primates include: cardiovascular changes and responsiveness, epigenetic modification and age-related effects on the rate of CSF clearance in the brain.

Specific Aim 5. Expansion of archival projects. Continuation of one of the long-term projects in PAR is the collection tissues for our archives. We will also continue to build our archive of MRI brain images to better define the patterns of normative aging.

Specific Aim 6. Data mining. A great deal of archived data, whose extraction and analysis could benefit primate model development and husbandry, is available. Programming for the extraction and analysis of such data is being pursued.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-AgingResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-AgingResource_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

ABSTRACTS

Excluded by Requester. Identifying regulators of synaptic stability during normal healthy ageing in non- human primates. Society for Neuroscience Abstracts, #515.12.

Excluded by Requester (2016). Characterization of the rhesus monkey suprachiasmatic nucleus during aging. Society for Neuroscience Abstracts, #815.06.

Excluded by Requester (2016). Retinal degeneration in a Japanese macaque model of neuronal ceroid lipofuscinosis. XVIIth International Symposium on Retinal Degeneration. Abstract 94. (Kyoto).

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

For 2017 it will be important to replenish the animal resource, if pending grants are indeed funded. The pursuit of pilot data will be important as well, in order to have preliminary information for new research arenas.

AGING RESOURCE: ACCOMPLISHMENTS

Specific Aim 1. In the past year, meetings with the Head of DCM have occurred, as well as with the animal resource and research support managers, clinic, pathology and surgery. Planned and spontaneous meetings help clarify and strengthen a synergistic relationship. Meeting with new members of the team is especially critical, which has occurred after a recent reorganization.

Specific Aim 2. The Primate Records and Information Management (PRIMe) system is the primary source for regularly scheduled queries of the Aging colony census, identification of replacement animals for PAR and associated animal costs (per diems, lease fees etc.). The latter informs reports from our financial analysts for budget proposals in applications.

Specific Aim 3. Biannual physicals are continuing for the animals in the Aging Resource, which is enhanced by continuity with the same primary contact in clinic. With this surveillance system in place, early animal health problems are captured and treated in a preemptive manner.

Specific Aim 4. While continuity of some long-term projects on aging research continue, new important areas of research continue to emerge and evolve. This reflects the maturation of exciting new research opportunities, which benefit from a highly translational model.

Specific Aim 5. Tissue distribution from the Aging Resource has continued and form the basis of scientific aims from on-going and proposed studies. This includes local, national and international collaborators. We have recently finished analyzing anatomical MRIs from a cross-sectional aging study, which will serve as a basis for comparison future studies.

Specific Aim 6. The data-mining effort, as recommended by the Office of Research Infrastructure Programs, has continued. Results looking at cross-sectional aging changes in macaque brain weight have been analyzed, figures generated, and this is in the process of being written up for peer-review. Currently, we are looking for possible secular effects on the development, mature and aged body weight in a cross-sectional design.

AGING RESOURCE: TRAINING AND PROFESSIONAL DEVELOPMENT

The Head of the Primate Aging Resource attended two national conferences: 1. The 2016 American Aging Association meeting; and, 2. The 2016 Society for Neuroscience meeting. In addition, two local meetings were also attended: 1. The Neurofutures and 2. Oregon Chapter of the Society for Neuroscience meetings. These meetings afforded the opportunity to see first-hand the current findings in areas of primary interest.

Other training opportunities presented themselves, with visiting scholars from Chile and Edinburgh (graduate students), as well as support of a student who was granted her doctorate.

This Resource provides post-doctoral laboratory animal veterinarians a unique opportunity to learn how to best manage and care for a group of geriatric macaques.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Models	There are opportunities for web-based search algorithms that utilize archived data, including information on longitudinal body weight measures and anatomical MRIs.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Research Material	The Primate Aging Resource continues to share information on the resource itself, as well discussing experimental design for grants, and provides animals and tissues for experimental use.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5562

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			78,092.00	28,113.00	106,205.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **106,205.00**

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						
2	Unit staff	18.0			58,998.00	21,240.00	80,238.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**80,238.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**186,443.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	5,600.00
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. Animal per diem	186,254.00
9. MRI fees, equipment maint & repair, software maint contract, memberships, morphology fees	8,818.00
Total Other Direct Costs	**200,672.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**389,115.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	389,115.00	108,952.00
		Total Indirect Costs	**108,952.00**

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)	**498,067.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Infectious Disease Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

This resource brings together a number of assets and capabilities that were previously in other Center entities, but which shared a focus on infectious disease research. In light of the significant focus on this research area and the concurrent presence of specialized SPF colonies supported by U24 and U42 grants, as well as the SIV-infected long-term survivor cohort. This resource provides professional and technical expertise to investigators who are performing infectious disease research in nonhuman primates and who would benefit from assistance with project performance as well as specialized SPF colonies supported by U24 and U42 grants. The Resource managed 40 study protocols utilizing 6 Risk Group 2 and 3 infectious agent models for 11 investigators totaling 803 macaques in calendar year 2016.

SPECIFIC AIM 1. Enhanced Resource Staffing. Additional professional expertise and management capacity is required to accommodate program growth, and the increasing effort necessary to manage expanding animal project compliance requirements. The growth in NHP infectious disease research activities hosted by the Infectious Disease Resource (IDR) has outstripped its professional personnel resources and additional professional expertise is critically needed. Of particular concern is the Resources ability to host and manage additional NHP studies for off-site, collaborative investigators in the spirit of a national resource, and to effectively manage the increasing number of NHPs on study in the ABSL-3 facility. A doctoral level scientist or veterinarian will be recruited to assist Excluded by Requester in managing the Resource. The staff scientist will assume principal investigator responsibility for a portion of the Center program project NHP cores and subcontracts from outside investigators, participate in the oversight of NHP research protocols and assist investigators with budget preparation, preparation of Institutional Animal Care and Use and Biosafety documents germane to their studies.

SPECIFIC AIM 2. Model development.
Development of a Plasmodium knowlesi (Pk) challenge model:
The Plasmodium knowlesi (PK) challenge model in rhesus macaques will be developed with the assistance of Excluded by Requester Naval Medical Research Center. Macaques will be intravenously inoculated with 100 sporozoites obtained 14 days after Anopheles dirus mosquitos are fed on a Pk-infected macaque using the Ozaki method. Beginning 6 days after sporozoite challenge, blood will be taken daily by ear prick at 1 pm. Pk infections are highly synchronized in the blood. Daily ear prick blood (10 µL) will be used for a PCR blot onto filter paper and for thin and thick malaria smears stained with Giemsa stain to quantify the percent of infected red blood cells according to standard procedures. When parasitemias exceed 2%, monkeys will be treated by IM injection of chloroquine 15 mg/kg on days 1, 3, and 5, and a single IM dose artesunate (AS; 5 mg/kg) to prevent death.

Development of an autologous bone marrow transplant model:
This rhesus macaque model will be developed with the assistance of Excluded by Requester and his transplant staff at the Fred Hutchinson Cancer Research Center. Briefly, macaques will be habituated to a jacket-tether system. Recombinant human granulocyte colony-stimulating factor (rhG-CSF, 100 µg/kg) will be given daily as subcutaneous injections for 5 days. On day 5, bone marrow will be harvested from the humeri and/or femora and cryopreserved. In preparation for transplant, a femoral vein catheter will be placed for continuous intravenous (iv) hydration with continuous iv administration of broad-spectrum antibiotics (cetazadime, vancomycin, gentamicin) and an antiviral agent (acyclovir) and the animals will receive myeloblative total-body irradiation. Twenty-four hours after transplantation, the animals will be started on intravenous G-CSF at 100 µg/kg daily until the animals have attained stable neutrophil engraftment with an absolute neutrophil count of greater than 0.5 × 109/L (500/µL). Standard supportive care, including blood product transfusions, fluid and electrolyte management, and antibiotics will be given as needed.

SPECIFIC AIM 3. Development of state-of the art immunological assays and analysis. We will make services available to support subcontracted grant work in the NHP model (design and implementation of full immunological studies), custom sample processing (isolation, counting, and cryopreservation of cells, fluids, and nucleic acids), performance of optimized and validated flow cytometric assays (phenotype staining, ICS, CFSE, tetramer, TruCount), specialized and customized high-throughput analysis, economies-of-scale reagent purchasing, and archiving of cryopreserved samples. This operation was previously the Cellular Immunology Unit of the Immunology Support Core during the previous grant period, but was felt to be more appropriate to function as a component of the IDR, and will continue to be managed by Excluded by Requester

SPECIFIC AIM 4. Maintenance of a National AIDS Macaque Resource. The resource will maintain a pool with an average census of 60 clinically stable and immunologically and virologically characterized SIV-infected macaques that have completed their initial research assignment. This pool of animals represents a unique and increasingly valuable research resource because of their value for priority research to identify strategies to eliminate HIV reservoirs. These animals will be made available to the US AIDS research community along with sufficient virologic and immunologic data to permit the identification of animals that are suitable for inclusion in additional studies. To maintain adequate immunologic characterization, animals in the pool will be bled and bronchoalveolar lavage will be performed at three week intervals to obtain serum, plasma, peripheral blood leukocytes and lung lymphocytes for virus-specific antibody, cellular immune, cellular proliferation and virus load analyses. The immunologic assays will be performed by the IDR. The ONPRC Molecular Virology Service Core will perform real-time PCR assays to quantify plasma SIV RNA.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-IDResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DCM-IDResource_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

SPECIFIC AIM 1. Enhanced Resource Staffing.
Recruiting a veterinarian with pathology expertise remains a high priority. Additional project management and technical staff recruitments will be necessary to support recently funded grants that will increase the number of animals on study and to support the challenge phases of funded and ongoing mycobacterium tuberculosis vaccine studies.

SPECIFIC AIM 2. Model development.
Future activities to development the Plasmodium knowlesi challenge model will focus on acquiring the expertise to maintain Anopheles dirus and infect them to eliminate the need to ship Pk-infected mosquitos from the east coast. Future activities to develop the bone marrow transplant model will focus on repeating our successful immunosuppressive protocol to achieve heterologous engraftment and further improve post-transplant management of GVHD. We will also initiate autologous bone marrow transplants in macaques to support studies aimed at eliminating the SIV reservoir that remains after anti retrovirus therapy as a model for eliminating the HIV reservoir.

SPECIFIC AIM 3. Development of state-of the art immunological assays and analysis.
The IDR LU will continue to provide immunological assay expertise as needed to support collaborative investigators including participation in grant applications, and design or modification of assays necessary to support their projects.

SPECIFIC AIM 4. Maintenance of a National AIDS Macaque Resource.
Activities will focus on managing the resource to maintain a cost effective balance between the numbers of animals maintained and projected investigator need for the animals as well as effective use of ABSL-2/3 housing.

INFECTIOUS DISEASE RESOURCE: ACCOMPLISHMENTS

Specific Aim 1. Enhanced Resource Staffing.
Seven research technicians were added to the IDR staff; 5 to replace technicians that left the resource and two to keep pace with the growth in the number of nonhuman primates assigned to infectious disease protocols managed by the resource and the increases in procedure complexity. The average daily census for protocols managed by the Resource was 590 macaques in calendar year 2016. Resource staff obtained 20,211 blood samples, 2,254 bronchoalveolar lavage samples, 315 intestinal mucosal biopsy samples, 559 lymph node biopsy samples, 458 bone marrow samples, 3,077 urine samples, and 1,483 mucosal secretion samples; and performed 863 infectious agent administration procedures, 11,381 drug administrations, 190 necropsies and 7,008 Complete blood counts in support of these protocols. The Resource is currently recruiting an additional veterinary pathologist, an additional project manager and two additional technicians to support recently funded grants that will increase the number of animals on study and to support the challenge phase of funded and ongoing SIV/HIV and *Mycobacterium tuberculosis* vaccine studies.

Specific Aim 2. Model development.
Development of a *Plasmodium knowlesi* (Pk) challenge model.
With the Assistance of Excluded by Requester Naval Medical Research Center the Infectious Disease Resource (IDR) staff acquired the expertise to complete its first 24-macaque Pk vaccine challenge study. *Plasmodium knowlesi*-infected *Anopheles dirus* mosquitos were obtained from the Naval Medical Research Center, sporozoites were harvested from them using the Ozaki method and the macaques were inoculated intravenously with 100 sporozoites. Parasitemia was quantified daily using Giemsa-stained thin blood smears and the animals were treated with chloroquine and artesunate when parasitemias exceeded 2% resulting in clearance in 100% of the animals. Therefore, the initial goals of this specific aim were achieved. The study provided evidence for partial vaccine efficacy. We will not further develop the Pk challenge model until additional funding is obtained.

Development of an autologous bone marrow transplant model.
With the Assistance of Excluded by Requester and his transplant staff at the Fred Hutchinson Cancer Research Center the IDR staff acquired the infrastructure, equipment and expertise to complete its first survival allogeneic bone marrow transplant in a cynomolgus macaque. A matched donor was mobilized with recombinant human granulocyte colony-stimulating factor, $1.5x10^9$ donor peripheral blood mononuclear cells were obtained using apheresis on day 5 post-mobilization and infused into a recipient maintained in a jacket-tether system following myeloblative total-body irradiation. Post-transplantation intensive care of the recipient consisted of continuous antibiotic infusion, treatment with rhG-CSF and infusion of irradiated matched donor platelets until its granulocyte numbers exceeded 0.5×10^9/L (500/μL. The allograft in this animal failed; however, the initial technical goals of this specific aim were accomplished. In the past year Excluded by Requester Excluded by Requester a bone marrow transplant expert with the OHSU Knight Cancer Center joined our transplant team and five additional transplants were attempted using successively refined immunosuppressive protocols. These attempts resulted in successful engraftments; however, four of five succumbed to graft vs. host disease (GVHD). We have now successful managed GVHD in 3 additional animals.

Specific Aim 3. Addition of state-of the art immunological assays and analysis.
The IDR Laboratory unit (LU) completed immunological assays supporting a collaborative study to test the efficacy of a computationally designed peptide, VG1177, as a therapeutic drug for treatment of SIV in rhesus macaques. The unit contributed expertise to two pending collaborator applications for vaccine efficacy studies in the SIV/rhesus macaque model.

Specific Aim 4. Maintenance of a National AIDS Macaque Resource.
The IDR maintained an average census of 9 clinically stable and immunologically and virologically characterized SIV-infected macaques in the National AIDS Macaque Resource. The average census of macaques maintained in the resource was reduced from the initially proposed target of 60 due to a budget reduction and a shortage of ABSL-2/3 caging. The overall goal of this specific aim was achieved. The SIV-infected macaques made available from the resource reduces overall use of rhesus macaques and provides a substantial cost savings to grants over infecting naive animals and maintaining them for 1-2 years to obtain a project-usable animal.

INFECTIOUS DISEASE RESOURCE: TRAINING AND PROFESSIONAL DEVELOPMENT

One-on-one training is provided to all members of the IDR with the goal of achieving a completely cross-trained staff. Formal classroom training was provided for nonhuman primate apheresis to the IDR staff as well as some of the Center's veterinary clinicians and veterinary technicians. The Resource acquired a Neurological CereTom Computed Tomography unit for use in the tuberculosis vaccine study. Formal classroom training in its use and applications will be extended to Center's veterinary clinicians and veterinary technicians. The IDR routinely provided one-on-one nonhuman primate protocol management and procedures training for graduate students and postdoctoral fellows from investigators laboratories. The Resource hosted two summer college student interns that aspire to attend veterinary school.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Protocols	Apheresis: The resource acquired a second Proprietary Info apheresis system and additional technical staff completed intensive training on the application of the system for nonhuman primate leukopheresis. The unit now performs leukopheresis procedures supporting bone marrow transplantation and large scale determination of T cell epitope specificity and major histocompatibility restriction of vaccine-induced T cell responses. Approximately 109 lymphocytes can be obtained in a single procedure permitting determinations to be completed on a single large cell sample eliminating the variability inherent in determinations from multiple blood samples and markedly reducing the number of blood sample experiences for the animals. The projected project use of leukopheresis is approximately 150 procedures annually.
Protocols	The Resource continues to expand immunohistochemistry and in situ hybridization applications of the Proprietary Info RX. Protocols for multi-labelled immunohistochemistry and combined immunohistochemistry in situ hybridization are being developed for precisely defining the proximity of immune effector cells to cells in tissues infected with study agents and vaccine vectors.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5563

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			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						
5	Unit staff	35.4			220,918.00	81,740.00	302,658.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**302,658.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**302,658.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	1,000.00
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. Rhesus macaque orphanage	32,317.00
Total Other Direct Costs	**33,317.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**335,975.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	335,975.00	94,073.00
		Total Indirect Costs	**94,073.00**

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)	**430,048.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Japanese Macaque Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The ONPRC Japanese Macaque Resource is increasingly recognized as an important reservoir of animals with unique and valuable phenotypes (associated with specific genetic susceptibilities) relevant to multiple sclerosis and age-related macular degeneration.

To maintain an appropriate population to take full advantage of these features, the Resource is pursuing the following steps in the next funding period:

Specific Aim 1. Expand breeding production, by rebalancing the demographic distribution, utilizing best practices to optimize colony and genetic health.

Specific Aim 2. Employ Information Systems (IS) capacities to model and inform JMR colony management decisions.

Specific Aim 3. Characterize colony members for pedigree relationships and risk for genetic diseases.

Specific Aim 4. Maintain centralized genetic and phenotypic records of the JMR to inform colony management decisions.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-JMacResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

An invited talk, “A nonhuman model of neuronal lipofuscinosis” was presented by Excluded by Requester at the 15th International Conference on Neuronal Lipofuscinosis in October 2016.

An invited talk, “Inhibition of hyaluronidase activity by modified flavonoids promotes functional remyelination.” was presented at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (London, UK) by Excluded by Requester

An invited talk, “Hyaluronidases as potential therapeutic targets for demyelination” on the JME model was also presented at the 12th Biennial International Society for Neurochemistry Satellite Meeting on Myelin Biology (Fitzroy Island, Australia) by Excluded by Requester

A poster entitled, “Retinal degeneration in a Japanese macaque model of Neuronal Ceroid Lipofuscinosis was presented at the XVIIth International Symposium on Retinal Degeneration (Kyoto Japan) Sept. 2016 by Excluded by Requester

An abstract entitled “Identification of a macaque model of neuronal ceroid lipofuscinosis” was submitted for presentation at the Association for Research in Vision and Ophthalmology annual meeting (Baltimore, MD) by Excluded by Requester

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Continue to support genetic and phenotypic characterization, breeding colony management and harem model production to promote improved health and productivity of this valuable population. In addition, we will continue to support the planning of JM-based research applications, and the expansion of genetic disease models to support the growing research demand from both internal and external investigators. Towards that goal, an R24 application to support expansion of the unique JM genetic disease models will be submitted in the coming year.

JAPANESE MACAQUE RESOURCE: ACCOMPLISHMENTS

We supported management of 2 breeding harem groups established to propagate genetic disease models (JME and macular degeneration) outside of the main colony. The value of the harems has been underscored by the federal funding of promising new MS therapies in NHPs, which is made feasible by the JME harem's success in producing genetically prone subjects.

The first NHP model of Batten disease, recently discovered in the JM colony, was characterized by a multidisciplinary team of ONPRC scientists in this past year. Batten disease, or neuroceroid lipofuscinosis (NCL) is the most common pediatric neurodegenerative disease. All aspects of human NCL are recapitulated in the JM model. In preparation for expanded breeding of the NCL model to enable disease treatment pre-clinical trials, genetic screening of the entire JM colony has begun, identifying candidates for a targeted breeding group.

The JMR continues to provide animals for ongoing studies on transgenerational effects of maternal obesity, which are managed through the Obese Resource (OR). As discussed in the RPPR for the OR, alternative macaques are being developed to enable a shift in focus of the JM colony to genetic disease models. This shift will allow the JMs to be managed for long-term sustainability and productivity and for the study of genetic disease models uniquely available in the JM population.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5564

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			13,097.00	4,322.00	17,419.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **17,419.00**

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 staff	1.8			10,325.00	3,407.00	13,732.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**13,732.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**31,151.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	35,000.00
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. Per diem	240,000.00
9. MRI fees, parentage analysis, quarantine housing, retinal characterization	44,629.00
Total Other Direct Costs	**319,629.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**350,780.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	350,780.00	98,218.00
		Total Indirect Costs	**98,218.00**

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)	**448,998.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Assisted Reproduction Technology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The overall objective of the ONPRC Assisted Reproductive Technologies (ART) Support Core is to provide ONPRC researchers as well as national and international scientists the expertise and materials necessary for the efficient use of nonhuman primates (NHPs) in studies relevant to human health and disease. Specifically, the ART Core offers investigators the means to acquire difficult to obtain NHP ovarian specimens (granulosa cells, follicular fluid), germ cells (sperm, oocytes), and embryos for research purposes. Embryos are generated by the ART Core using established in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) techniques. Additionally, the ART Core provides the expertise and technical support necessary to perform embryo transfers, such that the developmental potential of experimentally manipulated embryos can be evaluated based on the presence or absence of a successful pregnancy. Established ART Core embryo transfer and cryopreservation protocols also allow investigators to maintain animal lineages with valuable genotypes/phenotypes. Lastly, the ART Core also provides researchers with media and reagents that are necessary to culture nonhuman primate germ cells and embryos.

To ensure that the ART Core possesses the most up-to-date means to provide the aforementioned services in an efficient and cost-effective manner, continual refinement of existing protocols and the development of new technologies are required. Thus, the Core strives to be at the cutting edge of NHP ART by developing new techniques and protocols that will fully support ONPRC scientists and collaborators focusing on primate reproduction and development. An active technology-development arm of the Core enables the addition of services and expertise that advance the use of the NHP as a manipulatable and translationally relevant model system.

Therefore, to attain the same level of high quality and cutting-edge services provided in the previous funding interval, the ONPRC ART Core proposes the following objectives through the next 5-year period of support:

Specific Aim 1: To provide an efficient, responsive, and transparent operating structure that allows for the delivery of high-quality NHP ART services and support. The Core aims to offer the necessary services and expertise for researchers seeking to utilize NHPs as models for the treatment of diseases and regulation of fertility in humans. To achieve this goal, the Core will focus on maintaining current high standards of service and quality control, ensuring an uninterrupted source of nonhuman primate gametes, embryos, ovarian materials, and germ cell/embryo culture media. Regular review of resources, personnel training and performance, as well as quality of services offered will be performed by the Core director, oversight committee, and the ONPRC Associate Director for Research to ensure continued success of the Core.

Specific Aim 2: To develop new ART reagents, services, and expertise that advance the use of the NHP as a translationally relevant model system. The Core will develop the following tools and resources to advance the utility of NHP ART for ONPRC and external research projects. Technology development objectives for the next funding interval include: a) the identification of biomarkers in ovarian follicles that yield oocytes with the greatest potential to undergo fertilization and embryonic development; b) the development and optimization of ART protocols in cynomolgus macaques, an NHP species that is emerging as a valuable model system at ONPRC, as well as; c) to apply state-of-the-art molecular methodologies to the manipulation of the NHP genome, which will allow for the development of models of human disease critically important for advancing reproductive, regenerative, and stem cell-based medicine.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-ART_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Core-ART_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Based on suggestions by the ART Core Advisory Committee, advances in ART protocols and techniques will be made available to all Core users through the ONPRC PRIMe “Cores & Resources” management database. Adjustments will be made based on user feedback.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

With service and research objectives already well in progress, continuation of ART Core goals will be seamless. Funded grants from internal investigators have been reviewed and indicate a continued demand for ART Core services through the foreseeable future. Periodic review of routinely collected data (i.e., project income, animal expense, oocyte retrieval and embryo production rates) will provide an assessment of service quality and quantity provided to investigators. Updates to routine protocols will be evaluated through literature review and discussions with colleagues to ensure the optimal services are being provided to investigators.

Research goals will continue to be focused on investigator driven objectives in four areas.

1.Protocols for non-surgical artificial insemination will be optimized. This will provide investigators the ability to use sperm from genetically valuable males or time a pregnancy in specific females when in vitro embryo production is not desired. With the anticipated increase in the use of the Timed Mated Breeding (TMB) Resource, an optimized protocol will also provide an alternate method to specifically time pregnancies should demand outnumber available males for pairing at any given time. Protocol development will include optimizing the use of both fresh and frozen semen for increased accessibility to genetic selection and is expected to begin before the end of the breeding season in 2017.

2.As more investigators begin exploring the use of CRISPR technology to develop biomedical models, there will be an increase in th[Excluded by Requester] for recipients (surrogates) for transfer of genome modified embryos. Animals that undergo a controlled ovary stimulation [Excluded by Requester] for oocyte retrieval and in vitro embryo production are not suitable candidates for immediate surrogacy. As such, up to 4 additional animals must be available to try and match their ovarian cycle to that of the egg donor's to support a successful embryo transfer at any given time which increases the demand on animal use. To date there has been no successful protocol developed to synchronize the embryo transfer recipient to the stage of in vitro embryo development in the NHP model. In collaboration with [redacted] investigations will evaluate induction of estrous and synchronization protocols for the effect on uterine endometrium to predict receptivity to transferred embryos. Selected strategies will be further tested by transferring embryos and monitoring until delivery of a live animal. Health of the resultant offspring will be closely monitored and evaluated by standard clinical practice. Development of a successful synchronization program will reduce the number animals necessary to maintain available surrogates and increase the ability to transfer fresh (not cryopreserved) embryos which will have a positive impact on successful embryo implantation rates. Investigations will begin before the end of the breeding season in 2017.

Pending Support

4.Production of rhesus and cynomolgus macaque genome modified embryos for biomedical model development will continue. Efforts will focus on using the CRISPR/Cas9 system to both knock-in and knock-out genes of interest to recapitulate genotypes associated with specific human disease. Embryos produced will either be immediately transferred into a recipient to produce a pregnancy or undergo trophectoderm biopsy to confirm appropriate changes to the genome have occurred. Embryos that undergo genetic analysis will be cryopreserved until a suitable recipient becomes available for transfer.

ASSISTED REPRODUCTION TECHNOLOGY (ART): ACCOMPLISHMENTS

All specific aims are currently on track and/or being developed. One significant change that is pertinent to all the specific aims is the change in direct oversight of the core. Specifically, Excluded by Requester replaced Excluded by Requester as core director in December, 2016. This ccoincided with the appointment of Excluded by Requester as permanent Chief of the Division of Developmental and Reproductive Sciences. Excluded by Requester extensive experience with core techniques and operations make her an ideal replacement for Excluded by Requester and ths change allow Excluded by Requester to devote appropriate effort towards Division leadership duties.

Aim 1: An updated ART Core user survey was administered August 2015 in an anonymous digital format. Questions were designed to ascertain the perceived quality of service and value of ART Core access by internal users. The feedback was very positive with all respondents stating satisfaction and intentions to continue incorporation of ART Core services in their research. The most valued service was recovery of rhesus oocytes and follicle cells for experimental use by researchers and generation of embryos through in vitro fertilization techniques. Research services were provided for 11 ONPRC investigators and 4 external investigators Proprietary Info Proprietary Info Building on our previous success using CRISPER gene editing approaches for the development of valuable rhesus monkey disease models, the ART Core has continued to provide service for two investigators to generate specific genome modified embryos (Excluded by Requester ONPRC Division of Pathobiology and the Vaccine Gene Therapy Institute; Excluded by Requester Oregon Health & Science University) and have initiated an additional project to create gene knock-in models using CRISPR-homology driven repair to modify single cell rhesus embryos. For the reporting year, research services provided include controlled ovarian cycle stimulations, oocyte retrievals, follicle fluid isolation, in vitro fertilization, intracytoplasmic sperm injection, embryo culture, embryo cryopreservation, blastocyst biopsy, post-mortem sperm collection, semen cryopreservation, embryo cryopreservation, artificial insemination, embryo microinjection, embryo transfer, and follicle cell isolation. A cohort of 14 adult female and 4 adult male rhesus and 1 adult Cambodian cynomolgus macaque monkeys were managed by the Core to ensure the services and requested samples were available to meet investigator needs. In addition, 13 adult female and 2 adult male Mauritian cynomolgus macaques with specific major histocompatibility haplotypes were acquired to support individual ART Core user unique needs. New major equipment acquired included an ultrasound probe for evaluating follicle growth and pregnancy determination and a new cold storage unit for Core services and users. Meetings were regularly held with Core users whose research projects are heavily dependent on Core services to identify areas of additional program support and opportunities for protocol advancement. Biannual meetings with the ART Core Advisory Committee were also conducted to identify areas of growth and improvement.

Aim 2: Progress advancing the NHP as a translationally relevant model for this reporting period covers two major areas. First, ART protocol development continues for the cynomolgus macaque model including controlled ovary stimulation, in vitro fertilization, intracytoplasmic sperm injections, embryo culture, embryo microinjection, embryo biopsy, embryo and sperm cryopreservation and embryo transfer. While these techniques are established as common practice in rhesus macaques, few reports detail success in cynomolgus macaques and most require updating. Advances have been made developing a custom controlled ovary stimulation protocol specifically for the Mauritian cynomolgus species as their physiological response is varied compared to conventional (Cambodian) cynomolgus monkeys. Additionally, critical components for successful in vitro culture and fertilization with Mauritian oocytes and embryos have been defined overcoming a previous roadblock for using ART with this subspecies. Complementary to this, embryo transfers with genome modified embryos has begun with the goal to produce the first Mauritian cynomolgus monkey from embryo transfer and the first CRISPR engineered Mauritian biomedical model. Establishing these protocols directly supports a collaboration with an external investigator to create a NHP model for HIV-related therapies using a specific subspecies of cynomolgus monkeys (Mauritian cynomolgus macaques). The second area of protocol development is in direct response to the anticipated increase in use of the Timed Mated Breeding (TMB) Resource at ONPRC. Specifically, a program for monitoring serum levels of steroid hormones to pinpoint the optimal time and duration for pairing of animals for timed mating has been developed. Working in collaboration with TMB staff incorporation of this protocol into the TMB management program has increased pregnancy rates by over 50% since implantation and through continued collaboration future goals are being developed to identify areas to further enhance breeding success.

ASSISTED REPRODUCTION TECHNOLOGY (ART): TRAINING & PROFESSIONAL DEVELOPMENT

Training was provided for Core users across three different labs. Specifically, techniques in post mortem sperm recovery, semen vitrification and thawing, and oocyte recovery from ovarian follicle aspirates were demonstrated. Professional development was provided fo Excluded by Requester to attend the International Embryo Technology Society meeting in Austin, Texas in January 2017 to give a talk on the use of CRISPR technology to develop biomedical models in NHPs.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Protocols	Protocols for utilizing Mauritian cynomolgus macaques for ovary stimulation protocols, in vitro fertilization, embryo microinjection, and embryo culture have been developed and represent a resource of techniques not previously reported in the literature. These protocols directly support the research program of Excluded by Requester creating CCR5 knock-out animals for studies in HIV (SIV) infectivity.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Data or Databases	All data relating to the development of Mauritian cynomolgus ART protocols and the use of CRISPR technology will be submitted for publication in a peer-reviewed journal. The specific use of CRISPR in NHPs was presented at the International Embryo Technology Society conference. During this meeting, external investigators were encouraged to contact the Director of the ART Core to discuss the use of the NHP in their own projects centered on embryo production and genome modification.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5565

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			18,000.00	6,480.00	24,480.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **24,480.00**

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	Unit staff	28.8			118,955.00	42,824.00	161,779.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**161,779.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**186,259.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,000.00
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. Animal lease & setup, per diems, program income	27,790.00
9. Surgery fees, semen collection, blood draws, drug administration	32,070.00
10. Endocrine services, equipment maint contract, miscellaneous other expense	8,350.00
Total Other Direct Costs	**92,210.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**278,469.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	278,469.00	77,971.00
		Total Indirect Costs	**77,971.00**

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)	**356,440.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Endocrine

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The goal of the ONPRC Endocrine Technology and Support Core (ETSC) is to provide intramural (ONPRC and OHSU) and external (academic and industry) scientists with the expertise and facilities necessary for obtaining quality data supporting clinical and pre-clinical research using nonhuman primates (NHPs) and other species in studies relevant to human health and disease. Specifically, the ETSC provides services and support in traditional and new assay technologies, including radioiodination, radioimmunoassay (RIA), organic solvent extraction (Ext), Sephadex LH-20 liquid chromatography (LC), immunochemiluminescense technology using automated clinical platforms, XMAP-based technology (i.e., Luminex 200) for multiplexing protein assays, enzyme immunoassays (EIA), enzyme-linked immunosorbent assay (ELISA), enzyme-linked fluorescent immunoassay (ELFA), and unique bioassays such as those developed for mouse interstitial cell testosterone bioassay (MICT) and monkey luteinizing hormone (LH). Furthermore, the ETSC supports continuous developments in NHP research by validating commercial or existing assays using human antibodies, by developing new assays with antibodies generated in academia, and by partnering with companies to develop and validate single or multiplex assay panels specifically for NHPs. Regular review of resources, personnel training and performance, as well as quality of services offered will be performed by the Core director, oversight committee, and the ONPRC Associate Director for Research to ensure continued success of the Core.

To continue the high-quality services for NHP and non-NHP research provided in the previous funding period, the ONPRC ETSC proposes the following objectives through the next 5-year period of support:

Specific Aim 1: To provide a transparent operating structure for efficient and responsive services for NHP research programs with quality and validated analyses. This will be achieved through cooperation between the Core Director and his staff, the Core Oversight Committee, and the ONPRC Business office. Over the past 40 years, the ETSC has developed or validated more than 50 assays suitable for NHP serum, plasma, cell culture medium, or tissue extract samples. We expect to continue the high standards of service by maintaining close attention to all reagents and procedures, including multiple internal quality controls in all assays, and by enhancing our operation with electronic interactions with users, including sample requests, assay schedules, assay protocols, assay analysis, data reports, and invoicing. Immediate data-return, within an hour or less if necessary, is provided for time-dependent research projects, such as daily monitoring of the menstrual cycle in female NHPs. Regular review of resources, fee structure, performance and quality of services will be performed by the Core Director, the Core Oversight Committee, and the ONPRC Business office to ensure continued success of the Core.

Specific Aim 2: To support internal and external programs for clinical and basic sciences research. The ETSC focuses on providing scientists and clients with state-of-the-art equipment, knowledge, experience, reliability, skills, reasonable rates and well-proven technologies. The Core has acquired and validated assays on both a bench-top (e411) and a high-throughput (e170) Roche clinical automatic platform for analyzing large number of primate samples in clinical and basic research. The Core will continue to provide the capacity to analyze multiple steroid or protein hormones for primate and non-primate species, using chromatography and Luminex technologies, respectively, and to analyze a single steroid or protein parameter by traditional RIA and EIA methods following isolation and purification as necessary.

Specific Aim 3: To develop NHP-specific assays and share with NPRCs and other scientific institutions. The ETSC has initiated cooperation or partnership with academic laboratories or commercial companies to develop NHP-specific assays or panels, including custom-made multiplex monkey cytokine kits, appropriate multiplex metabolic hormonal panels, as well as steroid biosynthesis panels to monitor steroid intermediates and products in a single serum sample. The results of these developments will be shared with all NPRCs as well as the scientific community through specific organizations, NIH-sponsored programs, scientific annual meetings, and on our website.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Endocrine_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Core-Endocrine_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Excluded by Requester are co-authors on an abstract on LC-MS/MS analysis of contraceptive hormones presented at the 2016 Society for the Study of Reproduction Annual Meeting in San Diego. Excluded by plans to submit this work as a publication to the journal Contraception in the early part of 2017. Excluded by also plans to submit an abstract on newly developed LC-MS/MS methods to the American Society of Mass Spectrometry Annual Meeting in Indianapolis in June 2017. The ETSC sends an annual newsletter to Core users (most recently in June 2016), in order to update investigators on Core operations, new assays, and other lab news.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

During Year 58 (May 2017-April 2018) we plan to continue our expansion of sample analysis and method development on the LC-MS/MS platform. We will ultimately transition away from our in-house extraction-RIAs and extraction-chromatography-RIAs for steroids by mid-2017, as these assays will be completely replaced by LC-MS/MS methods. The ETSC will continue to provide high quality data to clients, and develop new methodologies as required by investigator request.

ENDOCRINE CORE: ACCOMPLISHMENTS

During Year 56 from May 1, 2015 through April 30, 2016, the ETSC served 41 internal investigators (ONPRC/OHSU) and 27 external investigators to process 56,982 tests for 69 different assay types, including 22 new assays, with chargeback income of $455,940.57. For the period in Year 57 from May 1, 2016 to December 31, 2016 covered in this progress report, the ETSC has served 290 internal investigators and 219 external investigators, including 5 investigators new to using our Core. We have performed 33,938 tests, with about 65% of these for internal clients and chargeback income of $269,102.52 to date. We anticipate that during Year 57 chargeback income will surpass $400,000.00 and approximately 50,000 tests will be completed for investigators.

Technologies Update: During Year 56, we validated and incorporated 22 new assays across our various platforms into our assay menu, including one new assay for NHP on our Roche Cobas e411 platform, and 19 new ELISAs for either NHP or rodents. In the current Year 57, we've focused on developing and incorporating high-throughput, affordable methods for quantifying steroid hormones and other compounds for investigators. Currently, we offer methods for analyzing 15 steroid and contraceptive hormones, with another 15-20 hormones of various classification, including steroids, peptides, and other small molecules, in some stage of development. We plan to have these assays validated for use in analysis of investigator samples sometime in 2017. We plan to move all steroid hormone assays currently available by in-house extraction-RIA or extraction-chromatography-RIA to LC-MS/MS during 2016. We continue to validate commercial assay kits for use on investigator samples as needed.

Investigator Base and Scientific Interactions: The ETSC maintains a group of investigators who have used the Core on a consistent basis while we continue to expand our client base. For Year 56, we served 68 investigators, with 15 of these being new users of the Core. In the current Year 57, we have worked with 29 internal investigators (2 new) and 19 external investigators (6 new). We continue to serve between 15 and 20 investigators new to the Core each fiscal year. We also continue to advise clients on assays and experimental design in the areas of reproduction, aging, metabolic disease, and cancer research, among others. We strive to serve our client base by providing assay services that focus on sensitivity, specificity, and selectivity.

Reduction of Manual Operations and Mistakes: We have instituted a data checking process for all assays, in which Excluded by Requester will audit all data generated by the Roche automated platforms before they are reported to investigators. Excluded by Requester reviews all data from RIA and ELISA platforms before they are reported to investigators. The addition of the LC-MS/MS platform allows multiple hormones to be simultaneously analyzed in a single sample, reducing the number of manually-operated assays while producing the same amount of data as assays run individually. These data are compiled by Excluded by Requester when they analyze the samples, reviewed by Excluded by Requester and then reported to investigators.

ENDOCRINE CORE: TRAINING & PROFESSIONAL DEVELOPMENT

Excluded by Requester nd staff continued to host Shimadzu scientists on multiple occasions for in-house training on the LC-MS/MS system.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5566

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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.	David		Erikson		Unit Head	78,797.00	1.98			13,002.00	4,941.00	17,943.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **17,943.00**

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						
5	Unit staff	8.91			29,460.00	11,195.00	40,655.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**40,655.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**58,598.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	260.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**260.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	30,412.00
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. Memberships, telecommunications, equipment maint & repair, biohazardous waste disposal	8,443.00
Total Other Direct Costs	**38,855.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**97,713.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	97,714.00	27,360.00
		Total Indirect Costs	**27,360.00**

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)	**125,073.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Flow Cytometry

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Flow Cytometry Support Core was created during the mid-1980s in response to the increase in non-human primate AIDS research. Both the technical capabilities and user base of this Core have significantly expanded in the intervening years, and the Core is now used by researchers from each of the ONPRC's scientific research divisions, animal care staff from the Division of Comparative Medicine, and collaborators from outside institutions.

The Specific Aims of the Flow Cytometry Core are:

Specific Aim 1: Provide an efficient, responsive, and transparent operating structure. The Core Director, Excluded by Requester directly interacts with the users, the Core Oversight committee, the ONPRC business office, and manufacturers to ensure appropriate provision of core services, regular assessment of chargeback fees, and assessment of technology needs. Excluded by Requester along with the other ONPRC research support core directors, reports to Excluded by Requester ONPRC Associate Direcotor for Research.

Specific Aim 2: Provide, maintain, and upgrade the Flow Core's equipment. The Flow Core currently has the same flow cytometers it had at the beginning of the 5-year grant; i.e., two BD FACS Calibur analyzers, two BD LSR2 analyzers, and a BD Aria II cell sorter, although all have had their computers and software upgraded, and both analyzers have been retrofitted with new UV lasers. The analyzers will be available to all users on a self-serve basis, while the sorter will be available only to a limited number of well-trained users. We will continue to have a full maintenance contract with BD to keep the cytometers in peak working condition. During the coming 5-year grant period, we will explore efforts to replace the two decommissioned BD FACS Caliburs with one newer analyzer and add to our cell sorting capabilities by purchasing a cell sorter that can sort very large cells, and can be located outside of a Biosafety Level 3 laboratory.

Specific Aim 3: Train users to operate the equipment in the Flow Core. We will continue training personnel to operate the analyzers on a self-service basis. The analyzers are available on a 24/7 basis to the users. The BD Aria-II cell sorter is operated by Flow Core personnel, or by only a few specially-certified users with independent BSL3 access. Many users require sorts that can take 8-16 hrs, running the instrument well beyond business hours. Core staff remains available at all times for problem-solving.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-FlowCytometry_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Core-FlowCytometry_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Excluded by Requester has incorporated lessons from the Aria training into a special version of the 'Flow 101' course, and has created checklists for instrument operations, and also written up new basic SOPs. By discussions with interested Core users, Excluded by Requester has disseminated information about apoptosis and RNA expression staining. Excluded by Requester also works closely and intensively with Core users who want to make use of cytometry in their research. Excluded by Requester has researched the technical literature to advise inexperienced users how best to prepare samples, and has helped them assess the effectiveness of their procedures on both the LSR analyzers and on the Aria sorter. In 2016, extensive assistance was provided to Excluded by Requester of the Excluded by Requester Lab (CFSE proliferation analysis), Excluded by Requester (budgeting for sort work), and Excluded by Requester (separate labs, panel development).

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In the next reporting period, the Core's two BD LSR-II analyzers will have the baseline voltages for their signal detectors optimized again, for alternate configurations (used by different users), so as to minimize spectral overlaps prior to compensation. This is a very time-consuming process which can dramatically improve data quality for users making use of more than 6 simultaneous colors. It was less necessary in the past, when most users were favoring use of only the blue and red lasers. Now that users are making more use of the Brilliant dyes on the violet laser, which have cross-laser overlap issues, this optimization is essential. In addition, this optimization will be extended to the BD Aria-II cell sorter, which until recently has been used with 6 or fewer colors.

FLOW CYTOMETRY CORE: ACCOMPLISHMENTS

Specific Aim 1: Provide an efficient, responsive, and transparent operating structure. The previous online scheduler was replaced during 2016 with a new scheduler developed by ONPRC IT staff, using PRIMe, the ONPRC implementation of Proprietary Info

Specific Aim 2: Provide, maintain, and upgrade the Flow Core's equipment. In December 2016, one of the BD LSR-II analyzers was moved from its original location (VGTI first floor) to the same room as the other BD LSR-II analyzer (NSI third floor). This move allowed the repurposing of the VGTI space, and provided some conveniences to both users and Flow Core staff.

Specific Aim 3: Train users to operate the equipment in the Flow Core Excluded by Requester created a 4-hr course titled "Flow 101." Day 1 is a classroom overview of the theory of flow cytometry, and the theoretical considerations of trouble-shooting, compensation, and panel design. Day 2 is a practicum at a cytometer (either analyzer or sorter), and goes over specific hardware and software operation. A Day 3 is available to any users who request it, and involves direct assistance with the setup of actual templates and the first running of samples from novel experiments. This class was conducted 6 times, for 14 users, in 2015. In addition, four users were assisted in challenging cell-sorting projects that expanded the skillset of the Core. In particular, the Core staff improved its expertise in performing single-cell sorts into multiwall plates for PCR work.

FLOW CYTOMETRY CORE: TRAINING & PROFESSIONAL DEVELOPMENT

In 2016, the Flow Core assistant attended the CYTO2016 conference held in Seattle, and attended workshops on quality assurance and automating methods.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

In 2016, the Core hopes to add a second sorter (BD FACSFusion), with money provided by OHSU (currently in process).

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5567

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			35,995.00	13,678.00	49,673.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **49,673.00**

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 staff	2.3			9,591.00	3,645.00	13,236.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**13,236.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**62,909.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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. Equipment maint contract, miscellaneous other expense	59,862.00
Total Other Direct Costs	**59,862.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**122,771.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	122,771.00	34,376.00
		Total Indirect Costs	**34,376.00**

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)	**157,147.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Imaging and Morphology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The overall goal of the Imaging and Morphology Support Core (IMSC) is to provide the ONPRC scientific community access to state-of-the-art instruments, expertise, and services in support of their light microscopy image acquisition and analysis needs. The IMSC offers advanced imaging, specialized for the needs of nonhuman primate (NHP) research, at the molecular and cellular level. Major groups of services include confocal microscopy and derived fluorescence techniques for studies of molecular localization and interactions, stereology for quantitative analysis of morphometric tissue features, and laser-capture microdissection for gene expression analyses in specific cells. Major instruments used to support IMSC goals include a Proprietary Info confocal Proprietary Info Proprietary Info a Marianas digital workstation Proprietary Info and Proprietary Info Core personnel provide expertise in experiment planning and choice of most adequate instrument and method, training for instrument use customized for each specific need, technical support in image acquisition and troubleshooting, and image analysis and stereology.

Specific Aim 1. Provide an efficient, responsive, and transparent operating structure. This will be achieved through cooperation between the Core Director and the staff, the Core Oversight Committee, and the ONPRC Business office.

Specific Aim 2. Provide state-of-the-art instruments that satisfy the major, most common needs for advanced microscopy techniques NHP studies. To this aim, the core is responsible for identifying instrument needs, procuring funds, and purchasing instruments. The Core currently offers a Proprietary Info confocal, a 3I's Marianas Imaging workstation, and an MBF Bioscience system. All instruments are covered by service contracts and undergo stringent periodical quality-control procedures to ensure optimum function. For each instrument, users receive a minimum three hours of one-on-one training before gaining independent access. We are in the process of identifying the best equipment that would serve most of the users using our annual user survey.

Specific Aim 3. Provide expertise, tools, and training for quantitative image analysis. To this goal, the IMSC has developed stereology and digital image processing and automated analysis expertise. The MBF system and the Marianas are the most appropriate tools for running a stereology-based analysis as they have the routines for uniform systematically subsampling large areas and (particularly the StereoInvestigator within MBF) collections of probes for estimating numbers, lengths of fibers, surface area, volumes, etc. Neurolucida is used for neuron tracing and analysis. ImageJ and FIJI are the tools of choice for image analysis for which the core offers basic and advanced training and automation macros. Volocity is used primarily for advanced 3D rendering. The core has acquired Olympus CellSens Dimension Desktop (for post-processing and analysis – can open different file formats) software and the Visiopharm VIS Stereology offline module for stereological analysis of images. The core also provides support for CellProfiler (Cell Image Analysis Software distributed under a GPL v2 public license).

Specific Aim 4. Provide expertise, training, and access to laser-capture microdissection (LCM) for the isolation of pure populations of cells. To this goal, IMSC maintains a list of protocols for tissue processing, an Arcturus XT LCM system and a close collaboration with ONPRC's Cell and Molecular Support Core and OHSU's Microarray Core to facilitate downstream applications for the microdissected materials.

Specific Aim 5. Act as an expert resource in microscopy and digital image analysis by providing consultation in experiment planning and execution, general microscopy and image-analysis knowledge, benefiting primarily the ONPRC and OHSU communities, but also serving as a regional resource in the field. To this goal, the IMSC keeps up-to-date with new methods, tools and applications, organizes periodic seminar and workshops and hosts trainees and student interns. The core has been providing support and training on slide scanners available on campus (Olympus Slide Scanner VS120 S5). Users were provided training using the CellSens Dimension Desktop software for image analysis.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Imaging_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Core-Imaging_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

A detailed description of IMSC services is available on the ONPRC website.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We have relocated the microscopes to the new space with minimal distruption to users. New protocols are been tested for imaging and image analysis using the available software. We are getting new users who wanted to use the available software for image analysis and post-processing. These images are obtained using individual lab microscopes and are saved in different formats like Big Tiff, JPEG2000, TIFF, JPEG and other proprietary formats and they are large, specialied images for other free software to handle. We are planning to write a Shared Instrumentation Grant (NIH S10) towards the purchase of a whole slide imaging slide scanning system.

IMAGING AND MORPHOLOGY SUPPORT CORE: ACCOMPLISHMENTS

The IMSC was used by 15 investigators in the current funding period. Usage comprised 476 hours for the confocal, 33.25 hours for the MBF Bioscience, 7.50 hours for Marianas, and 3 hours for Arcturus LCM systems.

IMAGING AND MORPHOLOGY SUPPORT CORE: TRAINING & PROFESSIONAL DEVELOPMENT

Within the first seven months of the last grant cycle, 7 new users were trained to use IMSC instruments. Training involved explanations on the theory of image formation and fluorescence as well as the design and preparation of imaging experiments.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Other	New experimental design to capture images and image analysis are continuously developed and refined.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Software	Macros for FIJI image analysis.
Software	We are providing support for training, troubleshooting and image analysis for microscopes available with other groups including the slide scanner. We are offering training to interested users to use our image analysis and post-processing software.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5568

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			50,738.00	12,915.00	63,653.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **63,653.00**

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 staff	1.58			5,335.00	1,358.00	6,693.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**6,693.00**
					Total Salary, Wages and Fringe Benefits (A+B)		**70,346.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	4,290.00
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. Equpment maint contract, registration fees, software upgrade, miscellaneous other expense	42,092.00
Total Other Direct Costs	**46,382.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**116,728.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	116,728.00	32,684.00
		Total Indirect Costs	**32,684.00**

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)	**149,412.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Molecular & Cell Biology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Molecular and Cellular Biology Support Core (MCBSC) provides services in support of molecular biology and cell culture for ONPRC investigators. The goal of the MCBSC is to provide flexible, state of the art, time-effective, cost-effective services to facilitate ONPRC investigators' utilization of molecular and cellular biology. Such services are absolutely fundamental to cutting-edge nonhuman primate research. Molecular biology services include both Next-Gen and capillary DNA sequencing, high-throughput genotyping, high-throughput real-time quantitative PCR, digital PCR, preparation of monkey genomic DNA, generation of monkey-specific cDNAs, establishment of monkey-specific, real-time quantitative PCR assays, large-scale plasmid and phage preparation, fully automated small-scale and medium scale DNA and RNA preps, and supply of a limited number of reagents and training. Cell biology services include preparation of lentiviral vectors, specialized media and reagents, storage, freezing and amplification of cell lines, preparation of coated culture ware and cover slips, transfection and cloning of cell lines, establishment of primary cell lines, training and access to specialized equipment including liquid handling robots, automated DNA/RNA/protein isolation platforms, real-time quantitative PCR platforms, scanning fluorometer, bioanalyzer and plate readers.

The focus of the next grant period will include continued delivery of existing services, provision of more automated and high-throughput services, delivery of medium-scale Next-Gen sequencing services, working closely with the ONPRC primate genetics program for analysis of colony genetics, ancestry, parentage and MHC genotyping, and meeting new needs of primate center investigators. Our specific aims for the next period are as follows:

Specific Aim 1: To provide an efficient, responsive, and transparent operating structure.

Specific Aim 2: To provide state-of-the-art, competitively priced molecular biology services.

Specific Aim 3: To provide state-of-the-art, competitively priced cell biology services.

Specific Aim 4: To work closely with the Primate Genetics Program to enhance colony management and genetic analysis of the colony.

Specific Aim 5: To work closely with similar cores at the OHSU main campus and Proprietary Info to leverage delivered services.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-MCB_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Core-MCB_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

By OHSU and ONPRC internal and external web sites as well as direct emails to all ONPRC scientific staff.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Continue to focus on next-generation sequencing in terms of library construction, quantitation, quality control, training, and sequencing. We will also continue to work with multiple center investigators to develop new methods to further the genetic characterization of the center colony and to facilitate new research directions in general. We will also continue to focus on emerging single-cell and limited cell population sequencing technologies using both oil droplet-based apporaches and closely coupling cell sorting to sequencing. For this our focus will primarily be on library construction and bioinformatic support. We will also continue our emphasis on excellent customer service with timely delivery, cost effectiveness and making sure we offer services most desired by customers.

MOLECULAR AND CELL BIOLOGY SUPPORT CORE: ACCOMPLISHMENTS

This has been another strong year for the MCB Core. The Core continues to reach new levels of delivered services to investigators. This reflects continuing focus on next-generation sequencing in terms of library construction, quantitation, quality control, training and sequencing. The Core is also working with multiple center investigators to develop new methods to further the genetic characterization of the center colony and to facilitate new research directions in general. High numbers of lentiviral vectors have also been delivered to facilitate gene expression and knockdown studies. Emphasis on excellent customer service with timely delivery and cost effectiveness continues.

MOLECULAR AND CELL BIOLOGY SUPPORT CORE: TRAINING AND PROFESSIONAL DEVELOPMENT

Emphasis on training of all services that the Molecular Core delivers continues. Particular emphasis on DNA sequencing, RNA and DNA quantification, viral vector and cell culture training continues. A new area of emphasis is training in preparation and quality control of libraries for Next-Gen sequencing as well as training investigators on newly acquired systems for automated DNA and RNA isolation platforms.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Research Material	Capillary sequencing, Next-Gen sequencing, library preparation, library quantification, library quality control, qPCR on multiple platformers, lentiviral vector construction, cell culture, transfection and infection, calcium kinetics, robotic liquid handling, automated DNA and RNA preparations, nucleic acid quantification and quality analysis. The technologies and results are shared primarily through the research papers and presentations of our customers. In addition, we spread technologies locally through trainings, one-on-one communications and seminars/presentations at division meetings.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Other, Other	Resource sharing is conducted as per NIH policy. Most sharing is the responsibility of investigators to whom services are delivered.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5569

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			12,495.00	3,748.00	16,243.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **16,243.00**

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						
4	Unit staff	14.26			73,699.00	22,110.00	95,809.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**95,809.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**112,052.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	1,080.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**1,080.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	48,600.00
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. Equipment maint contract, shipping, laboratory service	25,419.00
Total Other Direct Costs	**74,019.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**187,151.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	187,151.00	52,402.00
		Total Indirect Costs	**52,402.00**

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)	**239,553.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Molecular Virology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The overall purpose of the Molecular Virology Support Core (MVSC) is to provide high quality, affordable, and state-of-the-art virology services to support the local and national mission of the Oregon National Primate Research Center (ONPRC) that is centered on non-human primate (NHP) research. NHPs are an invaluable model for studies of viral pathobiology and immunology and for the evaluation of recombinant vaccines and viral gene therapies. The Core supports investigators through an array of specialized virology services and the provision of technical expertise. Key focus areas are 1) custom production and quality control of viral vectors, viral stocks, and antigens; 2) sensitive viral diagnostic assays to study virus spread after infection, to monitor viral tissue distribution, and to assess viral antibodies; and 3) provision and development of key reagents and standardized assays. In addition, the Core offers user training in virology techniques and safe handling of infectious agents, and assists in maintaining proper compliance with local institutional biosafety requirements.

In the previous grant period, the MVSC underwent structural and programmatic changes in order to position itself for success in a rapidly changing research environment and to best meet the virology needs of the local scientific community. In particular, the Core has made improvements to its management and infrastructure and has begun developing an array of new state-of-the-art virology services that capitalize on its expertise in viral production and diagnostics. Early indicators of success have been an increase in service utilization and user diversity. During the next grant period, we will continue building on these gains by further improving and tailoring our services to the programmatic needs of the ONPRC. To that end, the following specific aims are proposed:

Specific Aim 1. Provide an efficient, responsive, and transparent operating structure. This will be achieved through cooperation between the Virology Core Director and staff, the MVSC Oversight Committee, and the ONPRC Business office. The MVSC will further improve lab efficiency and administration in order to facilitate core operations, service use, and information flow. Key efforts will be 1) continuation of current efforts to standardize methods and improve efficiency in the MVSC laboratory through optimized protocols and automated procedures; 2) development and implementation of a viral load service module in the new campus-wide animal record and scientific database system to facilitate service requests, data analysis, and data sharing; and 3) evaluation of other potential service and administrative modules (e.g., billing, laboratory notes, inventory and freezer management, internal data storage, etc.) that would most benefit the Core and users.

Specific Aim 2. Provide high-quality virology services and to appropriately expand services and expertise in support of ONPRC's mission. The Core will continue to implement and improve its ongoing and new services, focusing on areas that foster growth of ONPRC's scientific programs and that are most important to investigators. These include cytomegalovirus (CMV) and HIV/SIV AIDS research, as well as gene transfer and gene therapy using adenoviral and adeno-associated virus (AAV) vectors to support diverse research areas such as neuroscience, reproduction, and metabolic disease. The goals, progress, service quality, and organization of the MVSC will be regularly reviewed by the MVSC Director, the Core Oversight Committee, and the Associate Director for Research.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Virology_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The MVSC director is regularly invited to give presentations at various venous to promote the services and technologies available and discuss latest developments, improvements, and collaborations.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The MVSC will continue responding to user needs by performing appropriate services and developing and improving services and capabilities as needed and in consultation with the core oversight committee.

MOLECULAR VIROLOGY: ACCOMPLISHMENTS

In the P51 core grant YR57, the overall demand for MVSC for virology services has continued to be strong and diverse. The user base has increased slightly to a total of 24 investigators (18 from OHSU/ONPRC, 6 external entities) that have utilized MVSC services so far this year.

In the area of viral diagnostics, the MVSC has performed nucleic acid extractions from PBMC (540) and tissues (602), and viral load determinations in those compartments (1,271). The MVSC also provided plasma viral load assays for simian-immunodeficiency virus (SIV) and simian-human immunodeficiency virus (SHIV) and related plasma processing services (983 samples each).

Viral production services include adeno-associated virus (AAV) vectors (41 small and 20 medium/large productions), and rhesus cytomegalovirus (RhCMV) (32 seed stocks and 94 large stocks). Other notable services provided were virus co-cultures (150) and AAV neutralizing antibody screening and titration (97). No adenoviral vector productions have been requested so far this year. The MVSC has also been providing purified antigens viral antigens for Expanded Simian Pathogen-Free (ESPF) surveillance.

Services have been continuously improved based on core and investigator needs. Some quantitative PCR (qPCR) assays for SIV and CMV dectection have been re-designed, in order to increase performance and sensitivity. Another example are improvements to mycoplasma testing methods used routinely used by the MVSC to screen virus cell cultures provided by collaborating investigators.

The MVSC continues to be a designated core component for a multi-investigator HIVRAD P01 (AI094417-01 Picker (PI), “Development of an Effector-Memory T cell AIDS Vaccine”; provides 10% salary support for MVSC Director). The core is closely involved with several current CMV and HIV research grants to different ONPRC investigators, which increasingly make use of its recently developed service capabilities for large tissue processing and ultrasensitive virus detection by nested qPCR. One example is an R01 on SIV reservoirs (HD080459-01 Haigwood (PI), “Reducing Latent Viral Reservoirs in Infant Macaques”; provides 5% salary support for MVSC Director).

The MVSC is one of the ONPRC cores selected for the development and beta-testing of new core service billing and scheduling modules in the PRIME Proprietary Info software, which are currently in development.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Protocols	The MVSC has recently developed a new method for rapid production (RP) of AAV vectors using ultrafiltration, which is scalable and cost-effective, and which does not require ultracentrifuges and density gradients. In addition, in collaboration with the [Excluded by Requester] laboratory at OHSU, we were able to demonstrate that RP-based AAV vectors can be effectively used for gene transfer to the mouse liver, without apparent toxicity and with transduction rates comparable to AAV vectors purified by iodixanol density gradient. The results of this collaboration have been summarized in a manuscript and recently submitted to a peer-reviewed journal.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5570

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			25,939.00	8,560.00	34,499.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **34,499.00**

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						
6	Unit staff	19.44			72,213.00	23,830.00	96,043.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**96,043.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**130,542.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	45,900.00
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. Equipment maint contract, shipping, laboratory services, hazardous waste disposal, telecommunication	2,228.00
Total Other Direct Costs	**48,128.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**178,670.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	178,670.00	50,028.00
		Total Indirect Costs	**50,028.00**

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)	**228,698.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: MRI

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Magnetic Resonance Imaging Support Core (MRISC) operates a Proprietary Info whole-body MRI system housed in a free-standing, 2500-sq. ft. facility in close proximity to the Animal Services Building. The MRISC's objective is to capitalize on the translational value of MRI-based investigations in non-human primate (NHP) research. The Core's mission is to enhance existing ONPRC research programs by providing flexible MRI facilities and expertise that are optimized for NHP subjects, enabling investigators to undertake strategies analogous to human clinical practices, and to utilize the close similarity between human and NHP anatomy and physiology to develop new MRI research and in vivo diagnosis techniques and applications. In order to facilitate these goals, the MRISC relies heavily on a mutually beneficial relationship with the OHSU Advanced Imaging Research Center (AIRC), in which the MRISC supports the efforts of several AIRC faculty and staff to provide infrastructure and technical support of the ONPRC MRISC.

The fundamental service provided by the MRISC to ONPRC investigators is assistance performing MRI exams of sedated NHP subjects. MRISC staff are available for each exam. Equipment and supplies for anesthesia and MRI-compatible physiological monitoring and regulation are provided by the MRI facility. A veterinary "on-call" system has been arranged with ONPRC surgical staff to address complications such as adverse reactions to anesthesia or experimental procedures immediately prior to, or during, the MRI exam. Imaging infrastructure services provided by the AIRC include safety and operator training sessions for ONPRC scientists, the construction of MRI-related instrumentation specialized for NHP MRI experiments, maintenance of computer resources for data access and archiving, quality/assurance oversight for the system, interface with ONPRC facilities staff to manage system requirements (such as electrical power, chilled water, etc.), and maintenance of a web-based scheduling system.

The overall goal of the MRISC is to provide ONPRC investigators state-of-the-art magnetic resonance imaging and spectroscopy services through pursuit of the following specific aims:

Specific Aim 1: Organization. Provide an efficient, responsive, and transparent operating structure. This will be accomplished by providing access to projected fees for MRISC for a 5-year period extending 5 years and through regular meetings with the MRISC oversight committee.

Specific Aim 2: Project Design. Provide the ONPRC research community with consultation and advice on appropriateness and/or feasibility of MRI experiments, and to assist with optimizing experiment design.

Specific Aim 3: Data Acquisition. Assist researchers in the development of data acquisition procedures, most typically through the development and implementation of imaging protocols.

Specific Aim 4: Data Analysis. Assist users of the ONPRC MRISC in the development of data analysis procedures, and train ONPRC personnel, either within the MRISC or within an investigator's laboratory, in implementation of the data-analysis plan.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-MRI_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Core-MRI_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Results from the MRI core has been shared through various publications and scientific meetings.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Continued support of ONPRC MRI core staff to provide services to ONPRC and OHSU investigators.

The next priority for instrumentation updates is to upgrade the MRI system to a Proprietary Info generation scanner. ONPRC scientists will benefit from the resulting improved gradient system capabilities. The cost of such an upgrade is approximately $1.5M, and therefore in the next year a strategic plan for obtaining funds for this upgrade will be developed.

MRI: ACCOMPLISHMENTS

The MRI core has provided data acquisition and analysis services to support laboratories from all four ONPRC scientific divisions, as well as multiple additional OHSU departments.

MRI: TRAINING AND PROFESSIONAL DEVELOPMENT

The primary objective of the MRI core is to provide services. However, ONPRC and broader OHSU research staff have been trained in data acquisition and analysis of MRI data. This takes place through ONPRC and OHSU research support of ONPRC MRI core staff.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Other	The ONPRC MRI core supports the development of resources which are shared, such as a rhesus macaque brain atlases which available through the NITRC data repository, and the nonhuman primate aging resource.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5571

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary		EFFORT		3,133.00	1,003.00	4,136.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **4,136.00**

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						
	Secretarial/Clerical						
6	Unit staff	3.24			15,873.00	5,079.00	20,952.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**20,952.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**25,088.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	100.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**100.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	550.00
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. Equipment maint contract, software maint contrat, services & fees	14,262.00
Total Other Direct Costs	**14,812.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**40,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	40,000.00	11,200.00
		Total Indirect Costs	**11,200.00**

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)	**51,200.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Primate Genetics

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The rapid development of the scope and sophistication of a number of capabilities in the Primate Genetics Program over the past funding period has justified their incorporation into a new Primate Genetics Support Core. The focus of the next grant period will include the systematic delivery of these services, using state-of-the-art methods to meet the expanding emphasis on genetic analysis in NHP management and research. Incorporation of next-generation sequence (NGS) methods and high-throughput genotyping analysis will continue to require integration to insure the seamless and efficient use of service resources. Our specific aims are as follows:

Specific Aim 1: Provide an efficient, responsive, and transparent operating structure. This will be achieved through cooperation between the Core Director and their staff, the Core Oversight Committee, and the ONPRC Business office.

Specific Aim 2: To collect and manage a comprehensive ONPRC NHP DNA Bank. The DNA Bank is a centralized resource to insure the availability of high quality genomic material for both colony and research analysis.

Specific Aim 3: To provide state-of-the-art genotyping services. Genotype assays to establish macaque parentage, ancestry and MHC expressed allele haplotypes inform colony management decisions. Additional genotype analyses, such as for TRIMCyp and 5-HTTLPR, are available as needed.

Specific Aim 4: To provide state-of-the-art bioinformatics services. Dedicated bioinformatics personnel provide state-of-the-art support for the analysis of high-density data, such as MHC expressed-allele analysis, user support for the Illumina MiSeq sequencer (operated by the MCBSC), and ONPRC genomics research applications.

Specific Aim 5: To provide comprehensive colony genetic analysis. This critical service informs ONPRC colony management decisions for breeding group formation and potential animal sale or research assignment, and to evaluate genetic diversity overall.

Specific Aim 6: To provide biostatistics support. This service leverages the Core's biostatistics expertise to evaluate NHP health measures and treatment efficacy, as well as pre- and post-award research grant support.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Genetics_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will continue to use cutting edge technologies to characterize the ONPRC macaque colonies. We will apply new fully developed genetic metrics analysis methods to analyze and monitor the diversity of the ONRPC rhesus macaque colony and to identify candidates for assignment or sale. We plan to continue providing Bioinformatics and Biostatisitcs Services to ONPRC investigators, pending P51 funding.

PRIMATE GENETICS: ACCOMPLISHMENTS

The request for ONPRC macaque breeding colony genetic characterization has accelerated in this past year for macaque ancestry analysis (increasing from 30 to 170 individuals) and MHC expressed allele assays (increasing from 515 to 720 individuals), with the additional new requests for custom MHC analysis of 50 additional subjects. The 96 SNP parentage assay was transitioned to the Fluidigm platform and was validated for accuracy and replication. The ONPRC DNA bank archived more than 690 NHP samples for future genomic extraction and distributed samples to 8 investigators. A new genotyping assay to enable the detection of the NCL – CLN7 mutation in Japanese macaques was developed and used to screen 120 subjects. Summary genetic analyses for the U24 ESPF colony were provided for the submission of the new U42 application. Genetic value analysis was performed to inform the colony genetic management of all rhesus and Japanese macaque breeding groups. The ONPRC Bioinformatics and Biostatistics services were evaluated using a survey format to gauge customer satisfaction of the users both at OHSU and in each ONPRC research division.

The new ONPRC PRIMeSeq database was expanded to provide a common resource to analyze or access genomic information gathered on the ONPRC macaques. PRIMe-Seq is now available for automated RNAseq analysis, DNA sequence variant calling, and DNA methylation analysis.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Protocols	We have developed novel protocols for characterizing sparse genome-wide genetic markers using genotyping-by-sequencing in the rhesus macaque genome, and for using these sparse markers to guide cost-effective, pedigree-based inference of dense genetic markers throughout the genome, without the requirement for expensive whole-genome sequencing on all animals. This approach was published in 2016 in BMC Genomics and is being implemented in a funded R24 grant aimed at whole-genome characterization in the pedigreed breeding colony of rhesus macaques at the ONPRC Excluded by Requester Excluded by Requester
Software	We have developed a R-based software package for implementing novel algorithms for managing population genetic diversity in large breeding colonies of non-human primates. These algorithms and software are aimed at using pedigree information to calculate colony kinship, allelic diversity, individual genetic value, and ideal breeding group design in order to maximize population genetic diversity and health. This software is being made available to genetic and/or colony managers at all national primate research centers this fiscal year, by the NIH-supported Genetic and Genomics working group.
Physical collections	During the past year, we have begun collecting EDTA plasma for the ONPRC DNA Bank, in addition to the standard DNA sample collection. This expansion of physical sampling for the DNA Bank was undertaken based on expressed interest by numerous investigators at the ONPRC and OHSU, and was approved by the Oversight Committee for the Colony Genetics unit of the Primate Genetics Section.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Data or Databases	Colony genotype data generated are deposited into PRIMe for access by ONPRC staff. Genomic data is downloaded to public databases (dbSNP, SRA) for public access.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

Reduced funding support may require the reduction in some provided services in the coming year.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5572

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary		EFFORT		14,669.00	5,134.00	19,803.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **19,803.00**

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						
11	Unit staff	45.02			194,649.00	64,700.00	259,349.00
11	**Total Number Other Personnel**					**Total Other Personnel**	**259,349.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**279,152.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,240.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,240.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	42,916.00
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. Laboratory service, software maintenance, ACC storage, miscellaneous other expense	75,692.00
Total Other Direct Costs	**118,608.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**400,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	400,000.00	112,000.00
		Total Indirect Costs	**112,000.00**

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)	**512,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Neuroscience

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Division of Neuroscience has established itself as a national and international leader in the fields of pubertal development, addiction, metabolic disease, healthy aging, macular degeneration, neurodegenerative diseases and primate genetics. Further, we have emerging expertise in therapeutic neural stem cell biology, motor system dysfunctions, epigenetics, primate informatics, in vivo MRI imaging and gene therapy in NHPs.
This research is organized within the Division along the lifespan of the organism, from in utero to advanced age. Scientists in this Division utilize NHP models of human disease processes as well as normative studies of NHP to understand fundamental aspects of brain development, puberty, biological rhythms, immune senescence, and cognitive decline. The Division produces and utilizes specific technologies that optimize the information obtained from our NHP models, including novel methods to acquire in vivo imaging data, measure cognitive performance, introduce and assess genetic therapeutics, provide functional neuroanatomical links to behavior, and identify informative phenotypes for genetic analysis of traits. Our longitudinal approaches in the NHP models provide translational bridges between animal models and human nervous system dysfunctions where baseline values or the impact of environmental variables are difficult if not impossible to measure/control in humans. This translational effort involves clinical partners at both our parent institution OHSU and in other national clinical centers. With the numerous high-throughput and repeated phenotypic measures gathered across all laboratories, the Division provides an unprecedented opportunity to provide tissue/data repositories as national resources for primate nervous system disorders. Further, these extensive phenotypic measures provide an opportunity to identify specific and sensitive biomarkers for disease progression or response to treatment.
The Division of Neuroscience also engages in specialized training to graduate students, postdoctoral research fellows, and visiting scientists and these activities increase our interactions with the basic science departments at OHSU. Our faculty members hold appointments in, and actively contribute to, the three main OHSU Graduate Programs, namely, the Department of Behavioral Neuroscience (BNS) graduate program and the cross-departmental graduate programs in Neuroscience (NGP) and in Molecular and Cellular Biosciences (MCB). Finally, the Division serves as a regional, national and international resource for integrative neuroscience research because of its unique capabilities to conceptually and experimentally link neural functions of invertebrate and other vertebrate laboratory animal models to those of nonhuman and human primates.

To advance our knowledge of primate nervous system development, function and disease we addressed the following specific aims:
Specific Aim 1: Develop and use NHP models of a human nervous system disease/disorders as well as normative processes to provide a deeper understanding of our primate neuroscience.
Specific Aim 2: Identify potential therapeutic target(s) to alter the course of the disease/disorder
Specific Aim 3: Promote the further development and implementation of specialized technologies that will uniquely inform NHP research.
Specific Aim 4: Continue to train the next generation of research neuroscientists using NHP models.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Neuro_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Neuro_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The Division of Neuroscience disseminates research findings through national and international conference presentations, publications in peer-reviewed journals, data repositories, and invited lectures. Since May, we have had 40 peer-reviewed publications in top rated journals including Nature Neuroscience, Cell, Neuron, Endocrinology, Clinical Science (London), J. Neuroscience, Addiction Biology, Frontiers Neural Circuits. etc. We also have 2 tissue banks (R24) based on monkey models of disease awarded to Division scientists that disseminate tissue and data nationally to requesting laboratories. We participate in all ONPRC outreach activities, in OHSU outreach activities and in community outreach, particularly the annual "brain fair" at the Portland Museum of Science and Industry. Finally, we participate in congressional staff visits as they arise and speak with the press when high impact findings are published.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The Division of Neuroscience now has a critical mass of investigators interested in understanding brain circuity at the level of manipulating circuitry to alter the course of disease. In the next year we plan to apply our advances in MRI imaging to define neural circuits mediating specific behaviors with resting state connectivity. We recently made progress in showing aggressive traits involve specific synchrony between the central amygdala and the prefrontal cortex. This demonstration will be expanded beyond temperament to neural adaptations in the addiction process, maternal-infant bonding, aging, and neurodegenerative disorders such as Batten and Huntington's. The U24 Excluded by Requester U24 Excluded by Requester U01 Excluded by Requester cluster of grants from the NIAAA under the consortium "Integrative

Neuroscience Initiative on Alcoholism" aka INIA) was competitively renewed for another 5 years anchoring in both large scale genomics and MRI imaging in the Division. Having now secured funding for alcohol use disorder and Huntington's disease, we will begin trials of neuron specific gene therapeutic approaches to treat neurodegenerative disorders. We will expand our cognitive testing in NHP models by providing a selection of on-line cognitive tasks for investigators to choose from and download to the computer controlled touch screens. Excluded by Requester plan on investigating, for the first time in a primate, the development of foveal vision and the cognitive implications of developmental trajectories of this circuitry Excluded by Requester will be continuing to develop the DREADD technique in NHP brains and will likely be instrumental in several collaborative grant applications developing this technique Excluded by Requester and colleagues are beginning to publish the in utero imaging of the developing brain, a milestone in brain development techniques that has an enormous potential for translational application. As in all previous years, our collaborative efforts with all other Divisions at the ONPRC will continue. Finally, we will continue to publish high quality papers and applications for federal, foundation, industry and philanthropic funding.

DIVISION OF NEUROSCIENCE: ACCOMPLISHMENTS

Major Activities:
The Division has integrated information across multiple levels of analysis and scientific disciplines, become a leading center for neuroscience research at OHSU, created resources for local, national and international neuroscience research, established clinical partners at OHSU and other universities and health centers to validate the NHP model, helped to train the next generation of scientists, successfully maintained a strong funding base, published our research findings in top tier neuroscience journals, extensively disseminated our research findings at international, national, regional and local neuroscience scientific meetings.

Specific Objectives and Significant Results: The Division is organized into scientific expertise groups that use common NHP models, common technologies and/or address common scientific approaches. Our objectives and results are best described within each of these scientific groups:

The genetics group: Leveraged the power of the ONPRC pedigreed macaque population and state-of-the-art genomic approaches to discover the genetic determinants of human diseases. They continue to make considerable progress in building the informatics infrastructure necessary for large scale genomic and epigenomic characterization of the NHP populations. This group tackled the arduous task of colony-wide phenotypic characterization. They have identified specific genes of interest and epigenetic changes of high relevance to alcohol addiction, macular degeneration, demyelinating disease and, most recently, Battens Disease. They utilize the pedigreed rhesus and Japanese macaque population of the ONPRC. They continue to show the uniqueness of epigenetic modifications that may provide breakthrough findings in cancer, cardiovascular disease, anxiety disorders, obesity/adiposity, and age- associated cognitive decline. Faculty members in this group head the genetic service core, the DCM Japanese Macaque resource and the Knight Cardiovascular Institute's epigenetics core.

The neuroendocrine group: Leveraged NHP models of normal development disease such as pubertal development and neuroendocrine dysfunction caused by alcohol addiction, age-related disorders, neurodegenerative diseases, and nutritional challenges. Sex differences and the effect of menstrual cycle on aging and addiction models is prominent. Newly emerging focus has been on neuroendocrine disorders caused by epigenetic misinformation, environmental toxins impacting neuroendocrine development, treatment of neuroendocrine and central nervous system disorders using modified viruses as delivery vectors for gene therapy.

The neurodegenerative group: Leveraged the power of the ONPRC rhesus and Japanese macaque population and state-of-the-art imaging, histological and surgical approaches to discover mechanisms underlying the initiation and progression of neurodegenerative diseases and to develop experimental therapies for these diseases. This group has made progress in understanding multiple sclerosis, Huntington's disease, Batten's disease, age-related macular degeneration, age-related cognitive decline, vascular cognitive impairment, chemotherapy-induced cognitive dysfunction, and alcohol-induced cognitive dysfunction. Progress was made towards translational gene therapeutics for Huntington and Batten's disease, the development of novel neurosurgical strategies to deliver viral vectors to the primate brain and the development of a non-human primate model of Huntington's disease.

The addiction group: Leveraged the translational significance of nonhuman primates with the Division of Neuroscience's expertise in addiction models to create a local, national and international resource for addiction research for biomedical (NIH) and Industry research into the causes and cures for substance use disorders. This group has developed state-of-the-art operant drinking and cognitive testing panels with computer automation. They have extended the NHP model to include nicotine self-administration and in utero models of fetal alcohol syndrome disorders. They have published extensively on longitudinal evaluations of brain damage through *in vivo* structural and functional MRI imaging, ex vivo slice recordings, and neuroimmune assessments of brain and organ damage. Through the Monkey Alcohol Tissue Research Resource (www.matrr.com), they have provided high quality tissues to over 32 laboratories to advance the understanding of the NHP model. Progress was made towards expanding new touch screen technology and the electronic infrastructure, with the goal of applying this to novel social group housing for assessing addictive behavior within a social setting.

Faculty member in this group also serves as the director of the ONPRC molecular biology core and the Divisional electrophysiology core.

The aging group: Used an integrated multidisciplinary approach to elucidate the mechanisms that underlie normal and pathological aging in order to help develop safe and effective therapies for human age-related disorders. This group made considerable progress in showing environmental and dietary factors that can influence the development of age-related neuropathologies. Specific projects of focus were age-related disruption of circadian rhythms and sleep-wake cycles, age related cognitive impairment, postmenopausal behavioral changes, and immune senescence. Progress was made on understanding the neurobiological basis of post-menopausal hot flashes, sex differences in cognitive decline and pathologies of the skeleto-muscular system and metabolism. Faculty member in this group also serves as the Director of the DCM Aging resource.

Key outcomes: An arguably key metric of outcome on a Divisional level is the amount of funding secured through the peer-review process, disease-specific foundation support and industry applications. Below is the current funding level of the Division of Neuroscience.

Our funding portfolio is diverse, reflecting the 5 major scientific groups represented in the Division. We have support from 9 NIH Institutes and the Office of the Director for a total of 28 NIH funded projects:

NINDS	NIAAA	NHLBI	NEI	NIA	NIAID	NICHD	NCI	NIMH	OD
R21 (2)	R00	R01 (2)	R01	R01	R01	R01	R01 (2 sub)	R01	R24
R01 (2)	P60	R01 (sub)		R01 (sub)		T32			UG3 (sub)
R01 (sub)	R01			R21 (sub)					
	U01 (2)								
	R24								
	R13								
	U44								

In addition, we have support from 9 foundations (some providing multiple awards), 4 industry partners and 8 other sources (university, research society or federal).

Foundations	Industry	Other
OHSU	Private Source	U of W (4)
Private Source		V.A.
		U-British Columbia
		DOD
		U-Iowa
		Ctr Women's Health
		Rutgers
		U-Illinois

Since May 2016 the Division Scientists applied for 35 grants, and 10 new grants were awarded.

DIVISION OF NEUROSCIENCE: TRAINING

The Division provides training and professional development encompassing summer internships for high school students, high school teachers, and undergraduates. Two graduate students obtained their PhD. and there are 3 current graduate students from the Behavioral Neuroscience graduate program that are conducting their doctorate research in the laboratory of a Division Scientist. The Division has a total of 7 post-doctoral trainees in 6 different laboratories. There are five junior faculty on the non-core track that receives close mentoring by their lab chiefs. At each level, training encompasses different activities. At the student level, Division scientists teach in graduate courses at the medical center. Our Scientists are members of NIH funded training grants (T32). We also provide lectures to student interns during the summer program. The Division has a seminar series that meets 3 times a month where students and trainees are expected to present their research progress. This seminar series also has guest presenters from OHSU and other Universities that provide new research and ideas to our community and help foster collaborations. Faculty is encouraged to have active roles in national and international societies and present their data at important scientific conferences. We help critique each other's grants, particularly helping junior investigators to secure their independent funding base. Finally, every faculty member (core or non-core) receive a yearly evaluation from the Division Chief where progress toward past professional goals is reviewed, and future goals to address career advancement are developed.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Protocols	Microarray or Deep Sequencing technologies: Development of the rodent postnatal hypothalamus is assessed by Microarray or Deep Sequencing technologies, generating gene expression as well as epigenetic posttranscriptional modification datasets. These data are stored securely and is made available to the scientific community trough Gene Expression Omnibus (GEO) (https://www.ncbi.nlm.nih.gov/gds)
Models	Macaque model of Huntington's disease (HD): We developed a rhesus macaque model of HD (an adult-onset-onset, fatal neurodegenerative disease) by injecting adeno-associated virus expressing mutant HTT in the caudate and putamen, the two brain regions most heavily affected in the disease. Monkeys display a progressive development of motor, cognitive and psychiatric symptoms, along with robust cellular dysfunction and degeneration, similar to what is seen in human HD. This model is unique and is being used to 1) better understand cortico-striatal connectivity changes in HD (Excluded by Requester nded R01), 2) to develop biomarkers of disease progression Excluded by funded Private Source and 3) Pending Support Pending Support (upcoming grant proposals).
Models	Murine mode of schwannomatosis: We have also developed a unique murine model of schwannomatosis, a rare disease characterized by multiple peripheral nerve tumors and intractable pain. Using this model, we have discovered a novel mechanism for neuropathic pain involving factors secreted by Schwann cells bearing mutations in the SMARCB1 gene typically observed in schwannomatosis patients. Our goal is to use this model to screen for agents that reduce pain phenotypes, possibly providing relief for the pain experienced by these patients.
Models	Model of reversible ischema in the brain and model of age-related Drusen: Our aging resource has helped to develop a model of reversible ischemia in the brain and a model of age-related drusen in the retina. Both of these models allow for the study of interventions that reduce the impact of disease processes, that occur with increasing frequency with age. A model of neuroendocrine aging has been developed which has examined the adrenal and gonadal steroid systems in females and males. Hormone treatment studies have examined the impact of hormone replacement in old animals, with functional endpoints at the tissue level and also at integrated levels, for example, behavior.
Instruments or equipment	These projects (INIA U01 and PARC) have necessitated the design and manufacturing of touch sensitive screens that can be safely and reliably functional within the monkey housing environment. The data acquisition and analyses required custom software to control the inputs and outputs needed in the cognitive testing as well as the ethanol self-administration.
Software	As part of the National Science Foundation Grant (IOS1121691) we designed algorithms and scripts for genomic data analysis and visualization. These new tools for miRNA targeting and 3D rendering of genomic/epigenomic information are under review by the Technology Transfer & business Development Office at OHSU.
Protocols	Genomic and Epigenomic Bioinformatics Pipeline: Capitalizing on the ONPRC pedigreed populations, and MiSeq sequencers we produce genome, exon, transcriptome and methylome sequencing and a team of full-time, skilled bioinformaticists provide support for large-scale sequence analysis and gene mapping studies. A custom genetic database (PRIMeSeq) now facilitates the storage and access of genomic data generated from the ONPRC macaque population. The ONPRC scientific advisory board has suggested that a systematic, genome sequencing effort, is established and will provide colony-wide genotype data sets. This initiative is underfunded at the present time but a pending R24 application will provide an unparalleled nonhuman primate resource with comprehensive colony genomic data made available to all investigators. In addition to informing genotype-phenotype studies, researchers will be able to search for variants by chromosome position, by similarity to

	known human variants or by animal. Currently, we have a handful of data collected on all research subjects that can be the basis of selecting animals based on genotype or haplotype.
Data or Databases	Phenotypic data on ethanol self-administration in relation to water and food intake is acquired in real time and in relation to all other monkeys in a cohort. These data are stored securely and available to the research community either through INIAstress.org or MATRR.com.
Physical collections	The MATRR is a repository for all organs, tissues and blood products from monkeys that have been studied with the alcohol self-administration protocol. Most tissue is flash frozen post-perfusion with artificial CSF at necropsy, however there are also custom prepared tissue (post-fixing in paraformaldehyde). Tissues are available to the alcohol research community through the website MATRR.com
Interventions (e.g., clinical or educational)	Together with collaborators at the Children's Hospital of Philadelphia and Spark Therapeutics, we have identified and screened a novel gene-lowering therapy to treat HD (AAV-miHDS1). We are currently working with the FDA to complete these IND-enabling studies in the rhesus macaque.
Interventions (e.g., clinical or educational)	Lithium was found to protect the infant brain from anesthesia induced Neurotoxicity. Lithium completely prevented the acute isoflurane-induced neuroapoptosis and significantly reduced the apoptosis of oligodendroglia.
Interventions (e.g., clinical or educational)	We have also characterized a number of novel compounds that target hyaluronidases and demonstrated that these compounds can promote demyelination in mouse models of demyelinating disease. We are presently moving forward with testing these compounds in Japanese macaques with Japanese macaque encephalomyelitis in hopes that one or more of these agents will be suitable for clinical trials in humans with multiple sclerosis.
Protocols	Gene therapy and chemogenetic therapy development: With the use of MRI compatible stereotactic devices, as well as efforts to develop viral vectors for most efficient delivery of nucleic acid constructs, we are developing gene therapeutic strategies targeting specific brain nuclei. This work has been spearheaded with an initial focus on Huntington's disease, but now includes pioneering work in alcohol addiction and targeting dopaminergic neurons in the ventral tegmental area. We are adding chemogenetic techniques this past year through introducing designer receptors exclusively activated by designer drugs (DREADDs).
Models	Macaque model of gestational protein deficiency: The macaque model of gestational protein deficiency is a translational nonhuman primate model in which to systematically dissect the complex physiological and behavioral outcomes in offspring associated with maternal malnutrition. This model will show a link between gestational protein restriction and the long-term impacts on brain genome, structure and function in a relevant primate species.
Models	The macaque model of chronic ethanol oral self-administration has face, construct and predictive validity for classifying individual differences in the propensity to acquire an alcoholic drinking phenotype. this model is unique and highly informative to the alcohol research community and is the basis of numerous NIH/NIAAA funding mechanisms to University and centers throughout the US.
Models	Macaque model of Batten disease (BD): The ONPRC Batten Disease Working Group characterized a novel, spontaneous model of BD (a juvenile-onset, fatal neurodegenerative disease) in our Japanese Macaque cohort. Monkeys display a mutation in the CLN7 gene, leading to the progressive development of retinal, cortical and cerebellar degeneration and corresponding visual decline, motor dysfunction, including ataxia and hypermetria. Histological analyses show the characteristic accumulation of lysosomal storage material. This is the only non-human primate model of a neuronal ceroid lipofuscinosis disease and it is rather unique. We are in the process of submitting an R24 grant to bank tissues from affected animals and have already identified several interested users of the model to 1) further study pathological processes, 2) to develop biomarkers of disease progression and 3) to assess novel therapeutics, including gene therapy for enzyme replacement.
Models	Macaque model of demyelinating disease: In collaboration with the Division of Pathobiology and Immunology, we have been characterizing a unique demyelinating disease in Japanese macaques housed at the ONPRC. This disease, called Japanese macaque encephalomyelitis, mimics many aspects of human multiple sclerosis. We are now pursuing novel pharmacological strategies to promote nervous system repair and demyelination with the aim of using this model for preclinical tests of the efficacy of new compounds with the potential to be carried to clinical trials.
Protocols	MRI Technical Advances: In the past year we helped develop tools that have

	significantly advanced our ability to identify and track how the brain adapts in normal development and disease states. These include: new informatic approaches, direct comparisons with human brain imaging results, novel applications of contrast agents, and optimal anesthetic conditions for measuring neurophysiological events, real time manipulation of brain connectivity.
Other	Development of cutting edge technology in visual sciences: The visual fovea is the region of the retina that is crucial for many basic functions such as reading, detail vision, color vision, visually guided manual manipulation, eye movement-directed attentional behavior, visual cognition and learning, and normal social behavior. However, little is known about the development of foveal representations in the brain and how abnormalities of this development might contribute to behavioral deficits. We have therefore developed an approach for studying the developing brain in infant monkeys in the first several postnatal months, a critical period for foveal maturation. This method includes: •PROTOCOL optical window methodology in infants through which areas representing foveal vision (e.g. V1, V2, and V4) can be studied using optical imaging, electrophysiology, optogenetics, and near infrared laser stimulation methods •PROTOCOL visual mapping procedures for studying cortical magnification, color representation, form representation, and binocular depth perception •INSTRUMENT/EQUIPMENT eye shutters for presentation of visual stimuli to individual eyes in infants •PROTOCOL in vivo functional tract tracing method for studying brain circuitry in infants •INSTRUMENT/EQUIPMENT a miniature head-mounted camera for monitoring cortical activity in vivo in infant and adult monkeys (in progress)
Protocols	A new surgical technique was developed for the subretinal implantation of therapeutic cells which avoids reflux of cells into the vitreous and the attendant deleterious side effects. The method has been communicated to the ophthalmology community through talks and a paper now in press.
Protocols	Fetal brain imaging: Recent technological developments have enabled characterization of moving fetal brain, in utero, using MRI. Although this approach is being implemented in human clinical studies and medical practice, a multitude of unanswered questions exist regarding the dynamic image contrast changes and their relationship to specific biological transformations. Nonhuman primate studies are absolutely critical for histological validation of interpretations of fetal brain MRI, and for developing sensitive measurements to detect abnormal development. ONPRC investigators are currently funded to characterize fetal brain development in contexts of maternal intrauterine infection, fetal exposure to alcohol and anesthetic agents, and under varying conditions of malnourishment.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Research Material	A new NIH (OD)-R24 for genomic sequencing of the ONPRC rhesus breeding population was funded this past July. This is a highly collaborative grant that will provide unique and essential genetic and genomic information for all scientific endeavors that utilize the rhesus macaque. We are in year 02 of a NIH-R24 (AA 013510) "Monkey Alcohol Tissue Research Resource" which disseminates tissue and plasma samples from rhesus and cynomolgus monkeys that have undergone chronic ethanol self-administration. We also have a unique aging resource of NHPs that is funded, in part, by the NIA and both facilitates research in the living NHP by outside investigators as well as provides tissue to study aspects of aging. We have shared resources on slice electrophysiology and voltammetry that have been used by OHSU and NIH intramural investigators over the past year.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

•Inherited retinal diseases: AAV gene therapies submitted to FDA for INDs for retinoschsin and Leber's optic neuropath Excluded by Requester
•Huntington's disease: AAV9 intrajugular route of administration Excluded by Requester
•West Nile virus encephalitis and vaccine development Excluded by Requester

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Project-5573

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			61,083.00	16,492.00	77,575.00
2.						Asst Scientist					46,360.00	12,517.00	58,877.00
3.						Assoc Scientist					6,548.00	1,768.00	8,316.00
4.						Asst Scientist					45,458.00	12,273.00	57,731.00
5.						Assoc Scientist					66,399.00	17,928.00	84,327.00
6.						Sr. Scientist					6,170.00	1,666.00	7,836.00
7.						Sr. Scientist					33,622.00	9,078.00	42,700.00
8.						Sr. Scientist					55,705.00	15,040.00	70,745.00
9.						Sr. Scientist					67,995.00	18,359.00	86,354.00
10.						Sr. Scientist					74,040.00	19,991.00	94,031.00
11.						Asst Scientist					21,538.00	5,815.00	27,353.00
12.						Sr. Scientist					73,707.00	19,900.00	93,607.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **709,452.00**

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						
4	Unit staff	33.0			147,027.00	39,699.00	186,726.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**186,726.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**896,178.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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. Equipment maint & repair, memberships, miscellaneous other expense	14,101.00
Total Other Direct Costs	**16,601.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**912,779.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	912,779.00	255,578.00
		Total Indirect Costs	**255,578.00**

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)	**1,168,357.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Reproductive & Developmental Sciences

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The main objective of the Division of Reproductive & Developmental Sciences (DRDS) at ONPRC is to understand the processes critical for primate reproduction and development, with the information gained being used to improve human health and quality of life. Currently it is estimated that 2 of 10 adult women are infertile, 4 of 10 pregnancies are "spontaneously" lost, and 1 of 10 children are born with a birth defect. It is also increasingly clear that environmental contaminants, lifestyle (e.g., the western-style diet), and clinical therapies (e.g., the chemo- and radiation therapy for cancer) can profoundly and negatively impact fertility. Conversely, approximately 5 of 10 pregnancies are unintended and human population growth (approaching 7.5 billion people) threatens our quality of life, if not life itself for many species, and threatens global resources. Thus, the rationale remains as great as ever to use advances in our knowledge of reproductive biology and fetal/neonatal development to better understand the causes of infertility and prevent its occurrence, as well as to develop the next generation of contraceptives to prevent fertility. Likewise, as our knowledge of gametes and early embryonic development expands, environmental effects on peri- or post-conception programming for subsequent postnatal disease can be determined and reproductive cells/tissues will serve as an important source of pluripotent cells than have unparalleled potential for applications to regenerative medicine.

Nonhuman primates are a valuable model for research advances pertaining to human reproductive and fetal/neonatal health. Many of the factors and mechanisms controlling reproductive processes (notably within the hypothalamic-pituitary-gonadal axis, the gonads, gametes, plus maternal recognition of pregnancy and term delivery) are more similar between monkeys, apes and man, than with typical laboratory rodent models. For logistical and ethical reasons, studies on humans and apes are very limited; consequently Old World monkeys (macaque, baboon species) are a preferred nonhuman primate (NHP) model for basic and applied studies on reproductive processes that are clinically relevant to human reproductive and developmental health.

The DRDS has a long and rich history in contributing significant advances in primate reproductive biology and its applications to women's health. Research and training activities span the continuum of reproductive processes from gamete (egg) and embryo development, to intrauterine pregnancy and maternal-fetal development, to delivery and neonatal health. A general theme of all laboratories is the use of NHP models for whole animal, cellular and molecular studies of direct relevance to women's reproductive and child health. The core, affiliate and visiting scientists embrace the objectives of the NPRC program in performing research on NHPs, developing NHP models of reproductive diseases, providing training opportunities in primatology, and disseminating our scientific advances. As such, our specific aims include:

Specific Aim 1: Promote research opportunities in existing fields of primate reproductive and developmental science.

Specific Aim 2: Expand opportunities in emerging fields of research.

Specific Aim 3: Ensure availability of primate resources for reproductive research.

Specific Aim 4: Promote efforts to train scientists that focus on primate and human reproductive health.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DRDS_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DRDS_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

OUTREACH ACTIVITIES
DRDS faculty were actively involved in outreach activities, which included sharing research expertise with U.S. and international scientists, as well as promoting and enhancing the understanding of research conducted in the division to members of the local community. Outreach activities included participation in hands-on courses sponsored by Saturday Academy that were held at the ONPRC demonstrating assisted reproductive technologies [Excluded by Requester] o local high school students. Through the ONPRC P50 National Centers for Translational Research in Reproduction and Infertility (NCTRI) supported Outreach Core, several hands-on laboratory courses were offered to Portland area middle and high school students. The NCTRI Outreach Core was also involved in working with local high school science teachers to promote the use of a curriculum developed 2 years ago that details cryopreservation and tissue bioengineering experiments that can be conducted in the classroom. This curriculum was presented at the Partners in Science Annual Conference, San Diego, CA, January 2017 [Excluded by Requester] ffers these materials to educators and provides related information for website visitors. [Excluded by Requester] NPRC Outreach Coordinator, and [Excluded by Requester] ontinued with a "Science Café" series that is held at the Willow Creek Campus of the Portland Community College (PCC), which is adjacent to ONPRC. Four consecutive lectures were offered 2

times this year: including October 2016 and February 2017. Topics for the October series included a panel discussion of "Zika Virus", as well as presentations covering "Preventing Fetal Brain Injury", "The Male Non-hormonal Contraception Pill", and "Fertility Preservation in Women and Giant Pandas". The February topics will include a panel discussion on "Editing Our DNA: Why, How, and Should We?" as well as presentations covering "Using 21st Century Genetic Technologies to Control Brain Function", "Curing Blindness", and "Three Parent Babies: Curing Mitochondrial Disease". The audience generally includes high school and undergraduate students, as well as adults form the community. Excluded by Requester arranged multiple programs for high school students and high school teachers at the center that involved all division scientists. For example, nearly all division faculty served as panelists to provide advice to high school students seeking careers in science. Several DRDS faculty members were involved in outreach presentations to the lay public in the Portland metro area.

CONFERENCES: Division scientists disseminate their research findings at regional, national, and international meetings, including the following:

REGIONAL CONFERENCES
•ONPRC Scientific Retreat, Stevenson, WA, March 2016. Participating scientists: All DRDS Faculty.
•Northwest Reproductive Sciences Symposium, Oregon State University, Corvallis, OR, June 2016. Participating DRDS faculty: Drs. Excluded by Requester (invited oral presentation), Excluded by Requester (invited oral presentation), Excluded by Requester

NATIONAL CONFERENCES
•NICHD Infertility (NCTRI) Center Research and Focus Group Meetings, Bethesda, MD, May 2016. Participating DRDS faculty: Dr. Excluded by (selected oral presentation).
•The Annual Meeting of the Society for the Study of Reproduction, San Diego, CA, July 2016. Participating DRDS faculty: Excluded by Requester (selected oral presentation) Excluded by Requester (invited oral presentation) Excluded by Requester
•StartART Annual Reproductive Endocrinology and Infertility Nursing Congress, Las Vegas, NV, August 2016. Participating DRDS faculty: Excluded by (selected oral presentation).
•The Annual Gilbert S. Greenwald Symposium on Reproduction and Regenerative Medicine, Kansas City, KS, September 2016. Participating DRDS faculty: Excluded by Requester (invited oral presentation).
•The Steering Committee Meeting for the NICHD Contraceptive Development & Research Centers, New York, NY, October 2016. Participating DRDS faculty: Excluded by Requester (invited oral presentations), Excluded by Requester (invited oral presentations), Excluded by Requester (invited oral presentations), and Excluded by
•The Annual Meeting of the Obesity Society, New Orleans, LA, October 2016. Participating DRDS faculty: Excluded by
•The Annual Meeting of the American Society of Reproductive Medicine, Salt Lake City, UT, October 2016. Participating DRDS faculty: Excluded by (selected oral presentation) Excluded by (selected oral presentation) Excluded by (selected oral presentation) Excluded by Requester
•NICHD Infertility (NCTRI) Ovarian Follicular and Oocyte Health Focus Group Meeting, Chicago, IL, November 2016. Participating DRDS faculty Excluded by Requester
•The Annual Meeting of the American Society for Reproductive Immunology, Baltimore, MD, November 2016. Participating DRDS faculty: Excluded by (selected oral presentation).
•The Annual Meeting of the Oncofertility Consortium, Chicago, IL, November 2016. Participating DRDS faculty Excluded by Requester
•The Annual Meeting of the Society for Maternal-Fetal Medicine, Las Vegas, NV, January 2017. Participating DRDS faculty: Excluded by (selected oral presentation).
•The Annual Meeting of the Murdock Trust Partners In Science, San Diego, CA, January 2017. Participating DRDS faculty: Excluded by
•The Annual Scientific Meeting of the Society for Reproductive Investigation, Orlando, FL, March 2017. Participating DRDS faculty: Drs. Excluded by Requester

INTERNATIONAL CONFERENCES
•International Conference on Cerebral Palsy and other Childhood-onset Disabilities, Stockholm, Sweden, May 2016. Participating DRDS faculty: Excluded by nvited oral presentation).
•The Annual Meeting & Exhibition of the International Society for Magnetic Resonance Medicine, Singapore, Malaysia, May 2016. Participating DRDS faculty: Excluded by vited oral presentation).
•World Biomaterials Congress, Montreal, Canada, May 2016. Participating DRDS faculty: Excluded by Requester invited oral presentation).
•Université de Montréal, Biomédecine Vétérinaire/Centre de Recherche en Reproduction Animale (CRRA), St-Hyacinthe, Quebec, May 2016. Participating DRDS faculty: Excluded by Requester invited oral presentation).
•International Congress of Animal Reproduction, Tours, France, June 2016. Participating DRDS faculty: Excluded by Requester selected oral presentation).
•Perinatal Brain Injury: Mechanisms, Consequences and Treatment, Gothenburg, Sweden, June 2016. Participating DRDS faculty: Dr. Excluded by Requester vited oral presentation).
•International Symposium on Equine Embryo Transfer, Ghent, Belgium, July 2016. Participating DRDS faculty: Excluded by Requester
•International Society for Serotonin Research, Seattle, WA, July 2016. Participating DRDS faculty: Excluded by Requester
•The Annual Meeting of the Society for Cryobiology, Ottawa, Canada, July 2016. Participating DRDS faculty: Excluded by Requester vited oral presentation).
•The Annual Meeting of International Federation of Placenta Associations, Portland, OR, September 2016. Participating DRDS faculty: Excluded by Requester selected oral presentation) Excluded by Requester lected oral presentation), and Excluded by Requester ected oral presentation).
•International Meeting of the Androgen Excess-Polycystic Ovary Syndrome (AE-PCOS) Society, Melbourne, Australia, November 2016. Participating DRDS faculty: Excluded by Requester (invited speaker).

Research results obtained by Division scientists are published in widely read reproductive sciences journals (see ONPRC publication list).

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

There are no anticipated deviations from the stated specific aims for the DRDS over the coming year. Current faculty will continue to focus on their respective areas of research, service and training. The division will continue with stated plans to expand opportunities in emerging fields of reproductive research. Specifically, the focus will be on further developing collaborative relationships with other ONPRC divisions and clinical departments at OHSU. For example, division scientists continue to be actively involved in the newly formed

Center for Developmental Health headed by Excluded by Requester which is part of the Knight Cardiovascular Institute and the Department of Cardiology. The Center for Developmental Health (CDH) aims to bring together researchers interested in dietary and environmental effects on embryogenesis and fetal development that subsequently lead to a greater propensity to develop disease after birth. It is anticipated that a concerted effort to bring together scientists interested in the developmental origins of health and disease will allow for the submission of individual investigator and multi-PI programmatic grant applications. Excluded by Requester s co-chairing the CDH Metabolism & Development working group, which focuses on defining how abnormalities in maternal nutrition and metabolism affect critical developmental processes that lead to later disease. DRDS faculty that are members of the various CDH working groups include Drs. Excluded by Requester Division scientists will also continue to work closely with ONPRC Neuroscience and Pathobiology/Immunology, as well as with VGTI and OHSU scientists to better understand how infectious agents such as Zika lead to placental dysfunction and fetal developmental abnormalities. Efforts in this area are also expected to lead to the submission of additional collaborative, multi-PI programmatic grant applications. Lastly, it is anticipated that the same level of mentoring and outreach activities will continue through the next funding interval.

DIVISION OF REPRODUCTIVE AND DEVELOPMENTAL SCIENCES: ACCOMPLISHMENTS

Specific Aim 1: Promote research opportunities in existing fields of primate reproductive and developmental science.

The DRDS continues to serve as a nationally and internationally recognized leader in reproductive sciences through the activities of its productive and collaborative scientific staff. In 2014 Excluded by Requester stepped down as the Chief of the Division in advance of his retirement. Excluded by Requester served as the Interim Division Chief from that time through June of 2016. On 7/1/2016 Excluded by Requester was hired as the permanent Chief of the Division following a national search and was promoted from Associate Professor to Professor. Dr. Excluded by Requester continues to be available to Excluded by Requester for consultation regarding divisional matters. Through this reporting period, there were 10 core scientists with a primary appointment in DRDS Excluded by Requester Excluded by Requester and 4 affiliate scientists that hold a joint appointment with other ONPRC/OHSU divisions Excluded by Requester ardiometabolic Health; Excluded by Requester nd Excluded by Requester Neuroscience; Excluded by Requester Department of Obstetrics & Gynecology in OHSU's School of Medicine). There were also 5 affiliate scientists in the DRDS at either the Senior Staff Scientist or Research Professor series rank Excluded by Requester Due to her accomplishments that include being selected for a Building Interdisciplinary Research Careers in Women's Health (BIRCWH) K12 fellowship and successfully competing for an independent R01 grant, Excluded by Requester became an Assistant Professor on 7/1/2016. An arrangement was made whereby Excluded by Requester alary support is shared between DRDS and the Department of Obstetrics & Gynecology (OB/GYN), demonstrating Excluded by Requester otential to utilize the nonhuman primate model to transform clinical practice. In addition t Excluded by Requester DRDS core scientists Excluded by Requester also have joint appointments and clinical responsibilities in OB/GYN. This close affiliation between OB/GYN and DRDS will only further strengthen an already highly collaborative working relationship between the two groups and sustain our emphasis on clinically relevant women's health research.

Division faculty continued to make progress in research programs that are translational in nature and of potential clinical significance in the following areas of reproductive biology:

Contraception: Studies performed in the division continue to focus on the identification and development of novel female contraceptives that reversibly or irreversibly block gamete transport and fertilization. Support for these studies included continued funding through an NICHD U54 Contraceptive Research & Development Center grant Excluded by Requester foundational grants Private Source Foundation; Excluded by Requester and pharmaceutical research contracts Private Source Dr. Excluded by Requester Private Source NIH SBIR/STTR subcontract Excluded by Requester Private Source solicited research proposals from internal and external scientists to develop nonsurgical approaches for women that permanently prevents pregnancy. Pending Support Pending Support

Infertility & Oncofertility: Division faculty continued to maintain active research programs focused on understanding the underlying causes of infertility. For example, a collaborative effort involving DRDS scientists Excluded by Requester and faculty from within the Division of Cardiometabolic Health Excluded by Requester supported by a P50 National Centers for Translational Research in Reproduction and Infertility (NCTRI) grant, aims to understand the role a Western style diet and hyperandrogenemia plays in the development of female infertility. Excluded by Requester in addition to her R01 that focuses on how anti-Müllerian hormone (AMH) regulates preantral follicle growth and antral follicle maturation in primates during the menstrual cycle, was awarded a pilot project grant through the NCTRI P50 grant wit Excluded by Requester hat focuses on the role that vitamin D3 plays in regulating ovarian follicle growth and development Excluded by Requester was awarded an R01 this past year that aims to identify the origins of chromosomal instability that occurs in pre-implantation embryos obtained through current infertility treatments, thereby allowing for the development of noninvasive approaches that will prevent the unnecessary transfer of embryos that are incapable of leading to a term pregnancy.

Development: Efforts in understanding primate development spanned the continuum of peri- or post-fertilization events through maternal-fetal pathologies that affect neonatal health. Excluded by Requester s continuing studies designed to assess the fertility of rhesus macaques that were born following somatic

cell nuclear transfer (SCNT), which serves as a model for preventing the transmission of mitochondrial disease. Through support from [Private Source] Innovation in Regulatory Science Award funded 9/1/2016, [Excluded by Requester] s currently performing studies that will provide critical evidence concerning the efficacy and long-term safety of mitochondrial replacement therapy. Using rhesus macaques, Dr. [Excluded by Requester] will determine if replacing donor mitochondria by spindle-transfer or pronuclear-transfer interferes with subsequent nuclear DNA- mitochondrial DNA compatibility and the normal development of offspring. This study will assess the feasibility and efficacy of pronuclear transfer in comparison to spindle transfer in primates. Studies will include evaluating growth, development and fertility of rhesus macaque offspring derived from both approaches through adulthood. Through the use of metabolomics profiling and real-time embryo imaging [Excluded by Requester] are conducting studies to assess the cellular activities in the ovarian follicle that are predictive of the ability of the resident oocyte to undergo fertilization and subsequent embryonic development. This effort is supported through a second year of funding provided by the [Private Source] [Private Source] [Excluded by Requester] ontinues to investigate the cellular and molecular mechanisms in primates that are responsible for the development of chromosomally abnormal embryos, which is associated with early pregnancy loss. [Excluded by Requester] esearch efforts are supported through an NICHD R01 funded in 2016. Through an NICHD funded R01, [Excluded by Requester] continued to study the effect of how premature birth initiated in response to infection results in lung disease and neurological impairment. [Excluded by Requester] s also serving as a Co-Investigator on an R01 grant that was awarded to [Excluded by Requester] this past year and aims to determine if routine use of CPAP (continuous positive airway pressure) in pre-term infants will stimulate lung growth to the same level observed in term infants, thereby preventing respiratory disease. [Excluded by Requester] hrough an NICHD funded Human Placenta Project R01, is continuing to develop and validate advanced non-invasive magnetic resonance imaging protocols in macaques for the *in vivo* assessment of placental perfusion and oxygenation, with the resultant information being used to improve the clinical management and early identification of pregnancies at-risk for placental insufficiency.

Specific Aim 2: Expand opportunities in emerging fields of research.
Opportunities to expand the DRDS' activities in emerging areas of reproductive science research included the development of multiple PI, center-based programs and the support of junior faculty that increase the breadth and expertise of the division. The Center for Embryonic Cell & Gene Therapy (CECGT; [Excluded by Requester] Director), which focuses on the use of nuclear transfer and stem cell-based therapies for disease therapies, continues to develop a close working relationship with DRDS. In this regard, [Excluded by Requester] ecame the 3rd member of DRDS to join the CECGT (other members include [Excluded by Requester]. The establishment of the CECGT and involvement of DRDS faculty will allow for translating basic science and proof-of-principle studies performed in NHP models into therapies for treating human infertility and disease.

In the past year, members from DRDS, the ONPRC Pathobiology and Immunology Division, as well as the OHSU Vaccine & Gene Therapy Institute (VGTI) formed a working group to study Zika virus pathogenesis, particularly as related to the development of a nonhuman primate model to study how infection during pregnancy leads to fetal developmental abnormalities. Studies supported through this P51 grant via a pilot project award allowed ONRPC/VGTI investigators to determine that Zika infection in rhesus macaques mirrors the tissue distribution and kinetics of infection observed in humans. Moreover, it was determined that infection during pregnancy negatively impacts placental function (i.e., blood flow, oxygenation) and leads to abnormal fetal brain development in macaques. The findings from this pilot project grant formed the basis for an NICHD R21 application that was funded summer 2016. The objective of this study will be to define when during pregnancy that Zika virus infection leads to the most severe developmental disability in the offspring. This collaborative effort spans a wide range of expertise (i.e., developmental biology, neuroscience, immunology and virology) and will provide a foundation for future projects focusing on how Zika infection during pregnancy leads to fetal brain abnormalities and whether vaccines can effectively protect mothers and fetuses from such effects.

Specific Aim 3: Ensure availability of primate resources for reproductive research.
It is imperative that the NHP needs for DRDS projects are effectively managed and balanced with those of the entire center. The need for adult female macaques by division scientists was historically in direct competition with the needs of the ONPRC Division of Comparative Medicine as this is the population that is required to sustain the center's breeding program. Thus, the division was involved in several activities that ensure

sufficient availability of NHP resources for projects focusing on reproduction and development. As Division Chief, Excluded by Requester continues to serve as a member of the ONPRC Animal Utilization Committee, which assesses all animal allocation requests for grant applications prior to their submission or activation. These requests are reviewed monthly for their feasibility based on animal availability and housing. Availability of animals for a given study is derived from a review of the current colony demographics and the effect removal of the requested cohort of animals would have on long-term colony stability. Division scientists also provided feedback and projections regarding their anticipated NHP needs. Through a real-time electronic health record system, division faculty now have access to the reproductive history of every animal at the center. This allowed investigators to assess ovarian cyclicity through daily menses reports and past fecundity, resulting in the selection of only those animals that are best suited for their studies. Lastly, utilization of the Timed Mated Breeding (TMB) Resource and the Assisted Reproductive Technologies (ART) Core allow for the most efficient use of valuable NHP resources. The TMB provided Excluded by Requester pregnancies suitable for their studies, whereas the ART Core provided multiple investigators in the division with the necessary gametes and embryos for their research projects.

Specific Aim 4: Promote efforts to train scientists that focus on primate and human reproductive health. Training efforts within the DRDS is detailed below in Section B.3.

DIVISION OF REPRODUCTIVE AND DEVELOPMENTAL SCIENCES: TRAINING AND PROFESSIONAL DEVELOPMENT

As stated in Specific Aim 4, a major goal of the DRDS is to train the next generation of reproductive biologists. Division faculty are involved in the training of 3 Ph.D. students through the OHSU graduate Program in Molecular & Cellular Biosciences (PMCB). Two of the students, Excluded by Requester are under the supervision of d Excluded by Requester A first year PMCB Ph.D. student, Excluded by Requester is being co-mentored by Excluded by Requester Excluded by Requester s providing mentorship to Excluded by Requester a Master's student in the OHSU Institute of Environmental Health. Faculty within the division (Excluded by Requester Excluded by Requester are also actively involved in the training of 4 postdoctoral fellows. Through the close ties between the DRDS, OB/GYN, and Department of Pediatrics faculty, 2 M.D. fellows were involved in research projects overseen by division faculty. Excluded by Requester both Family Planning fellows from OB/GYN, are working with division scientists Excluded by Requester Excluded by Requester esearch focus includes the development of contraceptives that function by blocking gamete transport. Excluded by Requester is developing a point-of-care test to aid in discerning uterine pregnancies from ectopic pregnancies before they can be visualized conclusively by ultrasound. Support for the development of independent research careers is also available to ONPRC postdoctoral fellows through an OHSU Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program. Moreover, a Women's Reproductive Health Research (WRHR) Career Development grant was funded in 2015 wit Excluded by Requester hair of the Department of Obstetrics & Excluded by Requester ecology, serving as the PI and DRDS faculty members Excluded by Requester acting as the Directors of esearch. The WRHR program will allow OB/GYN junior faculty the opportunity to conduct basic research, including the option of working with DRDS scientist to utilize NHP models. Lastly, DRDS continues to train international students and scientists in the use of NHP models for studying reproductive biology. Excluded by Requester visiting scientist from the Tianjin Medical University, Tianjin, China, is working with Excluded by Requester o investigate the direct effects of growth factors on macaque follicle development *in vitro*. Excluded by Requester also mentored an undergraduate student this past summer that is currently enrolled in a biomedical science Ph.D. program at the University of California-Davis.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
		Excluded by Requester					Institutional Base Salary	EFFORT					
1.						Unit Head					53,679.00	16,104.00	69,783.00
2.						Sr. Scientist					74,040.00	22,212.00	96,252.00
3.						Asst Scientist					46,134.00	13,840.00	59,974.00
4.						Asst Scientist					37,020.00	11,106.00	48,126.00
5.						Asst Scientist					43,819.00	13,146.00	56,965.00
6.						Sr. Scientist					37,020.00	11,106.00	48,126.00
7.						Sr. Scientist					11,569.00	3,471.00	15,040.00
8.						Assoc Scientist					26,067.00	7,820.00	33,887.00
9.						Sr. Scientist					9,255.00	2,777.00	12,032.00
10.						Asst Scientist					22,550.00	6,765.00	29,315.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **469,500.00**

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						
4	Unit staff	24.6			121,220.00	36,366.00	157,586.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**157,586.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**627,086.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	1,800.00
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. Supplies, memberships, biohazard waste disposal, equipment maint & repair, miscellaneous other expense	15,564.00
Total Other Direct Costs	**17,364.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**644,450.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	644,450.00	180,446.00
		Total Indirect Costs	**180,446.00**

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)	**824,896.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Pathobiology & Immunology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The World Health Organization (WHO) estimates that infectious disease is responsible for 25% of all deaths worldwide and that this number is likely to be even larger if certain cancers, cardiovascular and respiratory/digestive deaths, which can also be attributed to infection, are included. Interestingly, six diseases account for 90% of infectious disease deaths, and include acute respiratory infections (including pneumonia and influenza), AIDS and AIDS-associated disease, diarrheal diseases, tuberculosis, malaria and measles. To curb this growing global problem further elucidation of host-pathogen interactions is absolutely needed to better design therapeutics and vaccines to prevent morbidity and mortality from existing and newly emerging infectious agents. Commensurate with this need is the absolute requirement for an animal model that parallels and shares developmental, physiological and evolutionary relationships with humans, and are susceptible to the same or closely related infectious agents with similar, if not identical, sequelae. Addressing this challenge is the goal for the scientists within the Division of Pathobiology and Immunology (DPI), which is home to a team of outstanding virologists, immunologists and pathologists, many of whom are also scientists within the Vaccine and Gene Therapy Institute (VGTI), who are imbued with a team ethic and a commitment to nonhuman primate (NHP) models. The fundamental theme is that progress in these areas of investigation requires high level expertise and experience in virology, immunology and pathology, a combination that is rarely found in a single investigator, but that would be provided by a close-knit collaborative environment in which scientists encompassing these disciplines could interact on a daily basis. Furthermore, it was felt that NHP models would be an essential element of any truly clinically relevant investigations in these areas.

Within the next 5-year funding cycle of the P51 the Division will focus on expanding its research portfolio by building upon our existing strengths to develop new NHP models of infectious and chronic disease, and simultaneously train a new crop of scientists dedicated to the diligent use of NHP models to combat primate and human health concerns. Accomplishing these goals will be a challenge and we plan to tackle this by recruiting an established scientist who utilizes NHPs for both infectious and chronic disease research to lead the Division within the next two years, and recruit immunologists (senior and junior investigators) to fill the gaps generated by the departure of Excluded by Requester within three years. The specific aims for the Division are:

Specific Aim 1: To promote and expand research opportunities in existing areas of NHP Immunology and Infectious Disease Science

Specific Aim 2: Develop new NHP models of emerging infectious and chronic disease

Specific Aim 3: Train new era of scientists to expand NHP models of infectious disease

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Patho_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Patho_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Division Scientists continue to inform the public and scientific communities of our research activities. An example of our outreach is listed below.

Excluded by Requester

•ONPRC Public Tour, September 22, 2016
•Zika HIV Talk,September 23, 2016
•IMPAACT Conference, Washington DC, January 23-26, 2017
•Research Community, Australia National University, February 14, 2017
•Research Community, Lorne Infection & Immunology Conference 2017, Australia, February 15-17, 2017
•Research Community, Monash University, Australia, February 21, 2017
•Research Community, Translational Research Institute, Queensland, Australia, February 23, 2017
•Keystone Symposia on HIV Vaccines, March 2017
•Immunology Affinity Group, The Scripps Research Institute, April 27, 2017

Excluded by Requester

•Stanford University Immunology PhD Program Seminar Series, Stanford, CA, May 10, 2016
•AAI Presidential Symposium talk, Seattle, WA, May 13-17, 2016
•BMGF 2nd Annual CTVD Meeting, Seattle, WA, June 23-24, 2016
•From the Laboratory to the Clinic: Getting Closer to a Cure?, Trinity College, Oxford, Sept. 7-9, 2016

• IHV 18th Annual International Meeting, Baltimore, MD, Sept. 20, 2016
•2015/2016 Tyrrell Lectureship in Infection and Immunity at the University of Alberta, Edmonton, Alberta, Canada, Sept. 22, 2016
•Nature Conference: "Immune Profiling in Health and Disease"; Seattle, WA, Oct. 3-5, 2016
•HIVR4P (HIV Research for Prevention) - AIDS Vaccine, Microbicide and ARV-based Prevention Science, Chicago, IL, Oct. 17-20, 2016
•BMGF Grand Challenges Annual Meeting, London, UK, Oct. 23-26, 2016
•University College London UCL External Speaker Seminar Series - Division of Infection and Immunity Seminar Series, London, UK, Oct. 24, 2016
•Keystone Symposia on Translational Vaccinology for Global Health, London, UK, Oct. 25-29, 2016
•Invited speaker: K.G. Jebsen Center for Cancer Immunotherapy, Oslo, Norway, Oct. 31 - Nov. 2, 2016
•HIV Prevention Workshop, Magaliesburg, South Africa, Nov. 28-30, 2016
•Gates 11th Annual CAVD meeting, Seattle, WA, Dec. 4-9, 2016
•CROI 2017, Seattle, WA, Feb. 13-16, 2017
•NIH workshop on Non-Classical Monomorphic Molecules, Bethesda, MD, Mar. 16, 2017
•NIH Intramural Tuberculosis Research Initiative Seminar Series, Bethesda, MD, Mar. 17, 2017
•Johns Hopkins Seminar, Baltimore, MD, April 4, 2017
•Harvard 2016-2017 Virology Program Seminar Series, Boston, MA, April 5, 2017
•UCSF Seminar, San Francisco, CA, April 17, 2017

Excluded by Requester

•Stanford University Alumni Association, Oregon Chapter, October 8, 2016
•Lewis & Clark Law School: Center for Animal Law Studies, November 7, 2016
•Oregon Chinese Scientist, Engineer and Professionals Association, November 19, 2016

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Our studies with RM or other NHP species involve an OHSU Biostatistician to ensure that we utilize robust statistical analysis in our animal experiments. This includes Power analysis when appropriate. For pilot studies, we routinely use 4 animals (n=4) for each arm of a study. Four animals is the minimum number given the individual variation between animals.

We will continue to strive to accomplish the goals for the Division of Pathobiology and Immunology. One of our plans is to increase our scientific staff by recruiting an established senior immunologist to complement our current scientists. During this past year, we interviewed five potential candidates. One candidate will return for a second visit and a sixth candidate will arrive for their initial visit. The successful recruitment will lead to additional funding from these investigators and enhance opportunities to foster new collaborations that add to our research portfolio.

PATHOBIOLOGY & IMMUNOLOGY: ACCOMPLISHMENTS

The major activities for Division of Pathobiology and Immunology scientists were to pursue the Specific Aims put forth in our portion of the P51 competitive renewal.

Specific Aim 1: Promote and expand research opportunities in existing areas of NHP Immunology and Infectious Disease. Our Division scientists, core and affiliate, have continued to demonstrate success in this Specific Aim by receiving a number of new NIH and Foundation grants. These include a high priority R56 award, a new investigator R01, three UM1 cooperative agreements, one P01 program project and one AERAS Global TB Vaccine Foundation grant (**Table 1**).

Table 1. New grant awards to improve vaccines against HIV/SIV and TB

Principal Investigator	Title of application	Funding agency	Award number
Frueh, Klaus	Evasion of Antigen Presentation by RhCMV	NIH/NIAID	2 R56 AI059457
Hansen, Scott	Efficacy of Strain 68-1 RhCMV vectors Expressing 5' Leader polypeptides	NIH/NIAID	R01 AI124370
Hansen, Scott	CHAVI ID: Efficacy and Immunogenicity of 68-1 RhCMV Vectors Expressing Conserved SIV Antigens	NIH/NAID Subcontract from Duke University	5 UM1 AI100645-05 / #2035054
Picker, Louis	DARE: Delaney AIDS Research Enterprise to Find a Cure.	NIH/NIAID Subcontract from UC San Francisco	1 UM1 AI126611-01
Excluded by Requester	Development of Optimized CMV/TB Vectors: OHSU/AERAS Project 3 Proposal	Private Source	
Picker, Louis	Development of an Effector-Memory T Cell AIDS Vaccine	NIH/NIAID	3 P01 AI094417-05S1
Picker, Louis	Consortium for Innovative AIDS Research in Nonhuman Primates: Focus 1, Focus 2, Administrative Core, and Nonhuman Primate Core	NIH/NIAID Subcontract from Beth Israel Deaconess Medical Center	1 UM1 AI124377-01

Division scientists, core and affiliate, have also been awarded new grants to investigate novel HIV cure approaches that utilize ONPRC NHP resources. These include three foundation awards, an R44, and an R01 (Table 2).

Table 2. New grant awards to address HIV Cure

Principal Investigator	Title of application	Funding agency	Award number
Haigwood, Nancy	Plant-derived HIV Neutralizing mAbs for Passive Immunotherapy in Newborn Macaques	SBIR through PlantVax	2R44AI081621-04A1
Excluded by Requester	Combination Immune Checkpoint Blocker Inhibition to Eliminate HIV Latency (Lewin)	Private Source	
	To Determine the Effect of Toll-like Receptor (TLR) Agonists on SIV Production in Effectively Treated SIV-infected Macaques: Module E and Animal Core	Private Source	
Sacha, Jonah	A Nonhuman Primate Model of Stem Cell Transplantation to Understand Determinants of Post-transplant SIV Clearance	NHI/NIAID	R01 AI129703-01
Excluded by Requester	Evaluating Bromodomain Inhibitors for HIV Cure Therapy	Private Source	

We have also expanded our research efforts to investigate the increased frequency of cancer in AIDS patients, using the RM model (Table 3).

Table 3. New grant award that utilize NHPs for cancer research

Principal Investigator	Title of application	Funding agency	Award number
Wong, Scott	Investigating the Development of AIDS and non-AIDS Defining Cancers in Aged SIV-infected Rhesus Macaques	NIH/NCI	1 R01 CA206404-01

Specific Aim 2: Develop new NHP models of emerging infectious and chronic disease. The outbreak of Zika virus infection in the Americas and the effects of virus infection in utero has led to cross-divisional collaboration between Affiliate scientists from the Division of Pathobiology and Immunology, and the Division of Developmental and Reproductive Sciences to investigate the outcome of Zika virus infection in pregnant RM. The results from this collaborative effort were substantial; finding that infection during the first trimester of pregnancy resulted in some placental and neurological deficits. These findings were included in an R21 application (**Table 4**).

Table 4. New grant award that utilize NHPs for emerging infectious disease.

Principal Investigator	Title of application	Funding agency	Award number
Streblow, Daniel	Developing a model for determining the causal relationship between Zika virus infection during pregnancy and fetal microcephaly	NIH/NICHD	1 R21 HD091032-01

We are pleased with our success in acquiring new grant funding for SA 1 and 2, and will continue to submit new grant applications that utilize NHP resources.

Specific Aim 3: Train a new era of scientists to expand NHP models of infectious disease. Division scientists continue to train post-doctoral fellows, graduate students, and research assistants who apply to graduate and professional schools. Section B4 lists these types of trainees.

PATHOBIOLOGY & IMMUNOLOGY: TRAINING AND PROFESSIONAL DEVELOPMENT

Many of the research grants supporting the Division's mission have funds to train post-doctoral fellows and graduate students. These trainees investigate the mechanisms that infectious pathogens utilize to gain a foothold in hosts and induce disease. Similarly, some of our trainees investigate the host response to pathogen infection to better understand how to eliminate the pathogens. These talented young scientists routinely discuss their research findings at a weekly seminar series. This provides trainees a forum to develop and improve their presentation skills for when they attend national and international scientific meetings. Our graduate students are in the Department of Molecular Microbiology and Immunology at Oregon Health & Science University (OHSU) where they are required to present their research at a departmental seminar and are required to meet with visiting seminar speakers. These settings provide students and post-doctoral fellows opportunities to network with others. Additionally, these trainees are actively involved in a journal club to discuss recent published work that has broad interest to the Division. Some of our more senior trainees participate in national meetings that offer workshops to assist or advise trainees in career development. Finally, OHSU offers courses for grant writing and has an Office of Post-Doctoral Affairs to respond to career and professional development needs.

Type of trainee	Number of trainees
Postdoctoral Fellowes	9
Graduate Students	7
Undergraduate Student(s)	1
Other Type (1) Research Assistants	3
Other Type (2)	
Total	20

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Research Material	Recombinant rhesus CMV vectors, rhesus rhadinovirus reagents and other research reagents are routinely made available to requestors following the completion of institutional material transfer agreements executed by the OHSU Office of Technology Transfer & Business Development and the requestors' institutional official.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

ProprietaryInfo

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			37,020.00	9,995.00	47,015.00
2.						Assoc Scientis					56,456.00	15,243.00	71,699.00
3.						Sr. Scientist					37,020.00	9,995.00	47,015.00
4.						Sr. Scientist					0.00	0.00	0.00
5.						Assoc Scientis					29,665.00	8,009.00	37,674.00
6.						Sr. Scientist					37,020.00	9,995.00	47,015.00
7.						Sr. Scientist					37,020.00	9,995.00	47,015.00
8.						Asst Scientist					30,464.00	8,225.00	38,689.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **336,122.00**

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						
4	Unit staff	11.64			68,957.00	18,619.00	87,576.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**87,576.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**423,698.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	2,375.00
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. Supplies, memberships, biohazard waste disposal, miscellaneous other expense	11,194.00
Total Other Direct Costs	**13,569.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**437,267.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	437,267.00	122,435.00
		Total Indirect Costs	**122,435.00**

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)	**559,702.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Diabetes, Obesity, & Metabolism (now Cardiometabolic Health)

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Cardiovascular disease is the most common cause of death in the United States. Cardiovascular disease, when combined with the pathophysiologically related processes of obesity and diabetes (collectively termed cardiometabolic diseases), are by far the most important contributors to morbidity, loss of productivity, and health care costs in the United States. There are many inter-related factors that contribute to susceptibility to cardiometabolic diseases, including genetic factors (genome and epigenome), dysplipidemias, inflammatory status, sedentary life style, and diet. It is increasingly recognized that these processes lead to the initiation of insulin resistance and cardiovascular diseases such as atherosclerosis, which occurs years or even decades before becoming clinically evident. The ONPRC has fostered the development of a small but internationally recognized and well-funded group of investigators focused on various aspects of cardiometabolic disease, with a particular focus on adult and early-onset obesity and diabetes, with a recent addition of research programs in cardiovascular disease. Based on the supportive critiques of the most recent P51 grant renewal and by the ONPRC Scientific Advisory Board, the scope of the ONPRC Division of Diabetes, Obesity and Metabolism has been widened to include greater involvement from affiliated researchers in cardiovascular disease, resulting in the restructuring of the group as the Division of Cardiometabolic Health. Members of this group have developed several powerful nonhuman primate (NHP) models that uniquely mimic the complexities of the development and pathogenesis of metabolic diseases in humans. The group has also developed unique non-invasive assessment tools for studying disease pathophysiology in NHPs. Using these models and these unique research tools available at ONPRC, the members of the Division of Cardiometabolic Health have been highly successful in providing unique insight into disease pathophysiology and new treatment algorithms. The group has also established strong and productive collaborations with renowned investigators at OHSU, throughout the United States and internationally. Under the auspices of this Division, the ONPRC has continued to expand the scope of the Obese NHP Resource, which supports the development and maintenance of these powerful animal models and research tools, and has made them available to the national research community. Because of the continued success of this research program and the recognized importance to improving human health, ONPRC has partnered with the Knight Cardiovascular Institute (KCVI) at OHSU to expand core services and to foster collaborative research programs between basic scientists and physician scientists. This new division is led by senior scientists 1) [Excluded by Requester] Division Head; 2) [Excluded by Requester] ONPRC Associate Director for Research; 3) and [Excluded by Requester] along with a talented group of young scientists with primary affiliation at ONPRC and senior internationally-renowned affiliated KCVI investigators. Our scientists have set some fundamental goals for the next several years that will be key for the continued development and long-term success of this division.

Specific Aim 1: To develop a fully integrated and collaborative Division focused on the understanding of the biology and pathophysiology of cardiometabolic diseases, with a collective group of scientists focused on the diverse aspects of this health epidemic as a foundation. There will be a strong focus on increasing our understanding of the molecular and pathophysiological complications that develop during the progression of these diseases, as well as the investigation of new diagnostics and therapeutics to prevent or reverse complications associated with these diseases.

Specific Aim 2: To recruit new investigators to provide new expertise and technical approaches to allow a more diverse and integrated approach to the investigation of these complex diseases. These diverse approaches and areas of expertise will allow a more efficient use of these valuable research models, as well as providing a rich intellectual environment. The goal is to expand the Division with the recruitment of additional assistant core scientists in areas that complement our current faculty, but that expand into areas where we lack expertise.

Specific Aim 3: To develop a supportive and constructive environment for training the next generation of scientists in the use of complex and highly translatable NHP models of metabolic diseases. The NHP model has been identified nationally as a critical translational research tool. This is especially important in the areas of metabolic diseases since the NHP model so closely mimics the human disease. However, only a small number of national investigators that regularly use this valuable model. Thus, it is key to provide a rich training environment and resources to expand this research community.

B.1.a Have the major goals changed since the initial competing award or previous report?

Yes

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DOM_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-DOM_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The Division's scientists have a strong record of publications based upon their funded research.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The specific aims remain conceptually similar to those originally stated, but with the proviso that the research focus of the Division will progressively incorporate more emphasis on cardiovascular research in harmony with the recent Division relabeling, leadership change, and expansion of faculty. New research activities planned include projects using molecular imaging to assess the earliest stages of atherogenesis, assessment of lipoprotein genetics associated with vascular dysfunction, and assessment of mechanisms responsible for metabolic memory. Resources associated with the recruitment of a new Chief will be used to hold two research retreats to encourage greater collaboration with physician-scientists at OHSU, other academic institutions, and industry. There will be expansion of the Obese NHP Resource. Faculty members of the Division of Cardiometabolic health are tasked with the planning and construction of the new Primate Multimodality Imaging Center, the establishment of imaging procedures within the Center, and the integration of advanced imaging in existing or future research programs throughout campus.

DIVISION OF DIABETES, OBESITY, AND METABOLISM, NOW KNOWN AS CARDIOMETABOLIC HEALTH: ACCOMPLISHMENTS

Division name change and Specific Aim 2: Although the specific aims remain conceptually similar to those originally stated. Specific Aim 2 outlined plans to expand the scope of the research activities of the Division. There have been substantial strides towards this Aim, which have resulted in constructive changes in Division labeling, leadership, scope, and faculty composition. Accordingly, the Division of "Diabetes, Obesity, and Metabolism" has been restructured as the "Division of Cardiometabolic Health," which reflects a continued focus on obesity and insulin resistance, with additional contributions from researchers with a primary focus of cardiovascular disease (atherosclerosis, heart failure, cardiac aging) and diagnostic imaging. The expanded scope is now reflected by changes in the Specific Aims.

Excluded by Requester who is an expert in cardiovascular imaging, molecular imaging, atherosclerosis, and diabetic microvascular dysfunction, has been recruited as the new Division Chief. Excluded by Requester recruitment has come with resources for: (1) recruiting other core scientists and independent non-core scientists; (2) holding research retreats to explore unique collaborative research activities in the field of lipid disorders, obesity/diabetes, and cardiovascular disease; (3) funding for pilot grants to encourage cross-collaborative research programs between basic scientists and physician scientists; and (4) to develop novel non-invasive imaging methods for assessing adipose biology, muscle biology, and vascular biology.

The Division has been very successful in maintaining a robust level of funding from a variety of sources, including the NIH, NASA, non-profit foundations, and partners in industry. Several long-term partnerships with Private Source have been established.

Two former staff scientists Excluded by Requester, who have been successful in obtaining independent grant support, have been promoted, with Excluded by Requester becoming a core scientist and assistant professor and Dr. Excluded by Requester becoming a research assistant professor. There has been a marked increase in affiliated scientists, most of whom have a primary appointment at OHSU (KCVI, Biomedical Engineering, Pediatrics) but who have leveraged the unique resources at the ONPRC to make critical discoveries or translational steps in their research programs.

Research productivity has been robust in terms of scientific publications and discoveries that will lead to continued collaborative research support. New models of atherosclerotic disease are now being developed which will also enable better understanding of the relationship between diet, activity, obesity, insulin resistance and atherogenesis.

DIVISION OF DIABETES, OBESITY, AND METABOLISM: TRAINING & PROFESSIONAL DEVELOPMENT

The Division supports the training of postdoctoral and clinical fellows and also aims to provide opportunities for leadership for more junior members. The faculty status of all ONPRC investigators has changed according to new OHSU policies in faculty classifications. Excluded by Requester was promoted to Research Assistant Professor and Excluded by Requester was promoted to Assistant Core Scientist/Professor. With the restructuring of the Division, the KCVI T32 training grant (eligible for MD and PhD post-doctoral training) has prioritized the recruitment of a post-doctoral fellow in the Division of Cardiometabolic Health.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Research Material	The Obese NHP Resource based in the Division provides NHP samples to internal and external users based upon published rates. Reagents, novel molecular imaging protocols, and other resources developed through NIH-funded studies are shared according to NIH guidelines.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

The principal impact of Divisional activities on technology transfer is represented by the Private Source strategic partnership that is now in its third year. This project will employ the NHP model of diet-induced obesity for discovery of targets for obesity and diabetes treatments the rights to which will be licensed to Private Source by OHSU, with OHSU retaining IP rights to any targets not licensed to Private Source leaving the option of establishing a new company to develop these targets. IP rights will be sought for any truly novel molecular imaging tracers.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

The recruitment of a core scientist who will also serve to oversee day-to-day operation of the future Primate Multimodality Imaging Center represents a major challenge since the skill sets needed for the position (radionuclide imaging experience in large animal models of disease) will limit the applicant pool. This anticipated difficulty will be addressed primarily through personal communications in addition to standard advertised announcements.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			92,550.00	23,733.00	116,283.00
2.						Sr. Scientist					11,569.00	3,239.00	14,808.00
3.						Asst Scientist					11,217.00	3,141.00	14,358.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **145,449.00**

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 staff	6.0			26,973.00	7,544.00	34,517.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**34,517.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**179,966.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	1,500.00
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
Total Other Direct Costs	**1,500.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**181,466.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	181,466.00	50,810.00
		Total Indirect Costs	**50,810.00**

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)	**232,276.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Interdisciplinary Research Programs

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

In the previous P51 renewal, three Working Groups were established to foster areas that were not adequately represented by the existing Research Divisions. These included Biology of Aging, Metabolic Disease, and Stem Cells and Developmental Biology. The explicit goal of these was to establish interdisciplinary research programs that fostered interdivisional and inter- and intra-institutional collaborations. As expected, during the past funding period, each of these has evolved along different paths. As described below and in the research strategy section, the Biology of Aging Working Group has continued to mature and is now designated an IDRP at the Center. The Metabolic Disease Working Group has matured to become a new Research Division, as detailed in its designated section. The Stem Cell & Developmental Biology Working Group has been integrated into the original Division of Reproductive Sciences with its change in focus to the Division of Reproductive & Developmental Sciences. Two new Interdisciplinary Research Programs have been established based on recommendations from the 2011 Scientific Retreat. The Early Childhood Health & Development program represents the increasing interactions between the Center and the Departments of Ob-Gyn and Pediatrics at OHSU, and the Primate Genetics Program represents the growing importance of genetic and genomic aspects of the NHP model and the unique pedigreed NHP colonies at the Center. As with the Working Groups, these programs are supported minimally by the P51, to provide funds to enhance communication and interaction by supporting seminar speakers and symposia. The Specific Aims are:

Specific Aim 1: Biology of Aging. The Biology of Aging Program is a multi-disciplinary research program involving Core and Affiliate investigators from each of the four research Divisions, and it draws strength from the broad spectrum of scientific and technical expertise afforded by its members. Since nearly 20% of the US population will be 65+ years old by 2030, a universal goal is to find safe and effective ways of enhancing the health and quality of life in the elderly, and to find ways of reducing premature senescence. Unfortunately, the mechanisms that underlie normal and pathological human aging are still poorly understood, and this significantly hampers the development of effective therapies. NHPs are long-lived and show age-related physiological changes that more closely resemble those of humans. The associated Primate Aging Resource provides Center investigators an unique opportunity to study the etiology of normal and pathological human aging. The goals for the next funding period include: 1) strengthening existing NHP aging disease models and to developing new models; and 2) strengthen inter-disciplinary collaborations and increase their translational potential.

Specific Aim 2: Early Childhood Health & Development. The overall goal of the newly established Early Childhood Health & Development Program is to develop and utilize NHP models that encompass key developmental stages (i.e., prenatal and postnatal life) that have been demonstrated to strongly influence the risk of developing cardiovascular, pulmonary, metabolic and psychological disease during early childhood and throughout life. Specifically, program investigators collectively study events that occur during pregnancy (i.e., intra-amniotic infection, hypoxia, growth restriction, maternal nutrition, placental abnormalities and preterm birth), as well as broad aspects of human development (i.e., cardio-pulmonary physiology, neurodevelopment, immune function and vaccine development) as a means of understanding factors and/or events during prenatal and postnatal life that can have profound effect on the overall health of an individual and as an adult. The near-term goals of the program during the next funding period are to: 1) identify and develop key areas of research within the program to increase collaborative interactions and the scope of research in this area; 2) seek an array of funding opportunities to take advantage of the integrated interests of the program, in particular collaborative, team-science mechanisms; and 3) develop a strategic plan for longevity of the program.

Specific Aim 3: Primate Genetics Research. The goal of the Primate Genetics Program is to leverage the complementary genetics expertise of program investigators, unique ONPRC capabilities such as the Japanese Macaque Resource, and state-of-the-art technologies such as those available through the Molecular & Cellular Biology Research Support Core, to characterize the contribution of genetic and epigenetic variation to complex disease phenotypes in non-human primates, and to translate these findings to human disease. The goals of the program include :1) ongoing genetic studies in macular degereration and neuropsychiatric disorders, obesity, cardiovascular disease and obesity; 2) characterization of rhesus genome variation; 3) epigenetic studies in alcohol abuse and adiposity; and 4) NHP genomic analysis method development.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-IDRP_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-IDRP_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

BIOLOGY OF AGING

Presentations at Scientific conferences:

Excluded by Requester (2016). Identifying regulators of synaptic stability during normal healthy ageing in non- human primates. Society for Neuroscience Abstracts, #515.12.

Excluded by Requester 2016). Characterization of the rhesus monkey suprachiasmatic nucleus during aging. Society for Neuroscience Abstracts, #815.06.

Excluded by Requester (2016). Retinal degeneration in a Japanese macaque model of neuronal ceroid lipofuscinosis. XVIIth International Symposium on Retinal Degeneration. Abstract 94. (Kyoto).

EARLY CHILDHOOD HEALTH & DEVELOPMENT (ECHD)

Seminars:
•Perinatal Brain Injury: mechanisms, consequences and treatments. Gothenburg, Sweden. June 2016.
•International Conference on Cerebral Palsy and other Childhood-onset Disabilities; 5th International Conference of Cerebral Palsy (ICPC); 28th Annual Meeting of the European Academy of Childhood Disability (EACD); 1st International Alliance of Academics of Childhood Disability (IAACD). Stockholm, Sweden. June 2016.
•International Federation of Placenta Associations (IFPA) conference and the IFPA Workshop: Placenta and Fetal Brain Development. Portland, Oregon. September 2016.
•AVP/AALAS National Meeting. Charlotte, North Carolina. October 2016.
•36th Annual Meeting of the American Society of Reproductive Immunology. Baltimore, Maryland. November 2016.

ONPRC Educational Outreach Program:
Approximately 3000 students of varying educational levels have visited the Oregon National Primate Research Center over the past 12 months. In addition to touring the Center students have the opportunity to meet a variety of Investigators, many of which are part of the ECHD program (e.g., Science panels, Seminars, Job shadowing).

PRIMATE GENETICS

A symposium to present the breadth of genomic approaches currently being applied to the study of primates will be held at the ONRPC in April 2016, and will involve over 100 participants from the multiple research institutions.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

BIOLOGY OF AGING
There is growing awareness that nearly 50% of our genes have a circadian pattern of expression. Consequently, to better understand the etiology of normal and pathological aging we intend to continue with our gene expression profiling efforts, to establish which genes show circadian patterns and to determine if these patterns change during aging. In support of this goal Pending Support Pending Support

To make more efficient use of the limited primate aging resource, we intend to coordinate many of our aging-related research projects. In support of this goal, Pending Support

EARLY CHILDHOOD HEALTH & DEVELOPMENT
We have continued to build and strengthen our collaborative efforts through additional investigators and departments joining the ECHD (2015-2016). We now have expertise in the following disciplines:
•Neonatology/Pediatrics
•Neurobehavior & Cognitive Development
•Neuroscience and Advanced Imaging
•Immunology & Vaccine Development
•Nutrition & Metabolism
•Pregnancy (i.e., preterm birth, ART)
•Cardiovascular Physiology (i.e., preeclampsia)

Through these collaborations the current funding status for the ECHD is in excess of $25M via multiple NIH grant mechanisms (e.g., P51, G20, R01, R24, R21). Our 2020 Vision is to continue to expand the diversity of expertise including, but not limited to:
•Pediatric & Adolescent Oncology
•Psychiatry & Mental Health (mother and child)
•Pharmacology & Drug Metabolism

Our 2020 Funding Goal for the ECHD is $50M via NIH grants and expanded grant mechanisms (i.e., Private Source Private Source industry partnerships). ECHD members will continue to disseminate their research results at National and International Conferences.

PRIMATE GENETICS
We plan to launch large-scale genomic sequencing and genotype analysis of ONPRC rhesus macaques, pending R24 funding. These data would be made available to other investigators through the creation of a genotype and phenotype searchable database, thus will immediately be of value for expanding interdisciplinary genetic research across all divisions.

We will continue to advance the genetic study of alcohol addiction, chromosome missegregation, healthy aging, cardiovascular disease biomarkers, and adiposity/obesity, through other funding mechanisms.

We will evaluate the success of our first large-scale primate genetics symposium to determine if we will repeat that in the coming year, or

rather invite individual speakers to the ONPRC throughout the year.

INTERDISCIPLINARY RESEARCH PROGRAMS: ACCOMPLISHMENTS

BIOLOGY OF AGING

The Biology of Aging program continues to emphasize interdisciplinary approaches to elucidate the causal mechanisms that underlie aging-related pathologies, and to lay the foundation for safe and effective therapies. As in previous years, novel aging-related grant proposals were submitted; these focused on specific aspects of human aging and neurodegeneration that can be readily modeled in the rhesus monkey. Major accomplishments included: (1) The impact of age-related hormonal changes on cognitive function was examined in old females, and results from the completed studies were published in the Journal of Neuroscience and Genes, Brain and Behavior. (2) Development of a novel translational animal model in which to examine the etiology of hot flushes was initiated by securing a new R21 grant entitled “Establishment of a Primate Model for Menopausal Hot Flushes”. By showing that skin temperature changes can be monitored noninvasively, using a thermal-imaging camera, it will be possible to evaluate the efficacy of novel therapies for hot flushes in postmenopausal women. (3) New international collaborations were established with the University of Valparaíso in Chile (resulting in a publication in Neurobiology of Aging), and with the Roslin Institute in Scotland (resulting in a scientific abstract that was selected for presentation at the 2016 Society of Neuroscience annual conference as a Hot Topic).

EARLY CHILDHOOD HEALTH & DEVELOPMENT (ECHD)

Zika Virus has explosively spread throughout the Americas during the past year, possibly infecting up to 3-4 million people. With the global concern of Zika spreading, including the rise of microcephaly, health officials declared a Public Health Emergency. In an effort to respond to this new pandemic quickly the ECHD assembled a multidisciplinary team of investigators with expertise in Pathobiology & Immunology, Obstetrics & Gynecology, Fetal & Neonatal Physiology, Placenta Pathology, Pediatric Neurology and Advanced imaging techniques; many of who had not previously collaborated. In addition, the involvement of the Vaccine & Gene Therapy Institute has strengthened these collaborations. The Zika working group has already been successful in securing funding through the ONPRC Pilot Project Program, NICHD (R21) and NIAID (U01 pending Council review).

PRIMATE GENETICS

We continue to focus on advancing NHP genomic analysis methods as a means to accelerate the use of NHPs as models of biomedical disease and precision medicine approaches. Towards that goal, we submitted and were awarded R24 funding to support the large-scale genomic characterization of the ONPRC rhesus macaque breeding colony. In addition, the 2017 ONPRC Primate Genetics Seminar Series will feature four national leaders presenting work of the epigenetic, genetic, and microbiome’s contributions to disease.

In August 2016, we launched a national search for the recruitment of a senior faculty member to lead the expansion of a Primate Genetics Section over the next few years. Our priority is to recruit a faculty member with expertise in statistical genetics, genomic analysis of complex traits, or bioinformatics to enhance and expand the collaborative genetic analysis of NHP disease models.

INTERDISCIPLINARY RESEARCH PROGRAMS: TRAINING AND PROFESSIONAL DEVELOPMENT

BIOLOGY OF AGING

The Biology of Aging program provided a fertile environment for the training of 3 graduate students and two visiting scientists from the University of Valparaíso, Chile.

EARLY CHILDHOOD HEALTH & DEVELOPMENT (ECHD)

One graduate student is currently completing a rotation in an ONPRC laboratory, and we continue to regularly host an affiliate faculty member who has shared grants Excluded by Requester from University of California at Riverside).

PRIMATE GENETICS

OHSU was fortunate to host the International Federation of Placenta Associations (IFPA) conference in September 2016. Several members of the ECHD were on the local organizing committee. Collectively the ECHD was involved with the following:

Symposia (5 ONPRC Investigators):

- Viral Infection and the Placenta
- Trophoblast Specification/Progenitors
- Bioinformatics/Systems Biology applied to the Placenta

Workshops (8 ONPRC Investigators):

- Trophoblast Biology and Pathology
- Inflammation – what is it and how does it affect the placenta
- Sexual Dimorphism in placental function
- Systems Biology/Bioinformatics applied to the placenta
- Imaging and the Placenta
- Linkage between placenta and development of other organs

In our efforts to promote training opportunities within the framework of the ECHD, the group contributed funds to the IFPA Post-Doctoral Travel Awards to enable National / International graduate fellows to attend this meeting, thus providing training opportunities and exposure of the ECHD working group on the international research stage.

Over the last reporting period ECHD funds have also contributed to the purchase of a new advanced ultrasound machine Proprietary Info to replace our current Proprietary Info This upgrade has increased the scope of capabilities for our Interdisciplinary Research Program and has allowed additional investigators to be trained and utilize this equipment. The Proprietary Info is now housed in the containment facilities for use on multiple projects for which advanced ultrasounds were not previously available due to biosafety housing constraints, for example our investigations related to Zika Virus during pregnancy.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary		EFFORT		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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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. Interdisciplinary program	20,000.00
Total Other Direct Costs	**20,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**20,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	20,000.00	5,600.00
		Total Indirect Costs	**5,600.00**

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)	**25,600.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Pilot Research Program

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The goal of the ONPRC Pilot Project program is to encourage new avenues of investigation using appropriate nonhuman primate (NHP) models through the provision of funds for generation of preliminary data that can serve as the foundation for follow-up support from the NIH and other agencies and sources. This will be achieved through pursuit of the following Specific Aims:

Specific Aim 1. Solicit proposals from a wide spectrum of potential applicants through effective outreach at the institutional, local, and national levels. Annual announcements are circulated through e-mail and the ONPRC website to Center, OHSU, and NPRC consortium members to attract a robust response from interested parties.

Specific Aim 2. Employ a strong, credible, and transparent review process to select the most meritorious proposals. Proposals are evaluated through a two-step process that includes an initial assessment of letters of intent by the ONPRC Research Advisory Committee (RAC), followed by a request for full proposals from the highest-ranked preliminary proposals. These are then reviewed in depth by the ONPRC RAC and external ad hoc reviewers chosen from the ONPRC National Scientific Advisory Board (NSAB) and other entities as necessary for appropriate expertise.

Specific Aim 3. Monitor progress and outcomes to determine return on investment of allocated funds. Productivity in terms of manuscripts and grants submitted and awarded based on Pilot Program support are assessed through final reports and follow-up monitoring by the Associate Director for Research.

The ONPRC Pilot Project program plays a critical role in allowing investigators to develop research projects using NHPs, and is especially important for new investigators recruited to the ONPRC who lack significant prior NHP research experience. The program also provides funds for established investigators to develop new NHP models and preliminary data that are absolutely essential if new external grant funding is to be obtained.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Pilot_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Pilot_Trainings.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

These projects are still underway and results are not expected until the next reporting period.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The solicitation for the current year pilot grant program has been sent out and proposals will be evaluated for funding that will start May 1, 2017.

PILOT RESEARCH PROGRAM: ACCOMPLISHMENTS

The pilot projects listed below and detailed in Overall Section G. were funded in the most recent budget period.

1. Excluded by Requester (ONPRC, Neuroscience) was awarded $40,000 for a project entitled "Effects of chronic alcohol use on the sperm epigenome and ncRNA expression in rhesus macaques."
2. Excluded by Requester (UCLA AIDS Institute) was awarded $70,000 for a project entitled "Clearing HIV-1 reservoirs by delivery of bNAb within polymer nanocapsules."
3. Excluded by Requester (UCLA, Molecular Cell and Developmental Biology) was awarded $55,000 for a project entitled "Characterization of primate germline differentiation using the rhesus macaque."
4. Excluded by Requester Yale University School of Medicine) was awarded $60,000 for a project entitled "Development of Controlled Release Mitochondrial Protonophore (CRMP) as a novel treatment for Type 2 Diabetes and Non-Alcoholic Steatohepatitis in diet-induced obese nonhuman primates (DIO-NHP)"
5. Excluded by Requester (VGTI) was awarded $74,000 for a project entitled "Characterization of Zika Virus Infection during Pregnancy."

PILOT RESEARCH PROGRAM: TRAINING AND PROFESSIONAL DEVELOPMENT

A major objective of the pilot program is to generate preliminary data for more substantial follow-up on grant applications that, if successful, will facilitate the professional development of the applicants by demonstrating their ability to procure major independent research support.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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 program	200,000.00
Total Other Direct Costs	**200,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**200,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	200,000.00	56,000.00
		Total Indirect Costs	**56,000.00**

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)	**256,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Improvement & Modernization

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Improvement and Modernization (I&M) funds are provided up to a maximum of $600,000 per year. These funds can be used to upgrade the physical plant (repairs and renovation of facilities) and to replace obsolete shared resources and equipment (FOA, IV. G.). At ONPRC, Facilities, the Division of Comparative Medicine (DCM), Information Systems (IS), and the Research Support Cores provide shared resources to support the NHP research mission of ONPRC. Items are requested by each of these areas, individually justified, and then a committee works with the requestors to prioritize the requests to insure the continued improvement and modernization of these shared resources and that the requests contribute to the fulfillment of the goals of the ONPRC. A distinction is made between routine maintenance items provided by Facilities and specialized improvement/maintenance programs aimed toward the long-term preservation of the integrity and functionality of our facilities. Routine maintenance is included in the Facilities operations budget; specialized improvement/maintenance is included in the I&M budget. The amount provided through this mechanism is an integral part of a larger effort to provide for the comprehensive upkeep and improvement of the ONPRC facilities and resources that are used for NHP research and support.

Through these funds I&M supports:
•Improvement and modernization of buildings and equipment used in support of the NHP resources and research through Facilities requests.
•Improvement and modernization of Research Support Core equipment used in support of NHP Research through requests from the individual Research Support Cores.
•Improvement and modernization of Information Systems specific to the NHP related work of the ONPRC such as the PRIMe system and NHP research related bioinformatics through requests from the ONPRC Information Systems.
•Improvement and modernization of the DCM resources that provide for the care of our NHP colony through requests from DCM.

Specific Aim 1: To appropriately identify, justify, and prioritize requests for the improvement and modernization of ONPRC resulting in improved equipment and facilities specifically related to NHP research and support.

Specific Aim 2: To provide for the timely implementation of the approved requests through skilled professionals resulting in efficient and effective use of the improved resources.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-IM_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will be implementing a program to start replacing -80 freezer farms to liquid nitrogen freezers. This will require renovations to building to pipe in the liquid nitrogen so the freezers are not on individual tanks. This strategic change sets the Center up for the future to reduce energy costs and be able to have better stability with items stored in the LN freezers with power outages and natural disasters.

We will be finishing up an assessment with the HVAC systems on campus to prioritize and start upgrading them in the animal space.

IMPROVEMENT & MODERNIZATION: ACCOMPLISHMENTS

The host institution paid for consultants to perform a facilities assessment analysis for all structures on our campus. We used the new tool to help and assess and prioritized upgrades and renovations. It allowed us to be strategic in our decision making and is an integral part of future planning for campus.

The Center integrated the deferred maintenance and upgrade list with the host institutions annual process for reviewing and prioritizing. The host institution actively participates in the decision making and also provides supplemental funding to the campus.

The Center, with coordination from the host institution, completed a 20-year master plan with the City of Hillsboro. The purpose of the master plan is to describe campus improvements planned for the next ten and twenty year periods respectively. The master plan also addresses contingent issues such as infrastructure improvements, storm water management, circulation and parking needs.

The vision for the campus is that it will be an attractive, secure and vibrant Center of biomedical discovery and scholarship that integrates advanced research facilities, high performing workplaces, safe and enriching animal care spaces and the natural environment.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Major Infrastructure Improvements and Capital Equipment (Supported by ORIP)

Water Line Replacement, Administration Building: $245,000
Excluded by Requester Remodel: $68,199
Excluded by Requester VAC Panel Replacement: $33,121
Fan Replacement: $26,739
Fan Replacement: $17,808
ONPRC Remodel: $9,133

Sub-total Expense: $ 400,000

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary		EFFORT		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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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	500,000.00
Total Other Direct Costs	**500,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**500,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
		Total Indirect Costs	

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)	**500,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Outreach & Community Engagement

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Support for biomedical research depends in great part on public awareness of the value of such research and an understanding of the process by which medical science discoveries are made. A number of studies indicate that science proficiency in the United States lags behind that in many other countries, creating a significant challenge for maintaining public support for research. In addition, the dialog between researchers and the public about the essential need for animal models in biomedical research is important in maintaining support for research that requires animals. Providing multiple opportunities for the general public to learn about biomedical research at the ONPRC and its value is, therefore, of critical importance to the long-term success and productivity of the research enabled by the core grant.

During the previous funding period, education outreach at the ONPRC involved a multi-faceted program that targeted a number of different populations using a variety of strategies. Thousands of students, teachers and members of the public participated in these programs. Our strategies included tours, classroom visits, an informal science program that is held weekly during the school year called Science Ambassadors, a docent program, courses for high school students, veterinary externships, and high school, undergraduate, and teacher apprenticeships and/or volunteer opportunities. Relationships with surrounding school districts were cemented through our ability to host students tin hands-on learning opportunities conducted in our dedicated Learning Laboratory. A bi-annual lecture series, the ONPRC Science Café, was launched four years ago, and continues to flourish. This series provided an additional opportunity to inform the public (high school through mature adult) about research approaches to specific health issues as well as discussing the need for nonhuman primates in that research. The goal of each of these highly successful programs was to enhance science education and to provide unique experiences that strengthen public understanding of the value of biomedical research and the scientific process.

In the next funding period, we aim to continue and enhance these highly successful programs, and to expand their scope through additional outreach activities to the public and to state and federal legislators. Our specific aims are:

Specific Aim 1. To provide multiple outreach activities for the general public, teachers, and students. We will continue to offer the multiple successful programs developed at ONPRC to provide unique experiences that educate students and adults from multiple backgrounds. We will enhance existing programs and introduce additional new programs that will expand our outreach aims.

Specific Aim 2. To communicate the activities and discoveries of ONPRC personnel to the general public. In conjunction with our outreach activities, we will work closely with the Department of Strategic Communications at OHSU to highlight the exciting discoveries of Center scientists and other Center activities to the media and to state and federal legislators.

Specific Aim 3. To engage with the general public in a series of programs to foster discussions around science and the value of science. We will enhance our Science Café series by including sessions that focus on ethical questions that arise in science, specifically related to the use of gene editing and other cutting-edge technologies.

Specific Aim 4. To continue to represent ONPRC through participation in OHSU's public outreach events as appropriate. The ONPRC Outreach Program is an active participant in multiple OHSU-sponsored events. This affords multiple opportunities to educate the public about the role of the Center as an important component of OHSU's mission.

Specific Aim 5. To serve as a resource to other biomedical research institutions who wish to develop outreach programs. ONPRC has been an industry leader in the development of educational outreach programs. We will continue to improve and expand our own programs, and participate when invited to share our expertise with others in the biomedical research community.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Outreach_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-Outreach_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Aside from the Outreach accomplishments to disseminate information to the public as listed in Section B.2, we have shared our programmatic success stories with the NPRC Outreach Consortium and also with our NCTRI Outreach Core colleagues.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

•Identify additional sources of funding for programs in community/beyond
•Inaugurate, evaluate and refine the "Provost Scholar" apprenticeship program for underrepresented undergraduate students
•Promote the "Partners in Science Program" to qualified teachers through individual discussions with high school teachers who visit ONPRC with their students and through presentations at Science Faculty meetings
•Work with educational leaders in our community to implement our popular Science Ambassadors mentorship program at the district level.
•Assist in development/implementation of science fairs in the community
•Reach out to elected representatives at state and federal levels to invite them to learn more about the essential need for biomedical research leading to medical progress

OUTREACH & COMMUNITY ENGAGEMENT: ACCOMPLISHMENTS

Specific Aim 1: We hosted over 4000 visitors to our center during 2015, mostly through our popular tour program for school groups. Visitors enjoy an interactive presentation about biomedical research, as well as a tour of our outdoor-housed breeding colonies. Many groups also have the opportunity to meet our scientists, who participate frequently on interactive panels. To support our need to host visits from very large groups we continue to recruit and manage a group of volunteer docents. We have increased our efforts to engage underrepresented minorities and disadvantaged students in these programs. We provided a one-day event (Science Saturday) for 48 – 5th graders in May of 2016, and a one-day event (Camp Monkey) for 60 middle school students in August. Working closely with our parent institution, OHSU, we hosted two day-long lab experiences for underrepresented high school students and a one-week science camp for 20 underrepresented high school students during the summer of 2016. We will host similar events in 2017. Funding secured through yearly grant applications to a private donor and other sources allowed us to host nearly 20 students (high school and undergraduate) in apprenticeships during the summer of 2016. To complement this ongoing program, we worked with OHSU's Provost to inaugurate a program through that office that provided funding for the recruitment and support of two underrepresented undergraduate apprentices at ONPRC during the summer of 2016. This program will support two more students during the summer of 2017.

We continue to strengthen our ties with Beaverton School District's "Health & Science" School, the nearby science magnet. 2015-2016 was the fifth year of our Middle School Science Club program, in which ONPRC scientists and staff host a science activity for up to 30 students each month. In the 2015-2016 school year, we hosted a 10-session after-school program for high school students with the understanding that the activities we demonstrated would be assimilated into the school's curriculum on an ongoing basis.

Our Science Ambassadors mentorship program has become so popular that we have initiated talks with leading community educators to expand the program into the schools.

Many ONPRC scientists participated in science talks organized by non-ONPRC entities, including "Science on Tap," "Science Pub," the "Brain Awareness lecture series," and "Brain Fair." These venues offer additional opportunities for us to dialog with large audiences around the topic of biomedical research.

Specific Aim 2: Highlights from 2016 news stories related to scientific discoveries at ONPRC include:

Nature Medicine study led by Excluded by Requester is the first to show antibodies administered within one day of exposure can clear a nonhuman primate virus similar to HIV. Covered by *HealthDay/MedlinePlus; PR Newswire release picked up by dozens of media outlets around the country; Vaccine Daily News; KGW-TV story picked up by Northwest Cable News; KATU-TV; KPTV; KDRV (Medford); The Oregonian article picked up by The Register-Guard, Washington Times and others; Portland Business Journal; KEX-Radio; AMFAR.org; The Portland Physician Scribe (page 7); OHSU News press release; OHSU Research News blog post.*

Study led by Excluded by Requester suggests adults should get tetanus booster shots at ages 30 and 60, rather than every 10 years: *Forbes; HealthDay News article picked up by U.S. News & World Report, United Press International, MedlinePlus; The Columbian; OPB-Radio; KGW-TV story picked up by Northwest Cable News; KEX-Radio; KPTV story picked up by several TV station around the country, including KPAX-TV (Montana); OHSU News press release.*

HIV vaccine research led by Excluded by Requester is profiled in *Newsweek, Portland Monthly, Science.*

Excluded by Requester escribes Zika vaccine research currently underway in rhesus macaques at the OHSU Vaccine and Gene Therapy Institute: *Forbes.*

Excluded by Requester provides background, answers questions about Zika virus research: *The Oregonian, Portland Business Journal, Bend Bulletin, Portland Business Journal,*

Excluded by Requester describes advances made possible through research in nonhuman primates at National Institutes of Health Nonhuman Primate Workshop in Bethesda, Maryland: *Science.*

Excluded by Requester and team's use of gene-editing technology to aid in the understanding of several human diseases and disorders, including autism, congenital blindness and deafness and HIV, is profiled in *Portland Business Journal.*

Excluded by Requester shares her research into why 5 percent to 8 percent of all drinkers cross over into alcohol abuse at OHSU Brain Awareness lecture: *Portland Business Journal.*

Excluded by Requester describes her research into the known risk factors for alcohol abuse and the consequences of heavy alcohol consumption: *The Columbian.*

Private Source awards $200K to Excluded by Requester Excluded by Requester for their research into identifying eggs with the greatest potential of yielding a successful pregnancy: *PR Newswire release picked up by a number of media outlets around the country, including Yahoo! News.*

Oregon Sens. Jeff Merkley and Ron Wyden meet with Oregon National Primate Research Center researchers to discuss what's needed to fight Zika virus: *OPB-Radio story picked up by KUOW and Jefferson Public Radio; KPTV.*

Specific Aim 3: Funding available through the NCTRI grant supported the the third and fourth 4-part Science Café series during the Spring and Fall of 2016. This series is devoted to topics in female reproductive health; a second series, scheduled for February of 2017, will focus on the topic of "Genetic Approaches to Medical Progress." These series (scheduled on 4-consecutive weeknights in selected months) featured various Center scientists discussing their work and the importance of the NHP model to that work, as well as clinical colleagues from OHSU.

Specific Aim 4: Outreach personnel and volunteers represented ONPRC at the annual meetings of the Oregon State Science Teachers' Association and the Washington State Science Teachers' Association; the OHSU/OMSI "Brain Fair;" the OHSU "Brain Awareness Lecture Series," and continue to participate as active members in OHSU's "SOAR" Committee (Science Outreach and Resources).
The Education & Outreach Office worked closely with OHSU's Government Relations Office to arrange for several Oregon State representatives to visit the Center and meet with key personnel (Director, scientists, Outreach Coordinator).

Specific Aim 5: ONPRC's Outreach Coordinator presented a talk at the Northwest Association of Biomedical Research (NABR) "Connecting the I's" meeting, and has been invited to make presentations at the Public Responsibility in Medicine and Research Conference (PRIM&R) in March of 2017. These presentations focused on how to talk about biomedical research with the public and the importance of doing so. She is also participating in the Americans for Medical Progress initiatives related to public outreach.

OUTREACH & COMMUNITY ENGAGEMENT: TRAINING AND PROFESSIONAL DEVELOPMENT

Hands-on lab activities developed with the assistance of the ONPRC Office of Education & Outreach were piloted to educators at both the Oregon State Science Teachers Association and the Washington State Science Teachers' Association annual meetings during 2016. The Education and Outreach Coordinator actively recruits ONPRC scientist mentors and science teachers in nearby communities to participate in the Murdock Trust "Partners in Science" summer apprenticeship program.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5580

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			87,588.00	23,649.00	111,237.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **111,237.00**

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)	**111,237.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	3,000.00
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. Memberships, Hosting Groups & Guests	2,500.00
Total Other Direct Costs	**5,500.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**118,737.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	118,737.00	33,246.00
		Total Indirect Costs	**33,246.00**

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)	**151,983.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: NPRC Consortium-Based Activities

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The ONPRC takes an active role in promoting and contributing to each of the NPRC-based Consortium Working Groups. The major goals of each of these groups are listed below.

1.Behavioral Management (BMC). This group has the goal to strengthen communication and research collaboration to help to identify behavioral management best practices and promote psychological well-being for captive nonhuman primates (NHP). To this end, the BMC promotes resource sharing, standardization of terminology and assessment tools, and scientific collaboration among participants.

2.Breeding Colony Management (BCMC). This group enhances collaborations between NHP colony mangers of all national primate centers with regard to breeding management, herd health, regulatory compliance, SPF surveillance, facility management/design and resource sharing.

3.Clinical and Surgery Techniques (CAST). This group seeks to accelerate information transmission among NPRCs, to serve as a resource to develop best clinical and surgical practices among and within the NPRCs, and to facilitate networking among NPRCs and relevant institutes beyond NPRCs.

4.Computational Methods and Resources. The role of this group is to identify new and more productive synergies between people and computing technologies, to provide methods and software application resources to support other Consortium working groups, and to facilitate and make rigorous the sharing of data, practices and expertise between NPRCs.

5.Data Access Guidelines Group (DAGG). This group develops and maintains processes to ensure all website content and related access permissions are reviewed and approved by DAGG representatives. They educate working group participants on best practices to prevent unauthorized access or unnecessary exposure of shared information.

6.DNA Banking. This group has the goal of establishing and maintaining a National NHP DNA Bank to facilitate the distribution of NHP genomic resources for research use, establish a centralized web portal to enable direct access to DNA Bank content and distribution information and promote use of the National NHP DNA Bank through publications and targeted presentations.

7.Genetics and Genomics. This group has to goal of designing and developing a custom SNP-array for parentage analysis of rhesus macaques at all NPRCs, and an array for rhesus macaque ancestry analysis at all NPRCs. They are developing web-based analysis pipelines to facilitate parentage and ancestry genotype interpretation and to develop colony genetic management guidelines for optimizing the genetic health of NHP colonies across the NPRCs.

8.Integrity-Compliance. The purpose of this working group is to cultivate open discussions and critical thinking about matters related to compliance with federal regulations and NIH guidelines at the National Primate Research Centers (NPRCs). The first focus was the development of an on-line resource to provide information about IACUC protocol review and NPRC-specific attention to OLAW, USDA, and AAALAC regulations, guidelines and recommendations.

9.Occupational Health & Safety Working Group. This group plans to achieve a better understanding of the most updated information for those working with NHPs between the NPRCs, National B-virus lab and the Centers for Disease Control & Prevention, and to increase sharing of injury and exposure data between NPRCs to look for trends in data and share successful injury reduction strategies.

10.Outreach. The goal of this group is to share best practices with respect to handling issues that are unique to research involving animals, to identify opportunities to educate the public locally (near each NPRC, at public events, via the internet, and through the press), and to develop appropriate responses to persons who are opposed to biomedical research that involves animals. There is close communication with the Public Relations WG to assure that plans are coordinated.

11.Pathology. This group seeks to foster cooperation between the NPRC's to effect improved understanding of NHP pathology and to share best practices for greater efficiency. They have a goal to increase availability of the pathology resource (data, images, etc.) between and outside centers to better serve as a national resource for NHP Pathology.

12.Public Relations. This group was established this year and is responsible for working with the NPRC directors as the Consortium develops a public facing website, logo, and educational plan for national impact. They will share activities and information via the web and will develop marketing materials that can be used by all NPRCs at a national level within NIH and with other governmental and non-governmental agencies. There is close communication with the Outreach WG to assure that plans are coordinated.

13.Training. This group contributes to, and takes a leadership role in promoting, the exchange of clinical or operational case presentations of NHPs amongst NPRCs and other contributing institutions to foster a collegial and communicative environment amongst these institutions, and ultimately to promote best practices.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-NPRC_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: RPPR-NPRC_Training.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

1.Behavioral Management (BMC). Nothing to report

2.Breeding Colony Management (BCMC). Nothing to report.

3.Clinical and Surgery Techniques (CAST). We have expanded membership to 4 additional non-NPRC institutions (22 external institutions total).

4.Computational Methods and Resources. Installation of software tools at Tulane NPRC, CMRG page on the NHPRC Consortium website, presentation at 2016 AALAS National Meeting, presentations at monthly BCMC conference calls, and periodic briefings for Consortium working groups and technical staff across the NPRCs.

5.Data Access Guidelines Group (DAGG). Nothing to report.

6.DNA Banking. The availability of plasma collected by the ONPRC DNA Bank is indicated in our electronic records system (PRIMe), and samples are provided upon request.

7.Genetics and Genomics. A summary of the new parentage assay, and the genetic metrics software were presented to the BCMC by web conference. Genotyping-by-sequencing and imputation protocols have been published this year, are currently being shared by consultation with the YNPRC, and will be shared with other NPRCs as requested.

8.Integrity-Compliance. Nothing to report.

9.Occupational Health & Safety Working Group. The OHS Working Group members use the information and discussions from our meetings to be reflected in the policies (Measles Immunization Plan), trainings and SOPs at our respective NPRCs.

10.Outreach. This group has worked closely with Excluded by Requester to create and edit material for publication on the www.nprcresearch.org website, a site designed to assist scientists who are investigating the possibility of working with NHP models.

11.Pathology. Representatives for both laboratory animal medicine and veterinary pathology training groups are contacted each year in order to disseminate information about the availability of the PPID resource to current trainees. A monthly email is sent to each registered PPID user to highlight material within the PPID and to encourage sharing PPID contact information among colleagues.

12.Public Relations. The group has worked with Proprietary Info to develop the NPRC Public Relations Strategy including a new logo for the NPRC Consortium. The public relations plan has been shared with NPRC staff as well as home institution and NIH stakeholders. The group will be developing a new website that is public facing in 2017.

13.Training. VGR participation is open to non-NPRC institutions that hold NIH-sponsored training grants, as well as to other select institutions with postdoctoral training programs in laboratory animal medicine. External institutions currently participating in the monthly sessions include:

Proprietary Info

It is estimated that, with full participation, approximately 100-150 veterinarians, students, pathologists, technicians and scientists are exposed to the activities and clinical work being performed at the NPRCs.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

1.Behavioral Management (BMC). The BMC plans to establish a webinar series for vetted professionals within and outside of the NPRC system. We will also pilot test the protocol for the behavioral inhibition screening tool. We are also planning on develop our section of the NPRC external website. Finally, we plan to strengthen our collaboration with the BCMC, to develop common tools to optimize animal welfare.

2.Breeding Colony Management (BCMC).
The ONPRC will continue to actively participate in the monthly BCMC teleconferences and annual face-to-face meetings, in addition to

sharing information and ideas on issues related to breeding colony management. Within the BCMC and BMC, we are currently working to standardize wound scoring systems to facilitate sharing of data.

3.Clinical and Surgery Techniques (CAST). CAST will continue scheduled meetings that feature a specific topic presented on a rotational basis among the NPRCs. Additionally, members have shown interest in revisiting the "Limitations for Common Experimental Procedures in NHPs" survey conducted in 2015. The questionnaire will be revised, redistributed, results summarized and eventually published as a review article.

4.Computational Methods and Resources. Work will include deployment of the population modeling application at the Yerkes NPRC. Phase II of the Colony Health Benchmarking be a major activity as well, an effort restarted after time required to mature local NPRC record systems; here we will produce an automated system federating scheduled extracts from individual NPRCs to provide regular automatic updates on colony productivity. In interests of working toward more rigorous and reliable work design across the NPRCs, CMRG will support the BCMC with application specific support at any NPRC as required.

5.Data Access Guidelines Group (DAGG). Nothing to report.

6.DNA Banking. Nothing to report.

7.Genetics and Genomics. Finalize the distribution of the genetic metrics software to all NPRCs through the NHPRC Consortium website, and provide individual training sessions on the use of this software with managers at the NPRCs as requested. Additionally, provide maintenance of the software in its current version, including the fixing of reported problems if any.

8.Integrity-Compliance. Continue to share information and ideas on issues related to Integrity and compliance.

9.Occupational Health & Safety Working Group. A FY2017 annual meeting in April at the NPRC in Seattle, WA in order to share information and ideas on issues related to occupational health and safety as well as the B-virus working group re-initiation progress, on-going research at the NPRCs, injury/exposure rates, outstanding issues of concern, and standardization of data being used for comparisons between the NPRCs.

10.Outreach.
•Continue work to define roles of Media Relations and the Education Outreach arms of this group and focus on local activities at each NPRC.
•Represent NPRCs at outreach events (5th Biennial USA Science & Engineering Festival, April 2018; Society for Neuroscience, 2017;)
•Hold 5th Annual Outreach Working Group meeting, hosted by WaNPRC
•Work with the new Public Relations (PR) Working Group (see below #13) to coordinate a national effort to most effectively educate the public on the importance of NHP models in biomedical breakthroughs.
•Produce promotional marketing materials, including a new set of banners and signage to accompany staff to meetings, and other materials, as identified, in coordination with the PR group.

11.Pathology.
•Continuation of the monthly Virtual Slide Conferences with inclusion of administrative working session (in absence of face-to face meetings for this group)
•Continued enhancement and expansion of PPID content and utilization
•Expansion of PPID user community by promotion through professional organizations
•Continued engagement of PPID user community through regular email communications to provide enhanced teaching, provide a virtual platform for case consultation and gain increased feedback for improvement.
•Completion of the data collection for the PMNMD LVH screening at necropsy project
•Rollout and expansion of the Biomaterials Query System (BQS)

12.Public Relations. The Public Relations WG has the goal of developing and maintaining an externally facing, professionally-designed media and branding program to assist the NPRCs in handling public relations on a national level, in collaboration with but in many cases beyond the reach of individual home institutions. This group will be largely responsible for implementing the new program, in consultation with the Outreach WG and with Media and Communication offices at each home institution, to harmonize all communication.

13.Training. The ONPRC will continue to participate in the monthly Virtual Grand Rounds teleconferences. Institutions outside of the NPRCs that host training programs and manage NHPs have expressed an interest in participating in the VGR sessions. When institutions approach the consortium for participation in VGR presentations, an email is sent querying the group members for objections to expansion. If no objections exist and the requesting program provides evidence of a robust veterinary training program and houses NHPs for biomedical research, access to the teleconferences will be granted. This maximizes the use of the NHP resource and places the NPRCs as a leader in training laboratory animal veterinarians in the care and management of NHPs in the biomedical research setting. ONPRC has the goal of investigating the Training Consortium as an avenue for laboratory animal medicine trainees to participate in externships at other institutions within the Consortium.

NPRC-BASED CONSORTIUM ACTIVITIES: ACCOMPLISHMENTS

1. **Behavioral Management (BMC)** Excluded by Requester The BMC made great progress in the past year with active ONPRC participation. In 2016, the BMC implemented a technician forum, in an effort to provide a secure method for technicians at our facilities to communicate about behavioral management issues. Technicians at the ONPRC have been active participants in this forum, which leverages the sharing of capabilities and expertise across NPRCs in a secure environment. In addition, the ONPRC sent two behavioral technicians to the SNPRC, where they learned about behavioral management of squirrel monkeys and baboons. The BMC also participated in the Phenotype Mining and New Model Development initiative with a cross-facilities Behavioral Inhibition/Anxiety project. Excluded by Requester was involved in this group, which designed methodologies for assessing behavioral inhibition across multiple primate centers. The BMC established inter-observer reliability in standardized alopecia scoring both within and between two NPRCs (including the ONPRC). This goal is important as regulatory emphasis on alopecia dictates a uniform measure and approach toward hair coat quality. The BMC also held a joint meeting with members of the BCMC at Southwest NPRC in November 2016 in an effort to share resources with this working group. There was a high level of scientific collaboration among BMC members in the past year, including a co-authored book chapter Excluded by Requester
Excluded by Requester
Excluded by Requester and 5 additional co-authored publications, and a joint symposium at the 2016 American Association of Laboratory Animal Science (AALAS) meeting Excluded by Requester organized a joint symposium between the BMC and EUPRIM-Net (a European counterpart) on "Laboratory Animal Welfare", which was held at the 2016 American Society of Primatologists (ASP)/International Primatological Society (IPS) meeting. She co-organized and was an instructor in the *Workshop on Macaque Pair Housing (WOMPH)* at the YNPRC in May 2016 and *Teaching Monkeys to Cooperate with Restraint: Using Positive Reinforcement Training and Temperament Testing Methods* at the 2016 AALAS meeting. Both of these workshops will be repeated in the coming year.

2. **Breeding Colony Management (BCMC)** Excluded by Requester We completed a year-long pilot project with the CNPRC, entitled *Development of NHP Model of Environmental Enteric Disease*. The resulting data is the most extensive characterization yet of both the normal and abnormal gut of infant rhesus macaques, and resulted in funding for a 3-year study of preventative measures, including our Campylobacter coli vaccination. We are continuing our two other population focused studies, including a study focused on alopecia, and a study evaluating the efficacy of probiotics and fatty acids in the feed. Through the BCMC, we and the other NPRCs continued our work to improve and enhance communication with the USDA. The SPF testing algorithm was implemented, and updates to the National Animal Locator Database continue. Our work with the GGWG to develop a Phenotype Coordinating Committee continues, and now includes a model of Batten disease. Through the BCMC we continue to work on the cross-center crisis plan for sharing resources. During the joint Breeding Colony Management Consortium and Behavior Management Consortium meeting, we presented our breeding colony management modeling tool, an epidemiologic-based tool for managing group dynamics, and our wound scoring system. Additional topics covered in this meeting include management of young proposed male breeders to maximize breeding potential, nursery rearing effects on adult behavior, strategies to integrate nursery reared infants into breeding colonies, common measures of relevance to behaviorists and managers, and retrospective and prospective studies to improve behavioral management.

3. **Clinical and Surgery Techniques (CAST)** Excluded by Requester During the reporting period, CAST hosted eight web conferences. The range of topics presented included Immunosuppressive Therapy after Stem Cell Graft, Cranial Melange, Use of Operant Conditioning to Train Non-lactating Rhesus Macaques as Foster Mothers, C-section Surgery, and External Bone Fixation. After each presentation, participants asked questions for clarification or additional information; an open forum for general discussion followed this question/answer session. The web conferences were well attended and usually had at least one representative from each of the NPRCs, with most NPRCs signing on as a group of practitioners gathered in a conference room. The featured presentations were posted to the CAST section of the NHPRC Consortium website after DAGG review. This website serves as a reference library of past presentations

which may be accessed by members. CAST expanded membership base to include 4 additional external institutions (22 external institutions total).

4. **Computational Methods and Resources (** Excluded by Requester CMRG activities this past grant year continued to produce work-design solutions that substantially enhance the productivity, efficiency and/or reliability of mission-critical workflows in husbandry, research and administration. The weight management (WM) system developed by CMRG for the NPRCs now allows weight management of more than 600 animals at ONPRC (several-fold the amount possible previously), while reducing time to update WM cases from 9 to 4 min. These results were presented at the 2016 AALAS National Meeting. A similar system was deployed to manage infant growth, alerting clinicians to any among 160 ONPRC infants (0 to 1 YoA) that are below ONPRC-standard weight, or whose rate of growth over past 60 days is below standard (standard calculated from recent ONPRC demographics.) CMRG also developed an automated fasting-request (also called do-not-feed) list to virtually eliminate miscommunication and error in the scheduling and execution of fasting events (an animal fasted improperly cannot be manipulated, at best impacting timepoints if the animal is not fasted and a procedure delayed, and endangering animal health if a procedure is conducted on an unfasted animal). CMRG initiated collaboration with Yerkes NPRC to apply the CMRG population modelling (PM) application there, as proposed in their SPF renewal application, and is anticipated to facilitate additional CMRG applications at YNPRC. The PM application is also used at Tulane NPRC, where they also now have three CMRG-developed tools "scaffolding" their past-approval monitoring workflows. CMRG continued to work closely with the BCMC, in particular providing the data federation and analysis expertise for the Colony Health Benchmarks initiative which will facilitate discovery of better husbandry practices by data-mining across the NPRCs.

5. **Data Access Guidelines Group (DAGG)** Excluded by Requester The Data Access Guidelines Group completed its specific aims in the fall of 2013 and has not met since that time. Protocols and procedures were put into place for the working group chairs to handle most access requests. Potentially sensitive requests have the appropriate approvals secured through other channels. The full DAGG will be reconvened when necessary with a new chair and representatives from the centers to replace any vacancies caused by staff changes.

6. **DNA Bankin(** Excluded by Requester ONPRC DNA Bank inventories were updated, and 533 requested samples were delivered, including 20 National DNA Bank samples housed at the ONPRC.

7. **Genetics and Genomics** Excluded by Requester Excluded by Requester has led the NPRCs' transition of the SNP parentage assay from the Illumina platform to a Fluidigm platform, since Illumina has discontinued support for their platform. She adapted the SNP assay to the Fluidigm platform, and coordinated cross-center testing among the ONPRC, YNPRC, and CNPRC to ensure consistency of assay performance among centers. Additionally Excluded by Requester finalized a genetic metrics software package for use by all NPRCs, that will implement novel algorithms she developed for genetic management at the ONPRC.

8. **Integrity-Compliance** Excluded by Requester The integrity/compliance NPRC Consortium meets on a quarterly basis by teleconference. Discussions have focused on training requirements, occupational health systems, OLAW directives on modifications to IACUC protocols, and policies on reporting to federal agencies. Consortium members also communicate outside of regular meetings on matters related to compliance.

9. **Occupational Health & Safety Working Group** Excluded by Requester The OHS working group meets by teleconference regularly to discuss exposures/injuries, new experimental agents, and safe practices. At the 2016 in-person annual meeting in California, the ONPRC were able to send the EHRS Research Manager and the Occupational Health Nurse. In addition, OHSU Occupational Health sent a Nurse Practitioner along for training to provide support to the WC Occupational Health program. The development and implementation of Measles Immunization programs at the NPRCs were a prominent topic of discussion. In August of 2016, a letter was sent to the NIH requesting that the B-virus working group be re-initiated to review current practices and to provide support for making B-virus exposures and illness a Public Health reportable disease and that information for exposures and illness be shared between NHP users including non-NIH funded NHP research. Also, the 2017 meeting scheduled for April in Seattle, WA will develop a standard set of reporting parameters for each NPRC so that data exchanged between NPRCs can be directly comparable.

10. **Outreach** [Excluded by Requester]. During 2016, members of the NPRC Outreach Working Group (OWG) represented NPRC at the following meetings/events: USA Science & Engineering Festival (April 2016). This is the largest single public outreach event that the NPRCs participate in. We conservatively estimate speaking with 6,000 visitors over the 3-day event; Society for Neuroscience Annual Meeting (November 2016). Here we spoke with scores of scientists about the unique resources available to researchers through NPRCs. As a group, the OWG collaboratively developed answers to questions about and/or responding to attacks on biomedical research involving animal subjects that came from a variety of directions (elected representatives, websites such as "Speaking of Research," etc.)

11. **Pathology** [Excluded by Requester] In 2016, the Pathology Working Group (PWG) conducted ten Virtual Slide Conferences (VSC) featuring three to five NHP pathology cases from participating centers. The number of registered users of the Primate Pathology Image Database (PPID) expanded to 427 registered users as of December 2016 (an increase of 60% from previous year). Users now represent 107 institutions (in addition to NPRCs) in the U.S., Canada, Europe and Asia. Replacement of the BIRN platform with a new server at ONPRC allowed migration of the majority of PPID material which will provide a reliable environment at the ONPRC to support the most critical component of the PPID over the next five-years. In support of the Phenotype Mining and New Model Development (PMNMD) initiative, the PWG member pathology units have begun collecting data through necropsy protocols developed at CNPRC for standardized evaluation of the heart to aid in the characterization of HCM/LVH.

12. **Public Relations** [Excluded by Requester]. The Public Relations Working Group communicated regularly via email and conference calls, and met in October 2016 in New Orleans in conjunction with the NPRC Directors' meeting to develop a Public Relations strategy with [Proprietary Info] a firm headquartered in [Proprietary Info] They are working closely with the NPRC Directors to develop and implement this PR strategy, which includes a new logo and other materials.

13. **Training** [Excluded by Requester] The Training Consortium continues to serve as a forum for cross-center exchange of clinical experiences and provides both a speaking and education opportunity for laboratory animal medicine trainees and veterinary staff at many institutions utilizing nonhuman primates in biomedical research. During this past grant year, these Virtual Clinical Grand Round (VGR) sessions explored "best practices" and facilitated dissemination of clinical information to both new and seasoned members in the field. In general, VGR presentations also provided practice for residents and faculty alike in speaking to, and fielding questions from, a larger inter-institutional audience. Presentations, attendance, and participation in discussion are expectations of the residency program at the ONPRC. Laboratory animal veterinary residents are required to give VGR presentations and do so under the mentorship of faculty veterinarians. [Excluded by Requester] oversees scheduling of Center participation as the ONPRC representative for the VGR. ONPRC provided mentorship for one VGR presentation in Year 57. Dr. [Excluded by Requester] the first year ONPRC resident in laboratory animal medicine, presented "Interstitial Cystitis in Rhesus Macaques."

NPRC-BASED CONSORTIUM ACTIVITIES: TRAINING AND PROFESSIONAL DEVELOPMENT

1. **Behavioral Management (BMC).** The BMC meets annually for a face-to-face meeting, either during the American Society of Primatologists meeting, which we all attend, or separately along with the BCMC. We meet monthly via "GoToMeetings".

2. **Breeding Colony Management (BCMC).** Monthly telephone conferences, and annual face-to-face meetings have fostered increased collaboration across all NPRCs.

3. **Clinical and Surgery Techniques (CAST).** CAST meeting presentations, discussions, and the CAST Presentations library serve to expand members' procedural proficiencies and repertoire, encourage the development of best practices at each center, and identify expertise among the NPRCs. Rotational topic presentations allow participants to practice and improve public speaking skills and ability to concisely communicate and orient others about a specific technique.

4. **Computational Methods and Resources.** The project has produced results that ONPRC staff members have presented at professional meetings and seminars, such as those of the American Association of Laboratory Animal Science, the American Society of Primatologists, and various industry associations.

5. **Data Access Guidelines Group (DAGG).** Nothing to report.

6. **DNA Banking.** Nothing to report.

7. **Genetics and Genomics.** During the past year Excluded by Requester worked closely with Excluded by Requester and Excluded by Requester NIH-contracted IT consultants, to develop a set of instructional materials for the genetic metrics software package that will be distributed to all NPRCs through the NHPRC Consortium website.

8. **Integrity-Compliance.** The ability to interact with others in the same area provides for professional development. Members rotate in presenting a topic of interest to the group

9. **Occupational Health & Safety Working Group.** Meeting with OHSWG has provided exchanges of experience between members of the OHG and opportunities to review each other's processes and trainings.

10. **Outreach.** Monthly conference calls have provided insight into how other NPRCs address communication challenges as well as inspiration for outreach events that engage the public on the topic of biomedical research.

11. **Pathology.** The PPID is utilized extensively for basic training of laboratory animal medicine and veterinary pathology residents, including preparation for their respective certifying examinations. A majority of the new users in the past year represent these trainees and their mentors. The VSC's provide excellent sources of continuing education and collaboration opportunities for all participants.

12. **Public Relations.** Nothing to report.

13. **Training.** The training consortium has provided an excellent opportunity for laboratory animal medicine trainees to prepare and present presentations related the care of NHPs in biomedical research. Many of the VGR presentations lead to national presentations at high profile conferences such as the Annual Workshop of the Association of Primate Veterinarians and to the preparation of case report manuscripts that can be submitted for publication. As an example, the presentation by ONPRC veterinary resident Excluded by Requester n 2016 has led to the formation of a group collaboration to draft a case report describing cases of interstitial cystitis in rhesus macaques at ONPRC.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Nothing to report

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Category	Explanation
Software	Breeding Colony Management: Colony Health Benchmarks and Population Modeling projects utilize the Mathematica technical computing program using the Wolfram Language. The program builds robust and efficient algorithms capable of handling these large-scale problems, integrating nearly 5,000 built-in functions covering all areas of technical computing.
Other	Public Relations. All new PR materials will be shared amongst all of the NPRCs.
Software	Genetics and Genomics: Development of an R-based software package for implementing novel algorithms for managing population genetic diversity in large breeding colonies of non-human primates.
Data or Databases	Genetics and Genomics. Data developed is shared through the NHPRC consortium website, and through publications.
Protocols	Genetics and Genomics: Development of novel protocols for characterizing sparse genome-wide genetic markers using genotyping-by-sequencing in the rhesus macaque genome, and for using these sparse markers to guide cost-effective, pedigree-based inference of dense genetic markers throughout the genome.
Physical collections	Genetics and Genomics: Collection of EDTA plasma for the ONPRC DNA Bank, in addition to the standard DNA sample collection. This expansion of physical sampling for the DNA Bank was undertaken based on expressed interest by numerous investigators at the ONPRC and OHSU, and was approved by the Oversight Committee for the Colony Genetics unit of the Primate Genetics Section.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Genetics and Genomics. The genetic metrics software will be available using open-source licensing.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

1.Behavioral Management (BMC). One challenge towards meeting our goals is decreased funding for face-to-face meetings. We will continue to have our monthly meetings via "GoToMeeting".

2.Breeding Colony Management (BCMC). Nothing to report.

3.Clinical and Surgery Techniques (CAST). Nothing to report.

4.Computational Methods and Resources. Nothing to report.

5.Data Access Guidelines Group (DAGG). Nothing to report.

6.DNA Banking. Nothing to report.

7.Genetics and Genomics. Nothing to report.

8.Integrity-Compliance. Nothing to report.

9.Occupational Health & Safety Working Group. Nothing to report.

10.Outreach. We continue to explore the best way to assign outreach tasks so that the appropriate skills and abilities are engaged for the completion of each task.

11.Pathology. Preparation and curation of material for inclusion in the PPID remains time consuming and labor intensive. Locally, our plan to mitigate this will include efficient use of technicians to prepare material for inclusion, and regularly scheduled 1-2 hour curation sessions for each pathologist to achieve incremental expansion of content.

12.Public Relations. Agreement from the NPRC Directors on the new NPRC logo was delayed due to the Directors' schedules and NPRC priorities. The Directors and PR Working Group will revisit the public relations strategy timeline and move forward to finalize the NPRC logo design.

13.Training. Nothing to report.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5581

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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				Unit Head	Institutional Base Salary	EFFORT			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						
3	Unit staff	10.08			99,141.00	31,504.00	130,645.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**130,645.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**130,645.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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)	10,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**10,000.00**

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,000.00
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. ACC services, miscellaneous other expense	14,567.00
Total Other Direct Costs	**38,567.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**179,212.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. TMDC	28.0	179,212.00	50,179.00
		Total Indirect Costs	**50,179.00**

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)	**229,391.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.