Notice of Award

*PRIMATE RESEARCH CENTER GRANT* **Federal Award Date:** 06/11/2015

Department of Health and Human Services
National Institutes of Health
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

**Grant Number:** 5P51OD010425-54
**FAIN:** P51OD010425

**Principal Investigator(s):**
DAVID M ANDERSON, DVM

**Project Title:** Washington National Primate Research Center

Lynette Arias
Dir, Office of Ssponsored Programs
University of Washington
4333 Brooklyn Ave NE
Box 359472
Seattle, WA 981959472

**Award e-mailed to:** osp@uw.edu

**Period Of Performance:**
**Budget Period:** 05/01/2015 – 04/30/2016
**Project Period:** 06/10/1997 – 04/30/2017

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $12,795,503 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF WASHINGTON 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 P51OD010425. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

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

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

Sincerely yours,

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

Additional information follows

## SECTION I – AWARD DATA – 5P51OD010425-54

**Award Calculation (U.S. Dollars)**

| | |
|---|---|
| **Salaries and Wages** | $4,260,329 |
| **Fringe Benefits** | $1,521,573 |
| **Personnel Costs (Subtotal)** | $5,781,902 |
| **Consultant Services** | $23,497 |
| **Equipment** | $13,498 |
| **Supplies** | $1,638,342 |
| **Travel Costs** | $186,258 |
| **Alterations and Renovations** | $151,549 |
| **Other Costs** | $1,164,440 |
| **Consortium/Contractual Cost** | $142,352 |
| | |
| **Federal Direct Costs** | $9,101,838 |
| **Federal F&A Costs** | $3,693,665 |
| **Approved Budget** | $12,795,503 |
| **Total Amount of Federal Funds Obligated (Federal Share)** | $12,795,503 |
| **TOTAL FEDERAL AWARD AMOUNT** | $12,795,503 |
| | |
| **AMOUNT OF THIS ACTION (FEDERAL SHARE)** | $12,795,503 |

| SUMMARY TOTALS FOR ALL YEARS | | |
|---|---|---|
| **YR** | **THIS AWARD** | **CUMULATIVE TOTALS** |
| 54 | $12,795,503 | $12,795,503 |
| 55 | $13,055,420 | $13,055,420 |

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:** 1916001537A1
**Document Number:** POD010425I
**PMS Account Type:** G (Pooled)
**Fiscal Year:** 2015

| IC | CAN | 2015 | 2016 |
|---|---|---|---|
| OD | 8014499 | $12,795,503 | $13,055,420 |

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 06/10/2015
**Award Processed:** 03/23/2015 01:36:12 PM

## SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD010425-54

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

## SECTION III – TERMS AND CONDITIONS – 5P51OD010425-54

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

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 Central Contractor Registration. Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) P51OD010425. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

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

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

**Treatment of Program Income:**
Additional Costs

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**SECTION IV – OD Special Terms and Conditions – 5P51OD010425-54**

**SUBJECT FOA**
This award is subject to the conditions set forth in PAR-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.

**ORIP FUNDING PLAN FOR FY2015**

This non-competing award reflects the NIH Fiscal Policy for Grant Awards for FY2015 (see NIH Guide Notice NOT-OD-15-050) and the implementation of the ORIP FY2015 grants funding policy: http://dpcpsi.nih.gov/orip/rf/fyg_fp2015

**TOTAL COST COMMITMENT**
The requested budget provided in the non competing continuation application has been reviewed and accepted by ORIP. The costs requested did not represent significant rebudgeting from those previously committed. Therefore, the categorical amounts reflected in the NoA were used and an overall adjustment was made to arive at the ORIP recommended award amount of $12,795,503 total costs. The grantee may rebudget these funds to reflect those requested and accepted by ORIP in the non competing continuation. Future years were adjusted based on ORIP's funding guidance.

**GENOMIC ARRAYS**
For purposes of budgeting and accounting for high volume purchases of Gene Arrays, the standard treatment of these resources as supplies in determining the F&A base of an award is non-applicable. NIH classifies these costs as supplies for the first $50,000, but uses as a surrogate the budgeting and reimbursement concepts utilized for subcontracts on the excess over $50,000. See NIH Guide Notice NOT-OD-10-097 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-097.html).

**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.

**CONSORTIUM**
This award includes funds awarded for subcontractual/consortium activity with Oregon Health and Science University. Consortia are to be established and administered as described in the NIH Grants Policy Statement (NIH GPS). The referenced section of the NIH GPS is available at: http://grants.nih.gov/grants/policy/nihgps_2013/nihgps_ch15.htm.

**DESIGN DOCUMENT REVIEW**
The grantee shall submit Final Design Documents (95-100% complete construction design documents) for review to ORIP's architectural/engineering team. The documents must be sent in PDF format to ORIPCONSTRUCTION@mail.nih.gov, with the grant number in the subject line. Final Design Documents shall include detailed drawings, specifications, and detailed cost estimates.

**SALARY CAP**
None of the funds in this award shall be used to pay the salary of an individual at a rate in excess of the current salary cap. Current salary cap levels can be found at the following URL: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-049.html.

**GRADUATE STUDENT COMPENSATION**
The maximum amount NIH will award for compensation of a graduate student (salary, fringe benefits and tuition remission) receiving support from a research grant is the zero-level Kirschstein-NRSA stipend in effect when NIH issues the grant award (see current levels posted at http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-15-048.html

**DOMESTIC AIR CARRIER**
Grantees must comply with the requirement Fly America Act (49 U.S.C. 40118) which generally provides that foreign air travel funded by Federal funds may only be conducted on U.S flag air carriers. For additional information regarding the Fly America Act and its exceptions, see Public Policy Requirements and Objectives—Fly America Act.

**DIRECT CHARGES OF F&A TYPE COSTS**

Funds requested for satellite phone, laptops, computers, and office supplies 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.

**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_2013/nihgps_ch8.htm#prior_approval_requirements.

**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**: Dawn Walker
**Email**: walkerdaw@mail.nih.gov **Phone**: 301-435-0844 **Fax**: 301-480-3777

**Program Official:** John D. Harding
**Email**: hardingj@mail.nih.gov **Phone**: 301-435-0776 **Fax**: 30- 480-3819

**SPREADSHEET SUMMARY**
**GRANT NUMBER:** 5P51OD010425-54

**INSTITUTION:** UNIVERSITY OF WASHINGTON

| Budget | Year 54 | Year 55 |
|---|---|---|
| Salaries and Wages | $4,260,329 | $4,397,663 |
| Fringe Benefits | $1,521,573 | $1,582,173 |
| Personnel Costs (Subtotal) | $5,781,902 | $5,979,836 |
| Consultant Services | $23,497 | $25,344 |
| Equipment | $13,498 | |
| Supplies | $1,638,342 | $1,611,001 |
| Travel Costs | $186,258 | $200,899 |

| | | |
|---|---|---|
| Alterations and Renovations | $151,549 | $57,704 |
| Other Costs | $1,164,440 | $1,236,598 |
| Consortium/Contractual Cost | $142,352 | $141,494 |
| TOTAL FEDERAL DC | $9,101,838 | $9,252,876 |
| TOTAL FEDERAL F&A | $3,693,665 | $3,802,544 |
| TOTAL COST | $12,795,503 | $13,055,420 |

| Facilities and Administrative Costs | Year 54 | Year 55 |
|---|---|---|
| F&A Cost Rate 1 | 42% | 42% |
| F&A Cost Base 1 | $8,794,440 | $9,053,677 |
| F&A Costs 1 | $3,693,665 | $3,802,544 |

## A. OVERALL COVER PAGE

| | |
|---|---|
| **Project Title:** Washington National Primate Research Center | |
| **Grant Number:** 5P51OD010425-54 | **Project/Grant Period:** 06/10/1997 - 04/30/2017 |
| **Reporting Period:** 05/01/2014 - 04/30/2015 | **Requested Budget Period:** 05/01/2015 - 04/30/2016 |
| **Report Term Frequency:** Annual | **Date Submitted:** 03/02/2015 |
| **Program Director/Principal Investigator Information:**<br><br>DAVID M ANDERSON , DVM BA<br><br>**Phone number:** (206) 543-7202<br>**Email:** danderso@uw.edu | **Recipient Organization:**<br><br>UNIVERSITY OF WASHINGTON<br>UNIVERSITY OF WASHINGTON<br>Office of Sponsored Programs<br>4333 Brooklyn Ave NE<br>Box 359472<br>SEATTLE, WA 981959472<br><br>**DUNS:** 605799469<br>**EIN:** 1916001537A1<br><br>**RECIPIENT ID:** |
| **Change of Contact PD/PI:** N/A | |
| **Administrative Official:**<br><br>LYNETTE ARIAS<br>4333 Brooklyn Ave<br>Box 359472<br>Seattle, WA 98195<br><br>**Phone number:** 206-543-4043<br>**Email:** osp@uw.edu | **Signing Official:**<br><br>LYNETTE ARIAS<br>4333 Brooklyn Ave<br>Box 359472<br>Seattle, WA 98195<br><br>**Phone number:** 206-543-4043<br>**Email:** osp@uw.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 goal of this proposal is to support a broad-based research resources program, providing biomedical scientists the opportunity to conduct research using nonhuman primate (NHP) models for human health-related and NHP biologic issues. This goal will be attained through support for scientific intellectual resources, administration, animal support resources, facilities, and operations. Support is requested for translational and pre-clinical resource support in AIDS-related research, Neuroscience, NHP Systems Biology, Developmental and Reproductive Biology, and Global Programs (Research Cores). New research initiatives will develop novel NHP models and expand related research resources, including additional core scientists. Support for research resource related studies is requested to provide innovative research directions and better characterization of the NHP model. The WaNPRC will focus on efficient access to Center resources, with particular emphasis placed on
support for affiliate research activities. This proposal also includes support for a broad program of animal care and technical support for breeding, housing, and research activities (Primate Resources Division), including both domestic and international sites of operation. Administrative support ensures appropriate management of Center finances and operations, focusing on improved efficiency and effective support for research activities. All primates in WaNPRC facilities are housed and cared for under conditions that meet or exceed NIH standards per the Guide for the Care and Use of Laboratory Animals, ILAR recommendations, and the AAALAC accreditation standards for NHPs. All lentivirus-infected primates are housed in ABSL2/3 containment facilities with appropriate biosafety procedures. The University of Washington, including the WaNPRC, is fully accredited by AAALAC
International.

### 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

**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 OD010425-53S1 | WaNPRC-ABC supplement to expand nonhuman primate housing | The plan is to enhance the breeding program for a colony of specific-pathogen free (SPF) Macaca nemestrina, housed at our Arizona Breeding Colony (ABC), near Mesa, AZ. This species possess unique immunological characteristics that make them an invaluable experimental model, particularly in the field of AIDS-related studies. Our plan is to expand the animal care and housing facilities at ABC to provide a sustainable source of SPF quality M. nemestrina. Our indoor-outdoor modular design will provide additional capacity for breeding, clinical care and specialized space. The single Specific Aim is directed at renovating existing space to increase capacity at ABC by up to 200 animals. | The modular housing design for phase 2 at ABC has been completed and engineering drawings for a steel building are ready to submit for permit to the Specific Private Vendor construction office. The unit is Specific Animal Specific Animal Location Once permitting is approved, the lead time for the unit is approximately 6-8 weeks and a contracting company will be assembling the unit and custom building the concrete pad, and adding entry and exit areas to the building. This unit will house approximately 160-200 NHPs. |

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

File uploaded: Please_refer_to_individual_components_for_details.pdf

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

Specific details are provided with the component sections.

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

Please refer to individual components for plans for the next reporting period.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

## Overall Highlights

### A. Animal Census

1. Nonhuman primates supported partially, or in whole by the P51 base grant[1].

Census date: 01/29/2015

| Genus, Species | Breeding Colony[2] | | | | Animals not in breeding colony[3] | | | | Total Colony Census |
|---|---|---|---|---|---|---|---|---|---|
| | M | F | U[4] | Total | M | F | U[4] | Total | |
| M. fascicularis | | | | | 12 | 29 | | 41 | 41 |
| M. mulatta | 35 | 50 | 16 | 101 | 89 | 31 | | 120 | 221 |
| M. nemestrina | 222 | 728 | 88 | 1038 | 231 | 120 | | 351 | 1389 |
| Saimiri sciureus | | | | | 5 | 4 | | 9 | 9 |
| **Total** | **257** | **778** | **104** | **1139** | **337** | **184** | | **521** | **1660** |

[1] A portion of these animals are also supported by a SPF U42 grant
[2] Total number of animals in breeding colony including adult breeding animals and designated juvenile replacements at time of report.
[3] Animals on protocol or otherwise not in the breeding colony at the time of report.
[4] Sex undetermined

2. Nonhuman primates not supported by the P51 base grant[1].

All NHPs at the WaNPRC are supported by the P51OD010425 base grant

3. Non-primate colonies

The WaNPRC does not have any non-primate animals.

### B. TDP information

The Tissue Distribution Program filled 329 requests for tissue between March 1, 2014 and February 24, 2015. Of these requests filled, the tissues types distributed included:

- 19 fluid samples
- 131 tissue samples
- 178 organs

### C. Projects

| **Project type** | **Number** |
|---|---|
| Pilot | 5 |
| Management | 16 |
| Research | 74 |
| **Total** | **95** |

**D. AIDS-related P51OD010425 grant dollars:** 45.9%

Explanation of Y53 Support for AIDS Research

In the past year (Y53), the WaNPRC continued its strong commitment to AIDS related research, allocating 45.9% of P51 support towards the science, administration, husbandry and physical infrastructure of AIDS projects.

Over the years, different methods have been used to calculate the Center's support for AIDS related research yielding varying results. After consultation with the director, programmatic staff, and administrative personnel, a consistent and reproducible methodology has been devised using stable financial and husbandry data from our Animal Record Management System (ARMS).

The calculation determines the relative quantifiable administrative, facility, and husbandry resources devoted to AIDS projects, and adds it to the easily identified direct scientific expenditure on AIDS related projects and cores in the P51. The specific method is explained in **Table 1** below. This was deemed to be a logical approach for attributing administrative, facility, and husbandry resources because:

- Relative attribution of administrative, facility, and husbandry resources support varies as a function of work quantity and need;
- Work in the Center can be characterized by the number of animals assigned to projects because animals are the chief driver of both costs and program income;
- At a project/program level, the number of animals devoted to AIDS projects corresponds to quantity of work (and therefore support, as outlined above) devoted to AIDS research.

**Table 1: Methodology and Formulas for AIDS Support Calculation**

| | |
|---|---|
| **1.** Determine P51 values: | |
| **a.** Total direct cost funding for P51, excluding supplements; | $9,144,443 |
| **b.** Total direct cost funding from P51 for AIDS-related projects; | $412,956 |
| **c.** Total direct cost P51 funding administrative, primate resources, facilities, and modernization funding. | $6,688,435 |
| **2.** Using the period 5/1/14 to present, determine total number of animal-days (e.g. 1 animal x 7 days = 7 animal-days) on: | |
| **a.** All research projects; | 138912 |
| **b.** Any project in ARMS with the AIDS flag, or AIDS, HIV, SIV, SHIV, HSIV in the title. | 78687 |
| **3.** Percent of animal days devoted to AIDS research using the formula: [=(#2.b.) / #2.a] | 57% |
| **4.** Determine amount of administrative, facility, and husbandry (non-science) funding devoted to AIDS research using the formula: [= #3 * #1.c] | $3,788,678 |
| **5.** Determine dollar amount of AIDS support by adding direct science funding to non-science AIDS attribution using the formula: [= #4 + 1.b] | **$4,201,634** |
| **6.** Determine percent of total P51 devoted to AIDS research by the formula: [= #5 / #1.a] | **45.9%** |

## E. Investigators supported

| Investigator type | Number supported |
|---|---|
| Core Investigator | 14 |
| Affiliate Investigator | 90 |
| Visiting Investigator | 4 |
| **Total** | **108** |

## F. Publications directly attributed to P51 activity

| Publication type | Number produced |
|---|---|
| Peer-reviewed journal articles directly attributed to the P51 funding | 27 |
| Books | 1 |
| Other | 0 |
| **Total** | **28** |

## G. Training

| Investigator type | Number trained |
|---|---|
| Post-docs | 9 |
| Graduate students | 11 |
| Undergraduate students | 17 |
| Other: Veterinary Rotational Students | 32 |
| **Total trained** | **69** |

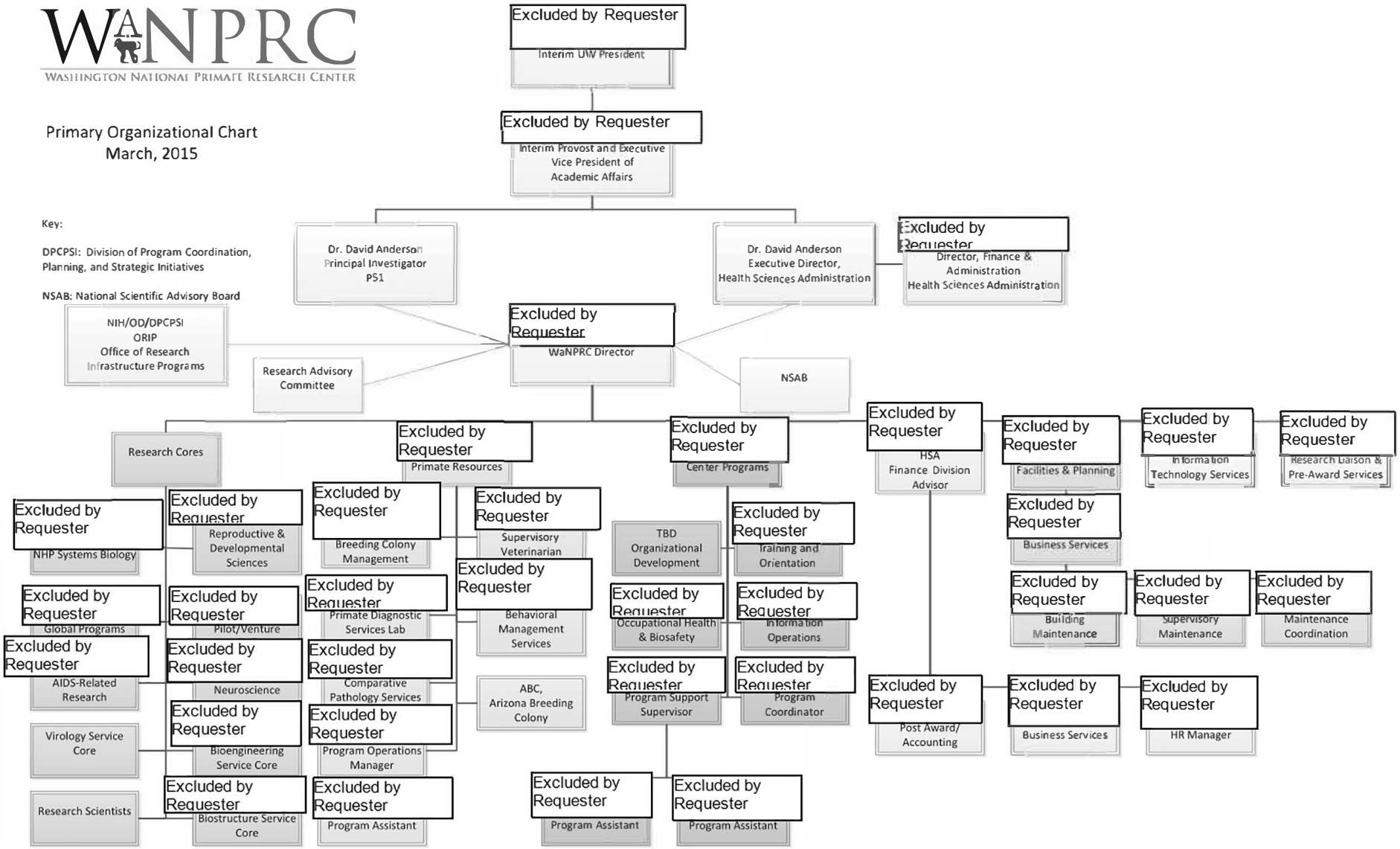
WaNPRC
WASHINGTON NATIONAL PRIMATE RESEARCH CENTER

Primary Organizational Chart
March, 2015

Key:

DPCPSI: Division of Program Coordination, Planning, and Strategic Initiatives

NSAB: National Scientific Advisory Board



# AIDS/VIROLOGY ANIMAL PROJECTS

**Project Title:** Efficacy of ALVAC-gp120 and NYVAC-gp120 for preventing SIV infection

**IACUC #** 2693-14 **IACUC Expiration:** 10/18/2014

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, U of Washington

**Principal Core Scientist:** PhD, WaNPRC, U of Washington

**Other affiliate scientists:**
Excluded by Requester MD, Virus Tumor Biology Section, NIH/NCI, MD
Excluded by Requester PhD, Virus Tumor Biology Section, NIH/NCI, MD

**Project Description**
Nonhuman primate models have played a significant role in preliminary HIV vaccine development. Numerous candidate vaccines have been examined preclinically at WaNPRC and other primate centers. Not uncommonly, similar immunization regimens have elicited different levels of protective efficacy in experiments often with several other experimental variables. This experiment was designed to carefully compare the host's immunological responses to two poxvirus-based candidate SIV vaccines during immunization and after SIV virus challenge. This will be the first such combined study of two poxvirus vector vaccines where all co-factors are controlled and will provide the basis for selecting the best vaccine vector system for future trials.

This study will compare two genetically engineered viral vector systems designated "NYVAC" and 'ALVAC'. Each recombinant vector will contain identical SIV DNA inserts. Neither vector replicates in mammalian cells. NYVAC was derived from the Copenhagen vaccinia virus strain following the deletion of 18 open reading frames from the viral genome. AL VAC is an attenuated canary pox virus that can replicate only in avian cells. The aim for this study is to identify the viral vector system which produces the best protection from SIV challenge in macaques.

**Publications associated with this project:** n/a

**Funding Sources**
NIH, Excluded by Requester PI; $3,283,375; HHSN266200600006C

**Project Title:** Efficacy of zinc-finger inhibitory compounds as vaginal microbicides for lentivirus infection

**IACUC #** 2693-07 **IACUC Expiration:** 7/18/2013

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, U. of Washington

**Principal Core Scientist:** PhD, WaNPRC, U. of Washington

**Other affiliate scientists:**
Excluded by Requester PhD, Private Source NY
Excluded by Requester MD, Laboratory of Cell Biology, NIH, MD
Excluded by Requester PhD, Laboratory of Cell Biology, NIH, MD
PhD, HIV& AIDS Prevention, CDC, GA

**Project Description**
This study involves the pre-clinical evaluation of a novel antiviral compound based upon inhibition of zinc-finger domains of viral protein processing and host cell infection which may be used to treat or block primate lentivirus (SIV/HIV/SHIV) infections of rhesus macaques (Macaca mulatta) as animal models for sexual transmission of humans AIDS. The zinc finger nucleocapsid protein (NCp7) of HIV-1 has been suggested as a target for therapeutic and microbicide intervention. NCp7 is a small highly basic protein containing two zinc-binding domains and generated by protease processing of the HIV-1 Gag protein during virus maturation. In research studies to date, S-acyl-2-mercaptobenzamide thioester ( SAMT) NCp7 inhibitors have prevented transmission of HIV-1 from infected cells, including primary cells, human cervical explant cultures, and in intra-vaginal SHIV vaginal challenge NHP models. Thus, SAMTs may be promising new drug candidates for further development in anti-HIV-1 topical microbicide applications. Importantly, viral resistance to NCp7 inhibitors has not been observed in treated cells. This SAMT-cell partnership mechanism opens new innovative avenues for development of inhibitors of HIV at a very early stage of viral replication. Since there are no vaccines yet proven efficacious for HIV, vaginal microbicides that target various phase of the virus life cycle from cell binding to virus replication may prove invaluable the fight against heterosexual transmission in the AIDS epidemic.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIAID/NIH | Excluded by Requester | PhD | $3,283,375.00 | HHSN266200600006C |

**Project Title:** Immunogenicity and efficacy of electroporated polyvalent DNA

**IACUC #** 2693-08 **IACUC Expiration:** 10/18/2014

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Private Source NY

Excluded by Requester PhD, Private Source NY

**Project Description**

This study intends to assess the immunogenicity and efficacy of a DNA prime and recombinant simian immunodeficiency virus (SIV) antigen boost immunization strategy for protection of rhesus macaques against repeat low-dose (RLD) SIV mucosal challenge. The DNA priming immunizations will be done by electroporation, which has previously been shown to elicit augmented immune responses when co-delivered with plasmids coding for the potent molecular adjuvant interleukin-12. We hypothesize that this combined immunization strategy will result in reduced or undetectable SIV provirus in peripheral blood samples of repeat low-dose intra-rectally SIV challenged rhesus macaques. Following immunization, the animals will be challenged with SIVmac251using our RLD method representative of natural HIV exposure by sexual intercourse, as detailed in other ongoing studies. Our proposed vaccine strategy is relevant for existing HIV vaccine candidates entering clinical evaluation and, in conjunction with our naturalistic SIV exposure model, may provide insights into control of retrovirus replication. Electroporation of protein subunit DNA (i.e., “pDNA”) vector vaccines engineered into recombinant (attenuated) vesicular stomatitis viral vectors as the immunizing method in this manner represents a platform technology well positioned for the development of efficacious products whose individual components have qualitative immunological differences when combined. The candidate prime and boost vaccines and their mock control, to be used in this study will be formulated and provided by Private Source

**Publications associated with this project:** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIAID/NIH | Excluded by Requester | PhD | $3,283,375.00 | HHSN266200600006C |

**Project Title:** Creating an in vivo simian model for genetically altered T-cells

**IACUC #** 2693-13 **IACUC Expiration:** 1/29/2014

**Unit:** AIDS/Virology

**Type of Project:** Pilot Project

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, University of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, University of Washington, WA

Excluded by Requester **Other affiliate scientists:** MD, PhD, Dept. of Medicine, Oregon Health Sciences University, OR

**Project Description**

Simian immunodeficiency virus (SIV) infection of Rhesus macaques (RM) is a large animal model for HIV. In both SIV and HIV the infection and destruction of T cells are key components to disease pathogenesis. In this study we hypothesize that RM T cells can be successfully transduced (genetically altered) and tracked in vivo for extended periods of time using a retrovirus vector. This is a proof-of-concept project for a RM model to study T cell biology through the tracking of genetically modified T cells in RMs. Studying the survival, kinetics and homing of genetically altered T cells is critical to better understand the in vivo dynamics of these cells which will aid in the development of improved therapeutic targets and vaccination strategies for SIVIHIV.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIAID/NIH | Excluded by Requester | PhD | $3,283,375.00 | HHSN266200600006C |

**Project Title:** Modulation of the immunogenicity of a GFP transgene expressed by AAV9

**IACUC #** 4266-04 **IACUC Expiration:** 12/18/2014

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**Principal investigator:** Excluded by Requester PhD, WaNPRC, Microbiology, U. Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Microbiology, U. Washington, WA

**Other affiliate scientists:** Excluded by Requester PhD, NY Dept of Health, NY

**Project Description**

Giant axonal neuropathy (GAN) is a rare neurodegenerative disease resulting in death in the second or third decade of life. The disease is due to homozygous loss-of-function mutations in the gene encoding gigaxonin, a Cul3 ubiquitin ligase adaptor protein. The absence of gigaxonin leads to disruption in the regulation of intermediate filaments (IF), accumulation of disordered microtubules and IF in axons, enlargement of axons, and degeneration of peripheral nerves. Pre-clinical data show that delivery of the GAN gene by an AAV9 vector in GAN-null mice results in resolution of IF aggregates and provide a rationale for a gene therapy approach in GAN patients. A concern is that GAN patients may not be tolerized to normal gigaxonin. If true, then introduction of gigaxonin will elicit an immune response against the normal protein thereby exacerbating the neurodegenerative disease. The present study is designed to model a GAN gene therapy protocol in monkeys. Since a monkey model lacking gigaxonin is not available, we have chosen GFP as the transgene because GFP is immunogenic in monkeys and models a 'worst case' scenario for GAN gene therapy. We will test the hypothesis that IL-10 coupled with transient rapamycin treatment will tolerize monkeys to GFP, delivered into the CNS using an AAV9 vector. The study will assess three treatments; AAV9/GFP alone; AAV9/GFP with transient rapamycin; and AAV9/GFP plus IL-10 nanoparticles with transient rapamycin. The aims: (1) Evaluate inflammatory / immune responses to trauma alone, the AAV9 capsid protein, and the GFP transgene, (2) Analyze GFP expression in CNS, and (3) Assess pathology in the CNS after gene delivery. This will determine if IL-10 with transient rapamycin treatment results in tolerization to GFP expressed in the CNS. The data will be used to inform the design of the GAN gene therapy protocol for use in the clinic.

**Publications associated with this project** N/A

**Funding Sources**

| | | | |
|---|---|---|---|
| Private Source | Excluded by Requester | PhD, PI | $352,915 | Private Source |

**Project Title:** Conserved Elements DNA Vaccine for HIV

**IACUC #** 4266-04 **IACUC Expiration:** 12/18/2014

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Microbiology, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Microbiology, U. of Washington, WA

**Other Core Scientists:**

Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
PhD, WaNPRC, U. of Washington, WA
PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
Excluded by PhD, WaNPRC, Microbiology, U. of Washington, WA
Excluded by Requester PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Microbiology, U. of Washington, WA
PhD, Microbiology, U. of Washington, WA
Excluded by Requester PhD, Microbiology, U. of Washington, WA

**Project Description**

We previously showed that therapeutic DNA vaccine induction of mucosal responses correlated with reduction of virus in the gut of SIV-infected macaques despite the use of a suboptimal ART regimen. This vaccine stimulated T cell responses that supressed virus to low/undetectable levels and afforded a durable viral remssion in ~50% of the animals after stopping ART. We are now investigating strategies to make therapeutic vaccination even more effective by 1) using a more potent combination of drugs (cART) 2) using a mucosal adjuvant (LT) to target immune responses to residual virus in the gut, and 3) use of a novel conserved elements (CE) DNA vaccine to focus T cell responses against highly conserved viral sequences that if mutated will impose greater fitness cost. We hypothesize that vaccine-induced viral remission is mediated by strong mucosal CD8 responses and focusing these responses to the gut in maximally suppressed infections and against more conserved epitopes will suppress a wider range of possible viral variants, select for fitness-cost escape mutations, and maximally disable the ability of residual viruses to emerge from the latent reservoir after stopping cART. Using optimized cART and mucosal targeting we are comparing traditional whole antigen and CE DNA vaccines for the ability to increase mucosal and systemic CD8 responses against conserved viral sequences, their impact on viral evolution and fitness, and their role in controlling virus. We are also investigating the role of inflammation on therapeutic efficacy. Our aims: 1) Determine efficacy of an LT-adjuvanted whole-antigen traditional SIV DNA vaccine when used with more potent cART. 2) Determine if an SIV CE immunogen will improve therapeutic efficacy. 3) Define immune and virological mechanisms underlying viral remission These studies will define the virological and immune profile of a vaccine-induced functional cure and the feasibility of a novel therapeutic CE DNA vaccine.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH | Excluded by Requester | (MPI) | $556,886 | R01 AI104679 |

**Project Title:** Immunogenicity of a human measles vaccine in pigtailed macaques

**IACUC #** 4202-07 **IACUC Expiration:** 6/12/2014

**Unit:** AIDS/Virology

**Type of Project:** Pilot Project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:**
Excluded by Requester DVM, PhD, WaNPRC, U. of Washington, WA
Excluded by Requester PhD, WaNPRC, U. of Washington, WA

**Principal Core Scientist:** **n/a**

**Other affiliate scientists:**
Excluded by Requester - DVM, PhD, Private Source WA

**Project Description**
This pilot project studied safety and immunogenicity of an attenuated, monovalent vaccine ("M-vac") for use in protecting Macaca nemestrina against measles. Reports from other institutions using M-vac indicated that rhesus macaques had responded well. Cost considerations and absence of other viral antigens also made this an attractive candidate for further study. We explored if serum neutralizing antibodies (SNAb) formed at levels considered protective against infection and to assure safety in this species. The study involved two phases; a 2-week acute safety study (Phase I) and a longer-term follow-up study (Phase 2) where safety and immunogenicity were monitored over 7-months.

**Project Progress**
In Phase I, five M. nemestrina (age 3 – 20 years; 2 F, 3 M) were used to provide baseline and post-immunization antibody titers, CBCs with lymphocyte subset analysis, clinical chemistry panels, necropsy, and histology of the immunization site. Each was also scored daily for two weeks based on 8 body-systems parameters. In Phase II, 36 M. nemestrina (age 1 – 12 years; 28 F, 8 M) were immunized then monitored for antibody responses two and seven months later; clinical scores, CBCs, and clinical chemistry panels were also obtained. Serum samples were tested against 3 different measles antigens, MRC-5 host cells, and negative and positive controls. Although binding antibody responses across assay formats were robust in most animals within weeks of immunization, neutralizing antibodies were virtually absent among 29 of the 36 M. nemestrina available for testing at the final time point. These findings provide an excellent example of unanticipated differences that may occur in features of biological response between macaque species, thus emphasizing the importance of validating applicable aspects of primate models prior to extrapolating results to human medicine. A manuscript comparing these results in M. nemestrina to the result in M. mulatta at other primate centers is in preparation.

**Publications associated with this project:** n/a

**Funding Sources**
P51OD010425 Pilot subproject. Excluded by Requester PI, No cost extension.

**Project Title:** Modulation of receptor/coreceptor binding for HIV-1 vaccine design

**IACUC #** 2370-23 **IACUC Expiration:** 9/4/2015

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:** Excluded by Requester MD, PhD, Medicine, U. of Massachusetts, MA

**Project Description**

Immunogens capable of inducing neutralizing antibodies (NtAb) against diverse isolates of human immunodeficiency virus (HIV) remains elusive. Multiple factors may contribute to the difficulty in generating broadly NtAb against HIV. We previously showed that removal of a single, highly conserved, N-linked glycan (N7) in HIV-1 gp120 resulted in increased sensitivity to broadly neutralizing monoclonal antibodies as well as the ability to mediate CD4-independent viral entry and to induce cross-reactive neutralizing antibody responses in macaques. Here, we examined if glycan modified Env from different isolates could induce cross-reactive NtAb and protect against heterologous SHIV challenge in macaques. We enrolled 36 animals to compare responses induced by WT and N7 mutant Env from different isolates in a DNA prime-gp120 boost regimen. Env were derived from a lymph node isolate (LN40) or a brain isolate (BR33) from a single patient. In addition, one group of animals received a mixture of gp120 from five heterologous isolates as a polyvalent vaccine boost. All animals in the vaccinated groups generated HIV Env-specific antibodies detectable by ELISA after DNA immunization. After the first gp120 boost, the majority of these animals also developed neutralization antibodies against a heterologous virus SHIV162P4. Protective efficacy against a heterologous virus was evaluated following a high dose intrarectal challenge with SHIV162P4. Although all but one animal were infected, vaccinated animals had significantly lower peak and setpoint viral loads and higher CD4 cell counts than those in control animals. Vaccinated animals also showed anamnestic responses after rectal challenge, but their anti-gp120 titers decreased quickly after peaking at Week 5, while titers in the control group continued to increase. Results indicate the effect of the N7 glycan may be isolate dependent. Although the vaccines were not protective against acquisition of a heterologous virus, they may have contributed to control virus replication and disease progression.

**Publications associated with this project** N/A

**Funding Sources**

| | | | |
|---|---|---|---|
| NIAID, NIH | Excluded by Requester PhD, PI | $736,956 | P01 AI082274 |

**Project Title:** Simian -tropic human immunodeficiency virus type -1 (st-HIV-1)

**IACUC #** 2370-29 **IACUC Expiration:** 9/25/2014

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 100%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:** Excluded by Requester PhD, Private Source

**Project Description**

The overall objective of this project is to establish a macaque model for HIV-1 infection and disease. Excluded by Requester We have collaborated with Private Source and with Excluded by Requester Private Source to test HIV-1 clones that express the Vif protein of SIV, which counteracts APOBEC3G/F-mediated restriction in macaques. Although these chimera were infectious in vivo, viral replication was controlled after the acute phase of infection and no disease progress was observed. Therefore, additional alterations may be needed to enhance their in vivo infectivity. To test this hypothesis, we tested a number of new chimeric viruses generated in the laboratory of Excluded by Requester Excluded by Private Source. These new chimera incorporate the regulatory proteins (Vpx, Vpr, Nef) of SIV replacing their counterparts in HIV-1. Two macaques were inoculated intravenously in a pilot study. Both animals became infected, but plasma viremia was controlled after 8-12 weeks. We previously reported that one animal developed significant weight loss and lymphocytopenia and was euthanized approximately at 40 weeks after infection. Although this was not the typical disease course of HIV-1 infection in human, this observation indicates the possibility of alternative pathogenic response to primate lentivirus infection in macaques. Plasma viremia in the other animal (A09166) persisted at approximately 100-400 copies/ml for >80 weeks, indicating continued viral replication. Over the last year, this animal continued to show detectable plasma viral load and its HIV-specific antibody titers increased almost 10-fold, consistent with persisting viral antigen stimulation. We are currently attempting to isolate virus from this animal to examine the changes that may have allowed this virus to adapt in pig-tailed macaques and maintain persistent infection.

**Publications associated with this project** N/A

**Funding Sources**

| | | | |
|---|---|---|---|
| NIH | David Anderson, DVM, PI | $464233 | P51 OD010425 |

**Project Title:** Macaque Model to Study Responses Against HIV-1 Quaternary Neutralizing Epitopes

**IACUC #** 2370-26 **IACUC Expiration:** 2/13/2015

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
PhD, WaNPRC, U. of Washington, WA

Excluded by Requester **Other affiliate scientists:** PhD, Pharmaceutics, U. of Washington, WA
Excluded by Requester PhD, Medicine, Rutgers U., NJ

**Project Description**

The overall objective of this proposal is to develop macaque models to study broadly neutralizing antibody (bNAb) responses to HIV-1 infection and factors that contribute to the generation of these antibodies. To determine if immunization with subunit proteins in animals previously infected with a SHIV virus would broaden the Env-specific antibody responses, we immunized animals previously infected with SHIV1157ipd3N4 WT or QNE mutant, ~ 1 year after the initial SHIV infection. The immunogen was a gp140 based on a consensus Clade C envelope sequence and was formulated in Adjuplex adjuvant. Four naïve animals were used as controls. All previously infected animals showed high anti-gp120 antibody titers after a single protein immunization. Prior to subunit protein boost, all infected animals showed Nab activities against only Tier 1B isolates and the homologous Tier 2 SHIV C virus. After the gp140 boost, all infected animals showed not only an increase in Nab titers, but also the breadth of Nab activity. Notably, 5 or the 6 animals that showed increased Nab titers generated Nab responses against a heterologous Tier 2 Clade C virus (SVPC13). Naïve animals did not show any Nab response after the first gp140 immunization. Nab was detected against only easy to neutralize Tier 1 viruses SS1196 and/or QA461 after the 2$^{nd}$ gp140 boost. No Tier 2 Nab response was detected. Importantly, Immunization did not affect the peripheral blood CD4 T cell counts or viral loads in previously infected animals, indicating the lack of potentially deleterious inflammatory responses due to gp140 immunization. Together these results demonstrate that Con C gp140 immunization in SHIV C infected animals can result in increased potency and breadth of Nab responses, albeit the breadth is still relatively restricted. Additional immunization or alternative immunogen may be needed to further increase the breadth of Nab response.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH NIAID | Excluded by Requester | PhD | $709,480 | P01 AI088610 |

**Project Title:** Oral Immunization against HIV/AIDS with prime boost strategies

**IACUC #** 2370-27 **IACUC Expiration:** 10/24/2015

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:** Excluded by Requester PhD, Pharmaceutics, U. of Washington, WA

**Project Description**

Mucosal transmission is the predominant mode of HIV acquisition. Oral transmission may occur in newborns at delivery, in infants through breast milk from HIV-infected mothers, and in adults through occupational exposure or oral-genital sex. The overall goal of this project is to test if oral delivery of poxvirus and protein vaccines in a prime-boost immunization regimen will generate protective immunity against mucosal challenge. As reported last year, we demonstrated the safety and immunogenicity of replication-competent poxviruses following oral administration.

**Project Progress**

To further examine the optimal dose and route for oral immunization, we inoculated two animals sublingually with twice the dose used in the 1st pilot study and two animals were inoculated with the same dose but at the tonsil. Oral lesions were found in all animals. However, all lesions were healed within 7-10 days and no other adverse effect was observed. These observations, together with previously reported findings, indicate that sublingual inoculation with $5x10^8$ PFU is likely to be the optimal dose and route for oral administration of a replication competent recombinant vaccinia virus in non-human primates. These animals generated HIV-specific antibodies which increased significantly after a single subunit gp120 boost. Neutralizing antibodies were detected in 3 of 4 immunized animals. We challenged the immunized animals with SHIVSF162P4to determine if immunity elicited would protect against a homologous high dose intrarectal challenge. Two animals were completely protected, one animal was infected and one showed delayed acquisition. The animal that was infected (i.e., did not show any sign of protection or delay of acquisition) did not have any virus neutralizing antibodies at the time of challenge, indicating the important role of neutralizing antibodies in vaccine protection. Together these results indicate that sublingual immunization recombinant vaccinia viruses was safe and effective in priming protective against a mucosal challenge with SHIVSF162.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH NIDCR | Excluded by Requester | PhD | $764,999 | R01 DE021223 |

**Project Title:** Unmasking Conserved Epitopes on HIV Envelope Protein for Vaccine Design

**IACUC #** 2370-23 **IACUC Expiration:** 9/4/2015

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA
PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:**
Excluded by Requester MD, PhD, Medicine, U. of Massachusetts, MA
Excluded by Requester MD, Medicine, U of Pennsylvania, PA
Excluded by Requester MD, Medicine, U of Pennsylvania, PA

**Project Description**
Although broadly neutralizing antibodies (bNAbs) can be found in some HIV-infected individuals, they are often directed against conserved epitopes on the envelope glycoprotein such as the Env CD4 binding site (CD4bs), which is masked by glycans. To date, efforts to generate bNAbs by immunization have largely been unsuccessful. The goal of this project is to explore approaches to optimize the design of Env immunogens that will elicit enhanced protective responses to HIV, including bNAbs. Because the N197 glycan occludes the CD4bs and is conserved among diverse HIV-1 isolates, we sought to determine if immunization with heterologous Env bearing the N197 mutation may increase the breadth of antibody response. Macaques were immunized in a poxvirus prime, protein boost regimen with homologous Env, or heterologous Env (either sequentially or as a mixture). As expected, animals immunized with N197 Env from a single isolate generated stronger antibody responses against the homologous Env than those immunized with heterologous N197 mutant Env (either sequentially or as a mixture). Interestingly, animals immunized with a mixture of N197 mutant Env from different isolates showed stronger and broader neutralizing antibody responses against heterologous Tier 1B than animals in all other groups. Furthermore, animals immunized with a mixture of N197 Env generated broadly reactive IgG responses against multiple epitopes in gp120, including CD4i epitopes, linear V3, V2, and C5 epitopes, V1V2 (clade B--gp70_B.CaseA_V1_V2) and conformation-dependent epitopes in the coreceptor binding region. These results support our hypothesis that specific glycan modification modulates the epitope specificity of immune responses against the Env protein and that the use of multivalent Env vaccines may focus antibody responses on epitopes shared by these immunogens.

**Publications associated with this project** N/A

**Funding Sources**

Private Source - Excluded by Requester PhD, PI $2,252,354 Private Source

**Project Title:** Chimeric Antigen Receptor (CAR) / UCLA

**IACUC #** 3235-01 **IACUC Expiration:** 9/25/15

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester MD, Private Sour œ WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description**
We are evaluating a potentially curative strategy involving the genetic modification of hematopoietic stem cells (HSCs) with a receptor that, following the development of these cells into mature T cells, target them to kill HIV infected cells in vivo. The overall goal of this project is to direct HSCs to become SHIV-specific by transduction with a custom-engineered chimeric antigen receptor (CAR), providing an inexhaustible source of SHIV-specific immune cells that are major histocompatibility complex (MHC)-unrestricted, superior to natural responses, and can be utilized in humans. We will develop a gene therapy vector to deliver a CAR with additional genes to protect transduced cells from SHIV infection, and will test this CAR for efficacy in controlling and/or clearing SHIV-infection in pigtailed macaques in vivo.

We will assess the ability of autologous, CAR-transduced HSCs to 1) engraft in pigtailed macaques, and 2) produce a measurable decrement in plasma viral load following SHIV challenge.

To generate cells expressing the optimized CAR- or control vector in every hematopoietic lineage, we will collect, transduce, and re-infuse autologous HSCs from primed bone marrow. Briefly, bone marrow hematopoietic cells will be mobilized by administration of granulocyte colony stimulating factor (GCSF) and stem cell factor (SCF). Bone marrow aspirates will then be collected, enriched for CD34+ HSCs, and transduced with CAR or control lentiviral vectors. During manipulation of HSCs ex vivo, each animal will receive a myeloablative conditioning regimen consisting of 1020 cGy total body irradiation. Following conditioning, transduced HSCs will be re-infused into the animal.

**Project Progress:** We have transplanted 5 animals on this study. Two have already been inoculated with SHIV and three are scheduled for inoculation later this year.

**Publications associated with this project**
None

**Funding Sources**
Private Source, Excluded by Requester (PI) Private Source

**Project Title:** Mucosal Immunity and SIV

**IACUC #** 4314-01 **IACUC Expiration:** 4/29/2015

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 63%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Pharmaceutics, U. of Washington, WA

**Other affiliate scientists:** n/a

**Project Description**

Currently, more than 33 million individuals are infected with human immunodeficiency virus (HIV) worldwide. HIV infection results in massive dysfunction of the immune system, particularly in mucosal tissues, which ultimately results in progression to Acquired Immunodeficiency Syndrome (AIDS) and death. The primary focus of Excluded by Requester lab is to understand the mechanisms by which mucosal immunity is altered in the context of lentiviral infections in order to develop novel therapeutic interventions aimed at enhancing mucosal immunity and thus decreasing HIV transmission and pathogenesis. We have recently demonstrated that SIV infection of Asian macaques results in damage to the structural barrier of the GI tract Excluded by Requester 2010 Excluded by Requester 2010), which is associated with translocation of microbial products and immune activation, both locally in mucosal tissues and systemically to peripheral tissues. Furthering these studies, we have better elucidated the mechanisms which underlie this damage to the tight epithelial barrier of the GI tract after SIV infection, including loss of homeostatic cells that produce IL-17 and IL-22 Excluded by Requester 2010 Excluded by Requester 2012).

Based on these data, we treated SIV-infected macaques with probiotics, and found that this treatment enhances mucosal immunity by decreasing inflammation Excluded by Requester 2012). We are also investigating the efficacy of fecal transplant therapy and probiotic treatment effect on the microbiome. Fecal transplants are a cutting edge therapy being developed for the treatment of many GI inflammatory diseases, such as Crohn's Disease, inflammatory bowel diseases, and antibiotic-resistant *C. difficile* infections. This study focuses on understanding mechanisms underlying mucosal dysfunction during HIV infection, and how they may be ameliorated using novel therapeutic interventions such as probiotic treatment and fecal transplant.

**Publications associated with this project** N/A

**Funding Sources**

| | | | |
|---|---|---|---|
| NIH | Excluded by Requester | $279,878 | P51OD010425 |
| NIH | | $162,000 | 1K22AI098440-01 |
| Pharmaceutics Start-up | | | |

**Project Title:** Toxicology studies with adenovirus derived proteins in NHPs

**IACUC #** 3108-03 **IACUC Expiration:** 6/9/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, PhD, Medicine, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description**

The goal was to study the safety of a new recombinant tumor junction opener (JO4) in combination with Doxil chemotherapy in preparation of a clinical trial.

JO4 was used at a dose that was effective in mouse tumor models (2mg/kg). Doxil was injected at a dose that will be used in the clinical trial (40mg/m2). Analysis of clinical symptoms and blood parameters did not show remarkable signs of toxicity. Upon necropsy, performed at 6 hours after the second injection cycle, no treatment related abnormalities in gross examination of organs and histological analysis of tissue sections was observed. Therefore, the combination of JO4 and Doxil was safe in an adequate animal model.

Considering the limitations of the study (N=1), a series of cautious conclusions can be made:
i) As expected, serum antibodies against JO4 develop after one week. These antibodies appear to be completely saturated when a second injection of JO4 is given. Corresponding immune complexes appear to be deposited in a series of lymphoid and non-lymphoid organs.
ii) Non-opsonized JO4 can be found in epithelial tissues, specifically in adrenal glands, epididymis, and kidneys. Some functional activity of JO4 with regards to junction opening is supported by an increased uptake of Doxil in the adrenal glands. On the other hand, JO4 appears to decrease Doxil concentrations in the liver, spleen, and lymphnodes. There was no JO4-related increase of Doxil in the heart or abnormalities in the ECG and the "heart panel" in blood chemistry analyses.

The data have been published in a recently accepted paper.

**Publications associated with this project:** n/a

**Funding Sources**

NIH, PI: Excluded by Requester $150,00, P50 CA83636, project 3 (PI Excluded by Requester
DoD, PI Excluded by Requester $200,000

**Project Title:** Model Refinement in Pig - Tailed Macaques

**IACUC #** 2195-18 **IACUC Expiration:** 5/19/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** **0%**

**AIDS?** No

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**
Chlamydia trachomatis, Trichomonas vaginalis and Mycoplasma genitalium are common sexually transmitted infections (STIs) in the United States as well as worldwide. Given the reproductive consequences, treatment limitations and economic impact of such STIs the potential role of Multipurpose Prevention Technologies (MPT) and/or therapeutic products in preventing these infections must be examined. The objective of these studies is to develop new protocols and/or modify existing protocols that are designed to evaluate safety and efficacy to further investigate the effectiveness of newly developed MPTs or other therapeutics in the preclinical pigtail macaque animal model. The pigtail macaque is an ideal model for studying the female reproductive tract in that the menstrual cycle is similar to that of human females in length and pattern, and the species is naturally susceptible to these human STIs without the need for exogenous hormone treatments.

**Publications associated with this project:** n/a

**Funding Sources**
NIH, Contractor: BIOQUAL/Subcontract PI: Excluded by Requester $2,008,836 HHSN272201000006I/Task Order Number HHSN27200008

**Project Title:** STD Prevention Primate Unit: Vaccine Development

**IACUC #** 2195-27 **IACUC Expiration:** 10/17/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

The overall objective of this project is to assess the safety and efficacy of a chlamydia vaccine candidate in preventing cervical infection in the macaque model. The Macaca nemestrina (pigtail macaque) model for Chlamydia trachomatis genital tract infection was established, and has been well characterized by this laboratory. We have used the model for over 25 years to investigate pathogenesis, treatment and prevention of chlamydial infections. Prior studies have noted that different serovars, indeed different isolates, may result in different rates of transmission efficiency and duration of shedding organisms (culture positivity) in the macaque model.

A recent study in this laboratory investigated the pathogenesis of the chlamydia vaccine candidate being explored in this project. Both the vaccine candidate (D/EC/P-) and its parental wild type strain (D/LC/P+) have been separately introduced to pigtail macaques, and the resulting disease progression for each isolate is being documented in the lower and upper reproductive tract tissues. These particular chlamydia isolates have been well characterized at the NIAID Rocky Mountain Laboratories where the vaccine candidate was documented to have a CT135 gene mutation consistent with decreased virulence/early clearance in a mouse model, in contrast to the parent isolate which has an intact CT135 plasmid. This differentiation in virulence and clearance are under investigation in the current macaque study. We intend to further investigate the usefulness of the plasmid free chlamydia as a mucosally delivered vaccine.

**Publications associated with this project:** n/a

**Funding Sources**

NIH/NIAID, PI Excluded by Requester $1,113,776 HHSN272201400016C

**Project Title:** Aminoglycoside microbicides restore natural expression of anti - HIV - 1 retrocy

**IACUC #** 2195-29 **IACUC Expiration:** 9/18/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

Research efforts to develop topical microbicides for intravaginal use for the prevention of sexually transmitted infections (STI) including HIV have been ongoing for over a decade. In the year an estimated 4.3 million people became newly infected with HIV. Women now represent almost half of all adults living with HIV/AIDS. The need for female controlled STI preventive products is well understood. Preclinical safety testing of topical microbicide products must be performed prior to human use to assess the product's effects on the vaginal ecosystem.

We have developed a useful model to evaluate the safety of topical microbicide products after vaginal use in the pigtailed macaques. We have used this model to study the effects of single and repeated applications of microbicides on vaginal microflora and epithelium. In this microbicide innovation program grant (MIP IV) vaginal films containing aminoglycoside formulations are being evaluated for safety in the macaque model.

**Publications associated with this project:** n/a

**Funding Sources**

NIH, PI: Excluded by Requester Project Leader Excluded by Requester $250,937, R33AI082693

**Project Title:** Project 2 Tenofovir

**IACUC #** 2195-18 **IACUC Expiration:** 5/19/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

In this cooperative agreement, a novel delivery system for topical microbicides, vaginal films, will be compared to vaginal gel formulations. We will use our macaque model to assess safety, dispersal and pharmacokinetic characteristics of various film formulations containing tenofovir and/or dapivirine, and compare these findings to those compiled for gel formulations. These studies will in part guide the optimization of a combination topical microbicide delivery system.

In the past year we have completed a series of pharmacokinetic, dispersal and safety evaluations.

**Publications associated with this project**

Excluded by Requester Expression and localization of P-glycoprotein, Multidrug Resistance Protein, and Breast Cancer Resistance Protein in the female lower genital tract of human and pigtailed macaque. AIDS Res Hum Retroviruses. 2014 Nov;30(11):1106-16. doi: 10.1089/AID.2013.0281 PMCID:PMC4212939

**Funding Sources**

NIH, PI: Excluded by Requester /Project 2 Leader Excluded by Requester $1,175,850 U19-AI-082639-01A1

**Project Title:** Chlamydia vaccine studies in the pigtail macaque model

**IACUC #** 2195-27 **IACUC Expiration:** 10/17/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

The long-term goal of this project is to explore the efficacy of vaccine candidates targeting chlamydial infection. Chlamydia trachomatis is a common sexually transmitted disease which is largely asymptomatic, can progress to infertility and has been associated with the facilitated acquisition of other STIs including HIV. The initial phases of this study will focus on determining an appropriate positive control to utilize in future preclinical vaccine studies to be carried out in the macaque model. With the determination of an appropriate positive control, further studies will be conducted in three- to four-arm study designs (test product; positive control; negative control; adjuvant control), where vaccine products can be developed to prevent chlamydial infection and subsequent sequelae.

This project assesses the clinical disease status and development of upper reproductive tract disease of two chlamydial serovars being considered for initial vaccine efficacy studies. Reproductive tract tissues of animals exposed to these test serovars undergo thorough assessments with a goal of establishing links between chlamydial infection status and pathologic tissue responses.

**Publications associated with this project:** n/a

**Funding Sources**

Private Source PI Excluded by Requester $2,589,529

**Project Title:** Improved Macaque safety model for topical microbicides: Post coital assessment

**IACUC #** 2195-18 **IACUC Expiration:** 5/19/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

Topical microbicides represent an emerging strategy for the prevention of transmission of HIV and other sexually transmitted infections. A successful topical microbicide product will be applied prior to intercourse, without necessitating partner consent, and will be active against a variety of STIs, including HIV. It will be acceptable to potential users in terms of physical characteristics, availability, ease of use, safety and efficacy properties.

We have utilized the macaque vaginal safety model (currently contracted by the NIH, HHSN266200700013C) to provide standardized preclinical safety data for numerous topical microbicide products in development. In the contract model, measures of product safety include cervicovaginal colposcopy, vaginal microbiologic evaluation, and vaginal pH monitoring. The model characterizes the vaginal environment's response to repeated topical product applications in the absence of the exogenous factors of intercourse and potentially infectious ejaculate.

With this project, we have enhanced our standardized vaginal safety evaluations conducted in the pigtailed macaque model to include evaluations after sexual activity and with the presence of seminal fluid.

This project has provided for the collection of baseline data from a cohort of 24 female macaques assessing the cervicovaginal environment before and after mating. In addition, we have collected parallel pre- and post-coital assessments, with a placebo gel (HEC universal placebo), and with placebo film formulations in place. We have also conducted post coital safety studies assessing potentially active Gel and Film formulation in this macaque model.

**Publications associated with this project:** n/a

**Funding Sources**

NIH, PI: Excluded by Requester $1,686,443, R33-AI-071939

**Project Title:** Topical microbicide safety and efficacy evaluation in nonhuman primates

**IACUC #** 2195-18 **IACUC Expiration:** 5/19/2015

**Unit:** AIDS/Virology

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

The objective of these studies is to further the development of topical microbicides aimed at the prevention and control of sexually transmitted infections (STIs) through preclinical testing in nonhuman primates (NHP), utilizing our established models for topical microbicide safety and efficacy evaluations. Macaque models of Chlamydia trachomatis and Trichomonas vaginalis are currently available for efficacy studies in this laboratory. All test products, provided by NIAID, will first complete safety evaluation with repeated intravaginal or intrarectal product application. Products with acceptable safety profiles may be enrolled (with NIAID approval) to efficacy studies involving one or more STI. Safety measures include microbiologic and pH assessments and documentation of mucosal tissue responses as evidenced by colposcopic evaluation or rectal lavage assessment. Efficacy is determined by a product's ability to prevent infection by the challenge pathogen. All test products are subject to confidentiality agreements. This NIH contract allows for some innovative studies designed to improve our understanding of various test products and to enhance our research model for topical microbicide development studies.

During the past year we have continued studies exploring M. nemestrina microbiota, T. vaginalis infection in female macaques, assessed safety of over the counter lubricants with vaginal and rectal use, and assessed safety and drug uptake of test compounds.

**Publications associated with this project:** n/a

**Funding Sources**

NIH/NIAID, PI Excluded by Requester $12,225,887 HHSN266200700013 C

**Project Title:** Risk of Neonatal Vaccination for HIV/SIV Exposed Infants

**IACUC #** 4213-03 **IACUC Expiration:** 10/30/2015

**Unit:** AIDS/Virology

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD, Private Source WA

**Principal Core Scientist:** PhD, WaNPRC, Microbiology, U. Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Global Health, U. Washington, WA

Excluded by Requester PhD, Microbiology, U. Washington, WA

**Project Description**

Infant HIV acquisition through mother-to-child HIV transmission persists at an unacceptably high rate in resource-poor settings. There are numerous reasons for this, including a lack of clean water for formula feeding, reduced access to/compliance with ART regimens, and dependence on breast-feeding for infant health. Additionally, the WHO recommends vaccination at birth using the Bacillus Calmette-Guerín (BCG) vaccine to protect infants against disseminated tuberculosis (TB). While vaccination has the potential to generate long-lasting immunity against TB, this vaccine could also increase the number of HIV target cells in an infant as well as increase immune activation. Taken together, BCG vaccination may act to enhance susceptibility to oral HIV acquisition through breast milk as well as affect disease progression in infants.

Using the established SIV infected rhesus macaque model, we will determine if vaccination with BCG results in an increased rate of SIV infection and disease progression. Over the past year, we have used 2 groups of 4 macaques to titer our SIV oral exposures and determine the optimal concentration of virus required for infection. We have also regularly monitored immune responses to both SIV infection and BCG vaccination in these infant macaques using immune phenotyping, cytokine quantification, RNA expression analyses, nd several other methods. In the coming years, we plan to use the data obtained during 2014 to early 2015 to direct further studies using infant macaques that are SIV infected following BCG vaccination.

**Publications associated with this project** N/A

**Funding Sources**

NIH, Excluded by Requester PhD, $872,386, R01DE023047

**Project Title:** Defining BCR evolution during immunization

**IACUC #** 3408-04 **IACUC Expiration:** 3/18/2015

**Unit:** AIDS/Virology

**Type of Project:** Pilot

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD Private Source WA

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, U. of Washington, WA

**Other affiliate scientists:** n/a

**Project Description**

The aim of this project is to determine a) whether our HIV-1 envelope-based protein immunogens are capable of stimulating B cells expressing specific B cell receptors (BCRs) that are known to give rise to broadly neutralizing antibodies against HIV-1 and b) how far along the pathway BCR affinity maturation we can drive this process with the tools presently at our disposal. Similar information is not currently available, and its absence is critically hindering our ability to guide B cell responses towards the development of broad neutralizing antibodies against HIV-1.

Research at University of Washington, under the direction of Excluded by Requester oversaw the administration of several of our HIV-1 vaccine candidates in a relevant animal model. To date, we have initiated *in vivo* testing of 3 Env immunogens in rhesus macaques. The evolution of vaccine-specific BCRs were monitored in the Bone Marrow (BM), blood and secondary lymph nodes (LN). In parallel, the binding and neutralizing antibody responses will be monitored in the blood against a panel of clade A, B, C, and D HIV-1 viruses. Using an extensive array of epitope-mapping reagents and protocols, we are fine mapping the epitope targets of the neutralizing activity in the vaccinated macaques. Vaccine specific B cells were isolated during the immunization protocol, their RNA was isolated and the sequences of their heavy and light antibody chains are being determined. BCR-sequencing throughout the immunization protocol will help us assess the extent and type of antibody affinity maturation taking place from each of our immunogens and whether specific immunogens are more conducive to stimulate B cells expressing BCRs that give rise to broadly anti-HIV Nabs. During this project period, there were 2 immunization groups with 4 animals per group for a total of 8 animals.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH/NIAID | Excluded by Requester | PhD, PI | $740,759 | R01AI104384 |

**Project Title:** Optimizing HIV immunogen-BCR interactions for vaccine development

**IACUC #** 3408-04 **IACUC Expiration:** 3/18/2015

**Unit:** AIDS/Virology

**Type of Project:** Pilot

**Percent P51 dollars:** 0%

**AIDS?** Yes

**PI:** Excluded by Requester PhD Private Source WA

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, U. Washington, WA

**Other affiliate scientists:** N/A

**Project Description**

The elicitation of potent and broad anti-HIV-1 neutralizing antibodies (NAbs) by immunization has been one of the major goals of HIV research since the beginning of the HIV/AIDS epidemic. So far, this goal has not been attained. The target of anti-HIV-1 NAbs is the viral envelope glycoprotein (Env) and several forms of HIV Env have been tested as immunogens over the past three decades. The lack of elicitation of antibodies with broad neutralizing activities by soluble Env immunogens is not due to the absence of relevant epitopes on such constructs. Understanding why conserved neutralization epitopes are poorly immunogenic during immunization by HIV Env constructs is the focus of this proposal. Our overall hypothesis is that the biophysical characteristics of the epitope-BCR interaction, especially the kon and koff binding rates of that interaction, dictate the downstream intracellular events that lead to either B cell-differentiation and antibody-production, or to B cell-anergy.

This project aims at (a) improving the engineering of protein constructs that express specific HIV neutralization epitopes; (b) improving our understanding of the structural and biophysical characteristics of epitope-BCR interactions; and (c) elucidating how these interactions influence downstream events that either lead to B cell-proliferation and antibody-production or to B cell-anergy.

A series of immunogens that bind with a range of affinities to the b12-B cell receptor were designed and tested as immunogens in NHP. Such controlled in vivo studies will improve our understanding of the evolution of B-cell responses linked with broadly neutralizing antibody responses.

**Project Progress**

Rhesus macaques were immunized with recombinant HIV Envelope glycoprotein constructs and the anti-envelope antibody responses were analyzed throughout the immunization schedule. During this project period, there were 2 immunization groups with 3 animals per group for a total of 6 animals.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH/NIAID | Excluded by Requester | PhD, PI | $1,958,486 | P01 AI094419 |

# DIVISION OF DEVELOPMENTAL AND REPRODUCTIVE SCIENCES

# ANIMAL PROJECTS

**Project Title:** Experimental Model for Chorioamnionitis and Preterm Labor

**IACUC #** 4165-01 **IACUC Expiration:** 02/2/2015

**Unit:** Division of Developmental and Reproductive Sciences

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, OB/GYN, U. of Washington, WA

**Principal Core Scientist:** N/A

**Other affiliate scientists:**

Excluded by Requester PhD, Private Source WA

Excluded by Requester PhD, Private Source WA

**Project Description**

Preterm birth remains a significant economic and public health burden and the incidence is rising. Predominant risk factors for preterm birth and neonatal morbidity are invasive bacterial infections, which mainly begin *in utero*. A large body of evidence links infection-associated fetal injury, preterm birth, stillbirth and early neonatal disease with the acquisition of pathogens *in utero.* Despite these advances, mechanisms that enable bacterial invasion of the amniotic fluid and fetus are unknown. The inability to repeatedly sample multiple compartments during human pregnancy (*e.g.* mother, fetus, amniotic fluid) and the lack of animal models which simulate *in utero* host-pathogen interactions occurring in humans has contributed to this knowledge gap. *We have overcome these limitations in our unique chronically catheterized nonhuman primate (NHP) model (3), which closely emulates human pregnancy and will allow us to determine key virulence mechanisms employed by bacteria to invade the amniotic cavity and fetus.* The model organism in this proposal is Group B Streptococcus (GBS), which resides as a commensal in the lower genital tract of healthy women. We hypothesize that invasion and/or breach of placental membranes is critical for ascending GBS infection and *in utero* fetal injury. The unifying hypothesis of our proposal is that upregulation of the pluripotent pore-forming toxin known as β-Hemolysin/Cytolysin (b-H/C) promotes Group B Streptococcal invasion of placental membranes, amniotic fluid and fetus leading to fetal injury. Using human placental membranes and the unique NHP model of preterm birth, we propose to establish how upregulation of b-H/C and other virulence factors enables GBS to breach placental membranes and traffic into the amniotic cavity leading to *in utero* fetal injury. These studies will have widespread relevance as regulated expression of virulence factors is critical for bacterial pathogenesis.

**Publications associated with this project**

Excluded by Requester Group B Streptococcal infection of the choriodecidua induces dysfunction of the cytokeratin network in amniotic epithelium: a pathway to membrane weakening. PLoS Pathogens 2014; 10(3): e1003920. PMCID: PMC3946355.

**Funding Sources**

| | | | |
|---|---|---|---|
| NIH R01 | Excluded by Requester | $2,491,146 (total) | R01A100989 |
| Private Source | | $64,676 | |
| Private Source | | $600,000 | |

**Project Title:** ESC Chimeras

**IACUC #** 4259-03 **IACUC Expiration:** 2/20/2015

**Unit:** Division of Developmental and Reproductive Sciences

**Type of Project:** Pilot project

**Percent P51 dollars:** 21%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

The primary goals of the RBSCC are to develop embryo and stem cell resources and investigate methodology for the efficient production of embryonic stem cell (ESC) chimeric M.fascicularis infants. ESC chimeras are individuals comprised of two genetically distinct cell populations, generated through the combination of undifferentiated ESCs with cells of a pre-implantation embryo. This technique has been extensively utilized for gene targeting studies and cell-based transplant therapy in the mouse but to date has been unsuccessful in the NHP. NHP-ESC chimeras offer a unique opportunity to establish clinically relevant and immune tolerant NHP models for a range of translational medicine applications. As a core service, this area of activity has driven interactions within the UW (IPRL,CHDD,ISCRM and UW Medicine) and at other US Institutes (Private Source Private Source). The specific aim of this pilot study is to determine the efficiencies of ESC-embryo aggregation techniques for the establishment of pregnancies and generation of liveborn ESC-chimeric NHPs. We have generated ESC-chimeric embryos at rates comparable to controls. Furthermore we have demonstrated significant contribution of the ESC derived cells to the embryo proper, which to date has not been achieved in the NHP. ESC-chimeric embryos have been transferred to recipient females for the establishment of pregnancy. Of the 7 successful transfers, 2 early pregnancies were established but unlike pregnancies derived from control embryos the pregnancies were not maintained beyond 60 days. In response to this ESC culture conditions have been modified to a feeder-free monolayer system that supports culture of a homogenous undifferentiated cell population more suitable for chimera production and embryo aggregation and culture protocols refined to support better embryo development. Testing of these new methods are underway with on-going embryo production and transfer.

**Publications associated with this project** n/a

**Funding Sources**

NIH, PI: David Anderson, Reproductive Biology and Stem Cell Core $39,014, P51OD010425

Center funded Pilot Research Project Excluded by Requester PhD (PI) $150,000

**Project Title:** A Nonhuman Primate Model of Fragile X Associated Primary Ovarian Insufficiency

**IACUC #** 4259-03 **IACUC Expiration:** 2/1/2015

**Unit:** Division of Developmental and Reproductive Sciences

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, U. of Washington, WA

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, Environmental Health, U. of Washington, WA

**Other affiliate scientists:** Excluded by Requester PhD, Biochemistry, U. of Washington, WA

**Project Description/Progress**

Fragile X is an X-linked disorder characterized by instability of CGG trinucleotide repeat length within the FMR1 gene and women who carry the Fragile X pre-mutation are at a significantly increased risk of developing Fragile X-associated premature ovarian Insufficiency (FXPOI), characterized by reduced fertility and early onset menopause. A limited understanding of FMR1 dysregulation on ovarian function is based largely on a paucity of translational animal model systems with which to study the molecular mechanisms of FXPOI. The primary objective of this application is the generation of a NHP whole animal based model system of FXPOI. To date we have generated a basic construct for both the knock-in, to support the pre-mutation CGG repeat, and the knock-out construct that represents the FMR1 full mutation (Fragile X Syndrome). While the knock-in construct is in final development we are testing the transduction efficiency of the knock-out construct in our NHP ESC lines and hope to have a NHP cellular model of Fragile X Syndrome shortly. We are also exploring recent advances in gene editing strategies such as TALEN and CRISPR/Cas9 systems to generate both the knock-out and pre-mutation knock-in models of Fragile X and associated disorders.

**Publications associated with this project**

Excluded by Requester Use of model systems to understand the etiology of fragile X-associated primary ovarian insufficiency (FXPOI). J Neurodev Disord. 2014;6(1):26. doi: 10.1186/1866-1955-6-26. Epub 2014 Aug 13. Review.

**Funding Sources**

NIH, Excluded by Requester PhD, $173,016, 1 R21 HD 071876-02

**Project Title:** Biomarkers of Neonatal Encephalopathy in a Nonhuman Primate Model

**IACUC #** 3328-05 **IACUC Expiration:** 4/8/2015

**Unit:** Division of Developmental and Reproductive Sciences

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, PhD, Pediatrics, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:**

Excluded by Requester MD, Pediatrics, U. of Washington, WA
Excluded by Requester MD, Pediatrics, U. of Washington, WA
Excluded by Requester PhD, Radiology, U. of Washington, WA
Excluded by Requester PhD, Pediatrics, U. of Washington, WA
Excluded by Requester MD, Pediatrics, U. of Washington, WA

**Project Description**

Hypoxic-ischemic encephalopathy (HIE) remains a significant problem in the US and globally, affecting 3-5/1000 liveborn infants in the US, and contributing to 23% of neonatal deaths globally. Therapeutic hypothermia decreases the outcomes of death and neurodevelopmental disability, but outcomes remain poor for 50% of affected, treated infants. Biomarkers that accurately reflect the degree of brain injury, the timing and evolution of injury, and response to therapy are critically needed for clinical management of these patients and for research. Ideal biomarkers would differentiate infants who do not require treatment from those at risk of permanent sequelae; infants that might benefit from intervention from those for whom treatment is futile; and would identify infants who are within a therapeutic window for a specific treatment. We hypothesize that by combining sequential targeted metabolomic, proteomic, and structural assessments in an established nonhuman primate model of HIE, we will develop an assessment panel for HIE that will identify early severity of illness, prognosis, and response to treatment with neurodevelopmental status as a final outcome. Using a macaque nemestrina model of HIE we will develop: 1) Sensitive and specific diagnostic early biomarkers of severity of acute brain injury. Neurobehavioral and structural (MRI and necropsy) outcomes at 6 months of age will be used as a gold standard; 2) Early prognostic biomarkers of long term outcomes of HIE, using sequential evaluations of the proteome, metabolome, MRI and MRS to correlate individual acute response to injury with long-term structural and functional outcomes; and 3) Biomarkers which predict an individual's response to therapeutic hypothermia. Results of this study will be directly applicable to both clinical practice, and will also advance the field by defining biomarkers that can be used for research purposes.

**Publications associated with this project** N/A

**Funding Sources**

| | | | |
|---|---|---|---|
| NIH | Excluded by Requester MD, PhD | $791,512 | 1 R01 HD073128-01A1 |

# DIVISION OF PRIMATE RESOURCES

# ANIMAL PROJECTS

**Project Title:** Stem Cell Derived - Strategies to Improve Hematopoetic Stem Cell Transduction

**IACUC #** 3220-01 **IACUC Expiration:** 7/15/2015

**Unit:** Research Resources

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, Private Source WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description**
We previously derived a stem cell line from macaque oral fibroblasts. We plan to take this macaque (Macaca nemestrina) cell line (MniPSC), differentiate the cells into hematopoietic stem cells, purify this population based on the CD34 marker, and infuse these into a macaque to test their ability to engraft and give rise to mature functional blood cells in the monkey.
The rational of this study is that using hematopoietic stem cells derived from induced pluripotent stem cells (iPSC) is a potentially attractive alternative compared to autologous hematopoietic stem cells especially for genetic disease (i.e. Fanconi Anemia and Thalassemia), because we can make hematopoietic stem cells, from iPSCs, for patient or animal specific cell transplantation.
We propose to infuse hematopoietic stem cells derived from Macaca nemestrina induced pluripotent stem cells (MniPSC). To assure that the monkeys will recover from myeloablative conditioning, autologous gene-modified bone marrow CD34 cells will also be infused. Based on data from our Endothelial Expansion Study, we intend to co-infuse human endothelial cells (EC) because EC co-infusion has shown to be beneficial to hematopoietic stem cell engraftment and does not cause any acute or long-term toxicity in the animals.

**Project Progress** Three animals have been transplanted with the co-infusion of human endothelial cells and are in long-tern followup.

**Publications associated with this project:** n/a

**Funding Sources**
NIH Excluded by Requester (PI), Total award amount $841,579, 5R01HL115128-02

**Project Title:** Toxicology studies with adenovirus derived proteins in NHPs

**IACUC #** 3108-03 **IACUC Expiration:** 6/9/2015

**Unit:** Primate Resources

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, PhD, Dept. of Medicine, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

The goal was to study the safety of a new recombinant tumor junction opener (JO4) in combination with Doxil chemotherapy in preparation of a clinical trial.

JO4 was used at a dose that was effective in mouse tumor models (2mg/kg). Doxil was injected at a dose that will be used in the clinical trial (40mg/m2). Analysis of clinical symptoms and blood parameters did not show remarkable signs of toxicity. Upon necropsy, performed at 6 hours after the second injection cycle, no treatment related abnormalities in gross examination of organs and histological analysis of tissue sections was observed. Therefore, the combination of JO4 and Doxil was safe in an adequate animal model.

Considering the limitations of the study (N=1), a series of cautious conclusions can be made:

i) As expected, serum antibodies against JO4 develop after one week. These antibodies appear to be completely saturated when a second injection of JO4 is given. Corresponding immune complexes appear to be deposited in a series of lymphoid and non-lymphoid organs.

ii) Non-opsonized JO4 can be found in epithelial tissues, specifically in adrenal glands, epididymis, and kidneys. Some functional activity of JO4 with regards to junction opening is supported by an increased uptake of Doxil in the adrenal glands. On the other hand, JO4 appears to decrease Doxil concentrations in the liver, spleen, and lymphnodes. There was no JO4-related increase of Doxil in the heart or abnormalities in the ECG and the "heart panel" in blood chemistry analyses.

The data have been published in a recently accepted paper.

**Publications associated with this project**

In Press

**Funding Sources**

NIH, PI: Excluded by Requester $150,00, P50 CA83636, project 3 (PI Excluded by Requester

DoD, PI Excluded by Requester MD, $200,000

**Project Title:** Development of stem cell therapies for myocardial infarction using primate model

**IACUC #** 2225-06 **IACUC Expiration:** 9/18/2015

**Unit:** Research Resources

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, PhD, Professor, Depts. of Pathology, Bioengineering, Medicine/Cardiology, U. of Washington, WA

**Principal Core Scientist:** **n/a**

**Other affiliate scientists:**

Excluded by Requester MD, Private Source WA
Excluded by Requester MD, Dept. of Pathology, U. of Washington, WA
Excluded by Requester MD, PhD, Dept. of Cardiology, U. of Washington, WA
Excluded by Requester MD, PhD, Dept. of Cardiology, U. of Washington, WA
Excluded by PhD, Dept. of Pathology, U. of Washington, WA
Excluded by Requester PhD, Dept. of Pathology, U. of Washington, WA
PhD, Dept. of Pathology, U. of Washington, WA
PhD, Dept. of Radiology, U. of Washington, WA
Excluded by Requester PhD, Dept. of Pathology, U. of Washington, WA
MD, PhD, Dept. of Pathology, U. of Washington, WA
Excluded by Requester PhD, Dept. of Pathology, U. of Washington, WA
Excluded by Requester PhD, Dept. of Pathology, U. of Washington, WA
Excluded by Requester PhD, Dept. of Pathology, U. of Washington, WA
Excluded by Requester MD, PhD, Dept. of Cardiology, Private Source

**Project Description**

Heart failure is a common result of many cardiovascular diseases including myocardial infarction. The natural course of heart failure is progressive deterioration resulting in death unless heart transplantation is performed. Novel therapies addressing this urgent problem include stem cell use to regenerate the injured or failing heart. Much progress has been made using cultured stem cells and rodent models. Many differences exist between rodents and humans that limits progression of stem cell therapies towards clinical treatments, making it difficult to evaluate the potential of human stem cell derivatives. In contrast, studies in nonhuman primates will enable the necessary research in a biological system with high degree of similarity to humans. We therefore developed a nonhuman primate myocardial infarction model that enables the study of engraftment and immune tolerance of stem cell derived cardiomyocytes. Our studies have shown that (1) large grafts of human embryonic stem cell derived cardiomyocyte (hESC-CM) were successfully achieved and, (2) all hESC-CM-treated macaques showed partial remuscularization of the infarct areas, but (3) exhibited ventricular tachycardia (VT) in the first 4 weeks after cell therapy. Post-infarct VT may result from re-entry (maybe due to the infarction or the transplanted cells) or enhanced automaticity (caused by the transplanted cells). From our previous studies, all cell-treated animals had ventricular arrhythmias which spontaneously resolved by 4 weeks after cell injection. Thus, the overall goals of the current project are to investigate mechanisms of ventricular arrhythmias after cell engraftment, to demonstrate the therapeutic effect of post-infarct cell therapy, and to identify the optimal therapeutic strategy of cell therapy for cardiac repair.

**Project Progress**

Our preliminary results show that cell therapy may improve heart function and reduce infarct scar size. We also identified a possible etiology of post-infarct VT after cell therapy.

**Publications associated with this project**

Excluded by Requester
Excluded by Requester Human embryonic-stem-cell-derived cardiomyocytes regenerate non-human primate hearts. Nature. 2014;510(7504):273-277.
Excluded by Requester Cardiac regeneration using pluripotent stem cells-Progression to large animal models. Stem Cell Res. 2014;13(3PB):654-665.

**Funding Sources**

Excluded by Requester $919,397, P01 HL094374
Excluded by Requester $2,500,000

**Project Title:** Strategies to improve the adoptive transfer of T cells

**IACUC #** 4159-01 **IACUC Expiration:** 05/29/2015

**Unit:** Research Resources

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, Private Source WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** Excluded by Requester MD Private Source WA

**Project Description**

Immunotherapy with T cells expressing chimeric antigen receptors (CARs) specific for a tumor cell-surface molecule is effective for $CD19^+$ B-cell malignancies. There is interest in extending CAR-T cell therapy to epithelial tumors, which requires identifying molecules that can be targeted safely without serious toxicity to normal cells. We identified a panel of target molecules expressed on some hematological malignancies and solid tumors, including ROR1, a conformationally exposed EGFR epitope ($EGFR_{v806}$), and CD171 (L1-CAM). CARs that recognize these molecules have been developed. However, safety evaluation is needed prior to clinical translation. Unlike the mouse, human and macaque ROR1, $EGFR_{v806}$, and CD171 proteins are highly homologous, and tissue expression is comparable in humans and macaques. Thus, we employed the macaque model as a platform to assess the safety of these novel CARs.

High doses ($1\text{-}5\times10^8$/kg) of ROR1-CAR-T cells were infused to macaques without toxicity and persisted in the blood for >3 weeks, albeit at lower levels than control T cells administered at the same dose. ROR1-CAR-T cells migrated efficiently to lymph nodes and bone marrow and eliminated endogenous $ROR1^+$ B cells, which coincided with transient increases in plasma IFN-γ and IL-6. ROR1-CAR-T cells remained functional in vivo as demonstrated by a 7.7-fold increase in number in response to infusion of $ROR1^+$ T cells. Preliminary analysis of the migration of ROR1 CAR-T cells to tissue sites demonstrated that these cells also migrated efficiently to spleen, lung, and liver. The induction of transgene product-specific immunity limited long-term persistence of CAR-T cells and analysis of late toxicity, however our data illustrate the value of this model for acute safety studies for candidate targets for CAR-T cells, and supports targeting ROR1 in human cancers with CAR-T cells. Additionally, studies with $EGFR_{v806}$- or CD171-CAR-T cells are in progress.

**Publications associated with this project**

Excluded by Requester

Excluded by Requester Safety of Targeting ROR1 in Primates with Chimeric Antigen Receptor-Modified T Cells. Cancer Immunol Res. 2014 Oct 29. [Epub ahead of print] doi: 10.1158/2326-6066.CIR-14-0163. PubMed PMID: 25355068; PubMed Central PMCID: n.a.

Excluded by Requester

Excluded by Requester Adoptive Therapy with Chimeric Antigen Receptor-Modified T cells of Defined Subset Composition. Cancer J. 2014 Mar-Apr;20(2):141-144. doi: 10.1097/PPO. 0000000000000036. PubMed PMID: 24667960 PubMed Central PMCID: n.a.

Excluded by Requester Design and Implementation of Adoptive Therapy with Chimeric Antigen Receptor-Modified T Cells. Immunol Rev. 2014 Jan;257(1):127-144. doi: 10.1111/Imr.12139. Erratum in Immunol Rev. 2014 Mar;258(1):259. PubMed PMID: 24329794; PubMed Central PMCID: PMC3991306.

**Funding Sources**

| | | | |
|---|---|---|---|
| NIH (NCI) | Excluded by Requester MD | $448,945 | 5 R01 CA114536-09 |

**Project Title:** Cytoxan induced tolerance to CAR-T cells in nonhuman primates

**IACUC #** 4159-01 **IACUC Expiration:** 05/29/2015

**Unit:** Research Resources

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester MD, Private Source WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** Excluded by Requester MD, Private Source WA

**Project Description**

The adoptive transfer of T cells modified to express a chimeric antigen receptor (CAR) is a promising strategy to treat human malignancies. To date, most CARs that are being used clinically consist of a single chain variable fragment (scFV) from a different species fused to several co-stimulation and/or signaling molecules. Based on this design, the induction of CAR-specific immune responses has become a major concern. Recent clinical trials of immunotherapy demonstrated that premature immune-mediated rejection limits the persistence of transferred CD19 CAR-T cells in some patients. "Humanized" CARs are being developed, but this approach does not address the potential immunogenicity of fusion sites between components of the CAR. Thus, broadly applicable strategies to induce tolerance to CAR-T cells are needed. Published work showed that 'post-transplantation" Cytoxan can be employed as a single agent to induce tolerance in murine allograft models and after allogeneic hematopoietic stem cell transplantation. Thus, here we examine if post-infusion Cytoxan can be used to induce tolerance to CAR-T cells in the *M. mulatta* model with the objective of defining a regimen that could be readily translated clinically. We first transferred CAR-T cells after the administration of Cytoxan to a control animal. As expected, the CAR-T cells were rapidly cleared from the circulation and clearance correlated with a CAR-specific immune response. A macaque was then primed with CAR-T cells followed by post-infusion Cytoxan (50 mg/kg), and a second CAR-T cell infusion to examine if we induced tolerance. The transferred CAR-T cells persisted in the peripheral blood for ~2-3 weeks, but then dropped to undetectable levels coincident with the induction of an anti-CAR-specific immune response. Thus, more profound immune modulation is needed to induce tolerance to CAR-T cells and we are now treating additional animals with both Fludarabine (30 mg/m$^2$/day) and Cytoxan.

**Publications associated with this project**

Excluded by Requester

Excluded by Requester Adoptive Therapy with Chimeric Antigen Receptor-Modified T cells of Defined Subset Composition. Cancer J. 2014 Mar-Apr;20(2):141-144. doi: 10.1097/PPO. 0000000000000036. PubMed PMID: 24667960 PubMed Central PMCID: n.a.

Excluded by Requester Design and Implementation of Adoptive Therapy with Chimeric Antigen Receptor-Modified T Cells. Immunol Rev. 2014 Jan;257(1):127-144. doi: 10.1111/Imr.12139. Erratum in Immunol Rev. 2014 Mar;258(1):259. PubMed PMID: 24329794; PubMed Central PMCID: PMC3991306.

**Funding Sources**

Private Source Excluded by Requester ~$190,293

**Project Title:** Self-injurious behavior and primate well-being

**IACUC #** 3054-07 **IACUC Expiration:**

**Unit:** Division of Primate Resources

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, U. Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, U. Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, U. Massachussetts-Amherst, MA
Excluded by Requester PhD, ONPRC, OR
Excluded by Requester PhD, SWNPRC, TX

**Project Description**

This project is a multi-center collaboration with Excluded by Requester at the University of Massachusetts Amherst (UMASS) Excluded by Requester at the Oregon National Primate Center (ORNPRC) and at the Excluded by Requester Southwest National Primate Research center (SWNPRC) to investigate the causes of self-injurious behavior (SIB) and alopecia in rhesus macaques. Work at the WaNPRC consists of collecting behavioral observations, evaluating stress reactivity, collecting and transferring photographs of alopecia for digital assessment at the UMASS, and collection of a small hair sample to be assayed for cortisol at the UMASS. In addition, the centers are creating a cross center life history database for all subjects to investigate demographic variables that may contribute to these disorders. Data from this project (5 abstracts) were presented at the 2014 meeting of the American Society of Primatologists and 3 articles were published in peer reviewed journals.

**Publications associated with this project**

Excluded by Requester (2014) Alopecia in three macaque species housed in a laboratory environment. American Journal of Primatology, doi:101002/ajp.22236.

Excluded by Requester (2014) A simple alopecia scoring system for use in colony management of laboratory-housed primates. Journal of Medical Primatology, doi 10.1111/jmp.12107.

Excluded by Requester (2014) Hair loss and hypothalamic-pituitary-adrenocortical (HPA) axis activity in captive rhesus macaques: a cautionary tale. Journal of the American Association for Laboratory animal Science, 53(3), 261-266.

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH | Excluded by Requester | PhD, PI | $83,374 | OD011180-15 |

# NEUROSCIENCE ANIMAL PROJECTS

**Project Title:** Neurobiology of Memory

**IACUC#** **4136-01** **IACUC Expiration:** 7/1/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 6%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, Physiology & Biophysics, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Physiology & Biophysics, U. of Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Physiology & Biophysics, U. of Washington, WA

PhD, Physiology & Biophysics, U. of Washington, WA

Excluded by Requester PhD, Psychology, Private Source GA

**Project Description**

Impaired memory is an important component of diseases such as Alzheimer's disease, temporal lobe epilepsy, depression, and schizophrenia that collectively affect over twenty million Americans. Our long-range goal is to contribute to a better understanding of the neural mechanisms that underlie memory processes, in order to bring us closer to developing new therapies for these disabled patients. The objective of the research in this project is to characterize neural signals that support memory formation and retrieval. The experiments in this project examine the role of medial temporal lobe structures, including the hippocampus and underlying cortices, in memory. This is accomplished using multi-electrode recording techniques, lesion techniques and neural stimulation in monkeys trained to perform a variety of memory tasks. In particular, we are examining neuronal activity in the hippocampus and entorhinal cortex that underlies visual recognition memory, relational memory, and spatial navigation. We are also identifying the role of the hippocampus in these forms of memory through an investigation of the effects of targeted lesions. Finally, we are investigating the effects of electrical stimulation on memory formation and retrieval.

**Project Progress**

We have made significant progress over the past year of this project. In the studies of spatial navigation, we have trained monkeys to use a joystick to navigate in a virtual reality environment and have initiated training in a memory version of the navigation task. With our collaborators, we have developed novel thin-film electrodes to allow for chronic recordings with many channels throughout the medial temporal lobe. We have implanted one monkey with 3 arrays of 12 channels each and have performed daily hippocampal recordings for over five months. In addition, we have developed novel methods for automated classification of eye movement traces for use in free-viewing tasks.

**Publications associated with this project**

Excluded by Requester (2014). A nonparametric method for detecting fixations and saccades using cluster analysis: Removing the need for arbitrary thresholds. Journal of Neuroscience Methods. 227:121-131. PMID: 24509130

Excluded by Requester (2014). Social relevance drives viewing behavior independent of low-level salience in rhesus macaques. Frontiers in Neuroscience. 8:354. PMID:25414633

Excluded by Requester (2014). Distinct frequencies mark the direction of cortical communication. Proceedings of the National Academy of Sciences. 111(40):14316-7. PMID: 25267647

**Funding Sources**

NIH P51 Base Grant Excluded by Requester $96,540 P51OD010425

NIH Excluded by Requester $513,365,R01 MH093807

NIH $505,611,2R01 MH080007

DARPA, Excluded by Requester $583,804, BAA-14-08I

**Project Title:** Systemic Gene Transfer in Nonhuman Primates via rAAV Vectors

**IACUC #** 3333-02 **IACUC Expiration:** 8/15/2014

**Unit:** Neuroscience

**Type of Project:** Research Project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Neurology, University of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:**

Excluded by Requester PhD, Neurology, U. of Washington, WA
, MD, Nephrology, U. of Washington, WA

**Project Description**

The proposed experiments will be conducted in Macaca nemestrina given the similar size to young humans. This proposal is designed to generate pre-clinical data supporting systemic delivery of AAV-micro-dystrophin vectors to patients with Duchenne muscular dystrophy/Becker muscular dystrophy (DMD/BMD). Aim 1 will develop efficient methods for limb muscle delivery while Aim 2 will adapt approaches to target forearms, heart and diaphragm. Finally, aim 3 will combine multiple approaches to test the ability to achieve systemic gene delivery to all the critical striated muscle targets in non-human primates. Duchenne muscular dystrophy is an X-linked genetic disorder caused by mutations in the gene encoding the cytoskeleton protein dystrophin, resulting in muscle degeneration. Affected patients die as a result of respiratory and/or cardiac complications due to progressive striated muscular weakness and wasting. There is no effective therapy for this disease, but we have demonstrated that delivery of a dystrophin-based gene to muscles using an AAV vector can dramatically reduce pathophysiology in dystrophic mice by halting muscle wasting and significantly decreasing weakness. An effective therapy for patients will need to treat muscles throughout the entire body. Recombinant vectors based on adeno-associated virus can deliver genes to the entire striated musculature of the body. We hypothesize that delivery of dystrophin-based genes to the striated muscles of patients will lead to a highly effective therapy for this disorder. However, we need to assay the efficiency and efficacy of vector-based approaches and also their safety in mammals more closely related to humans.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH | Excluded by Requester | PhD | $510,000 | R37 AR40864-25 |

**Project Title:** Neural Organization of Primate Inner Retina: Synaptic mechanisms of color and luminance coding

**IACUC #** 2309-01 **IACUC Expiration:** 5/9/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, Biological Structure, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Biological Structure, U. of Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Biological Structure, U. of Washington, WA
Excluded by Requester MS, Biological Structure, U. of Washington, WA
Excluded by PhD, Bioengineering, Private Source IL
Excluded by Requester PhD, Optometry, SUNY, NY
PhD, Ophthalmology, U. Illinois, IL
PhD, Vision Sciences, U. of Alabama, AL
Excluded by Requester PhD, Biological Structure, U. of Washington, WA

**Project Description**

The midget ganglion cell and its specialized circuitry in the foveal retina are unique to the primate visual system and gives rise to the primary visual pathway that initiates the perception of form and color. Despite this fundamental importance in the human visual process for the treatment of retinal disease the underlying synaptic mechanisms and circuits that mediate the complex physiological properties of the midget cell population remain poorly understood. Our project plan is to specifically advance understanding of the synaptic mechanisms that underlie the spatial and color coding properties of the unique midget circuit in the fovea. During the previous project period we developed methods to access and characterize the synaptic physiology of the macular midget ganglion cell circuitry. First, we have discovered that NMDA type glutamate receptors surprisingly mediate the major fraction of light-evoked excitatory synaptic input to midget ganglion cells and that a strong glycinergic synaptic inhibition acts to modulate this distinctive excitatory pathway. We propose to determine the role of these newly identified circuits in both 'red-green' color coding and achromatic contrast sensitivity. In addition we will test the hypothesis that NMDA receptors mediate the achromatic contrast sensitivity of the midget pathway. Second, we have identified a controversial S-cone input to OFF midget ganglion cells and we will determine the underlying synaptic mechanisms and role in color coding for this distinctive circuit. We will test the hypothesis that this pathway shows novel chromatic tuning not previously found at the retinal level and will investigate the underlying synaptic mechanisms. Third, we have discovered an unexpected high sensitivity rod signal pathway input to midget ganglion cells and we will determine the synaptic pathways that comprise the midget-rod circuit. We will directly test the hypothesis that the primary rod bipolar-AII amacrine pathway mediates the transmission of high sensitivity rod signals to midget ganglion cells. Taken together these projects will advance knowledge of synaptic mechanisms in the unique and dominant retinal circuitry that initiates spatial and color coding in primate visual system.

**Publications associated with this project**

Excluded by Requester (2014). Central projections of intrinsically photosensitive retinal ganglion cells in the macaque monkey. *Journal of Comparative Neurology*, 522(10):2231-48 [Epub 2014 April 19]. PMID: 24752533

Excluded by Requester (2014). Distinct synaptic mechanisms create parallel S-ON and S-OFF color opponent pathways in the primate retina. *Visual Neuroscience,* Mar;31(2):139-51 [Epub 2013 Jul 29]. PMID: 23895762

Excluded by Requester (2014). A synaptic signature for ON- and OFF-center parasol ganglion cells of the primate retina. *Visual Neuroscience,* Jan;31(1):57-84 [Epub 2013 Nov 27]. PMID: 24801624

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH NEI | Excluded by Requester | PhD | $516,608 | R01-EY06678-28 |

**Project Title:** Serial Blockface Electron Microscopic (SBEM) reconstruction of primate foveal circuits

**IACUC #** 2309-01 **IACUC Expiration:** 5/9/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** NO

**PI:** Excluded by Requester PhD, WaNPRC, Biological Structure, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Biological Structure, U. of Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Biological Structure, U. of Washington, WA
Excluded by Requester PhD, Biological Structure, U. of Washington, WA
Excluded by Requester MS, Biological Structure, U. of Washington, WA

**Project Description**

The foveal retina of the non-human primate and human retina is one of the most specialized neuronal structures in the central nervous system. Because of its small size and complex structure knowledge of the circuits that comprise the foveal retina and mediate all spatial and color vision are only poorly understood. In a companion project we are intensively studying the physiological properties of foveal neurons in a macaque in vitro model. In this project we are initiating studies using new and innovative methodology to reconstruct the complete synaptic circuit of the primate foveal retina. Serial Blockface Electron Microscopy (SBEM) will be employed to generated thousands of aligned serial digital image stacks through the fovea at high ultrastructural resolution using a newly acquired facility via the Vision Core. We will reconstruct all circuits linked to the three cone photoreceptor types that comprise and initiate the foveal circuits. Our overall goal is to produce the first complete "connectome" of the primate fovea and address several major questions regarding the structure and function of this neural network. Specific goals include a characterization of the unique circuits linked to short-wavelength sensitive (S) cones and the "midget" circuits linked to the long (L) and middle (M) wavelength sensitive cone types and the rod photoreceptor circuits linked to the unique All amacrine cell type.

**Publications associated with this project** N/A

**Funding Sources**

| | | | | |
|---|---|---|---|---|
| NIH | Excluded by Requester | PhD | $806,123 | 5P30EY001730-39 |
| NIH | | PhD | $516,608 | R01-EY06678-28 |

**Project Title:** Neuron Transcriptome Classification of Primate Visual Pathways

**IACUC #** 2309-01 **IACUC Expiration:** 5/9/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** NO

**PI:** Excluded by Requester PhD, WaNPRC, Biological Structure, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Biological Structure, U. of Washington, WA

**Other affiliate scientists:**

Excluded by Requester PhD, Biological Structure, U. of Washington, WA
Excluded by Requester MS, Biological Structure, U. of Washington, WA
Excluded by Requester PhD, Center for Neuroscience, UC Davis, CA
Excluded by Requester PhD, Center for Neuroscience, UC Davis, CA

**Project Description**

Understanding brain function and how it is altered by degenerative disease ultimately requires detailed knowledge of how the genome specifies the extreme diversity of neuronal cell types that is the sine qua non of central nervous system organization. Transcriptional profiles of nervous tissue suggest that functional cell types can be distinguished by gene expression patterns, yet linking gene expression to a comprehensive functional and anatomical classification of neuronal cell types has not been achieved. The goal of this project is to address this question directly in the non-human primate and human retina, where cell type complexity is extreme yet uniquely accessible for physiological, anatomical and genetic analyses. Specifically we will combine novel methods of visual physiology and cell type identification in an in vitro preparation of both the macaque and human retina with single-neuron, next generation RNA-sequencing to determine the distinct transcriptome for each of the 19 currently identified ganglion cell types that give rise to the central visual pathways. Our long range translational goals are to apply these methods to the full diversity of ~80 neuronal cell types present in the primate retina and to extend this analysis to cell type-specific gene expression changes linked to human retinal degenerative disease and aging.

**Publications associated with this project** N/A

**Funding Sources**

| | | | |
|---|---|---|---|
| NIH | Excluded by Requester PhD, | $516,608 | R01-EY06678-28 |

**Project Title:** Brain Computer Interface for Primates

**IACUC #** 2326-08 **IACUC Expiration:** 6/29/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester Ph.D., WaNPRC, Physiology & Biophysics, U. Of Washington

**Principal Core Scientist:** Ph.D., WaNPRC, Physiology & Biophysics, U. Of Washington

**Other affiliate scientists:**

Excluded by Requester Ph.D., Physiology & Biophysics, U. Of Washington
Excluded by Requester Ph.D., Rehabilitation Medicine and Physiology & Biophysics, U. of Washington
Excluded by Requester Ph.D., M.D., Physiology & Biophysics, U. Of Washington

**Project Description**

We are investigating several applications of head-fixed bidirectional brain-computer interfaces (BBCI) that operate continuously during free behavior and generate activity-dependent stimulation of the brain or spinal cord. These so-called "Neurochips" are connected to electrodes that record the activity of cortical cells and/or muscles; this activity is processed by a programmable computer chip and converted in real-time to activity-contingent electrical stimuli delivered to nervous system sites. A promising application is to bridge impaired biological connections, as we demonstrated for cortically controlled intraspinal stimulation, allowing a monkey with spinal cord injury to generate task-appropriate movements. A second application is to produce synaptic plasticity through spike-triggered stimulation, which can strengthen weak physiological connections. This year we analyzed data from a study in which intraspinal stimulation was triggered from corticospinal cells; this procedure produced changes in the strength of the cells' corticospinal connections and also produced changes in the way that these cells were related to limb movements. We are making good progress developing the next-generation "Neurochip 3", which will empower more sophisticated BBCI paradigms. NC3 will provide 16 channels of high-resolution recording, multiple feedback loops programmed in FPGA logic and greater on-board storage.

**Project Progress**

Our studies indicate that the BBCI has clinical potential to aid patients paralyzed by ALS or spinal injury to regain some motor control directly from cortical cells and may also be used to strengthen weak connections impaired by stroke.

**Publications associated with this project**

Excluded by Requester Editorial: Closed-Loop Neuroscience and Neuroengineering, Frontiers in Neural Circuits 8:115. doi: 10.3389/fncir.2014.00115, 2014.

Excluded by Requester eds. (2014). Closing the Loop Around Neural Systems. Lausanne: Frontiers Media. doi: 10.3389/978-2-88919-356-1

**Funding Sources**

NIH PI: Excluded by Requester $689,939 RO1 NS 12542-39

Private Source PI: Excluded by Requester $105,000

**Project Title:** Neurophysiology of vision

**IACUC #** 4167-01 **IACUC Expiration:** 4/21/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, Physiology & Biophysics, U. of Washington, WA

**Principal Core Scientist:** PhD, WaNPRC, Physiology & Biophysics, U. of Washington, WA

**Other affiliate scientists:** n/a

**Project Description/Progress**

The visual system has emerged as a premier model for understanding information processing by neurons. Within vision, the submodality of color provides a particularly attractive experimental platform: we know a tremendous amount about the phenomenology of color perception and can explain some aspects of color perception, quantitatively and with high precision, by well-understood physiological processes. As a result of this progress, we can quickly and accurately diagnose many distinct forms of color blindness and can build devices that render colors accurately. On the other hand, surprising holes in our knowledge remain. The proposed research will fill this hole in our knowledge by determining where the temporal bottlenecks for detection and appearance reside. Three specific aims are planned: 1) Electrophysiological and modeling to determine where in the visual system luminance signaling is limited. 2) Electrophysiological and modeling to determine where in the visual system red-green chromatic signaling is limited. 3) Comparison of stimulus categories as classified by monkeys and by their component neurons to determine whether the dynamics of neuronal signals are responsible for changes in stimulus appearance as a function of temporal frequency. The proposed experiments will extend our knowledge toward an understanding of the principles that give rise to perception and its disorders. Such an understanding promises to provide the means to promote recovery of visual function following trauma or neurological disease.

**Publications associated with this project**

Excluded by Requester 2014, "What studies of macaque monkeys have told us about human color vision." Neuroscience DOI:10.1016/j.neuroscience.2014.10.007.

Excluded by Requester 2014, Spectral sensitivity differences between rhesus monkeys and humans: Implications for neurophysiology. J. Neurophysiol. 112:3164-72.

Excluded by Requester 2014, Object-centered shifts of receptive field positions in monkey primary visual cortex. Curr. Biol. 24:1-6.

Excluded by Requester 2014, Bayesian active learning of neural firing rate maps with transformed Gaussian process priors. Neural Comput.30:1-23.

**Funding Sources**

NIH, PI: Excluded by Requester $2,187,500, R01ET018849

NIH, PI: Excluded by Requester $481,250, R21EY020622

NIH, PI: Excluded by Requester $489,500, R21EY024362

**Project Title:** A Neuronal Process of the Error Signal that Drives Saccade Adaptation

**IACUC #** 4310-01 **IACUC Expiration:** 4/28/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Physiology & Biophysics, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

I. Project of superior colliculus (SC):Examine whether SC visual activity reflects the characteristics of the visual error that drives saccade adaptation.

The result showed that the SC visual activity mirrored changes in the adaptation rate. This result supports our hypothesis that SC visual activity reflects characteristics of the error signal that drives saccade adaptation. This result was presented in a meeting at the National Institute of Advanced Industrial Science and Technology (4/18/2014).

II. Project of oculomotor vermis (OMV):Examine whether the Purkinje cell complex spikes in oculomotor vermis directionally modulate saccade adaptation.

The results suggest that Purkinje cells' complex spikes might signal the direction of the next-trial adaptation. This result was presented in the annual meeting of the Society for Neuroscience (11/15-19/2014, Washington, DC).

III. Project of Optogenetic:Optogenetics is a new set of tools to manipulate neural activity. These tools have been used effectively to study the neural basis of behavior in fruit flies, zebrafish, and mice. However, optogenetic effects on monkey behavior have been elusive. In this study we attempted to replicate the three behavioral effects of electrical stimulation of the SC with optogenetic activation.

Optogenetic activation using ChR2 in the SC was able to produce effects similar to, but weaker than, those produced by electrical stimulation.

IV. Project of caudal fastigial nucleus (cFN):Characterize the cerebellar influence on motoneurons in the abducens (ABD) nucleus.

The results suggest that the cerebellum controls ipsilateral ABD activity by truncating on-direction bursts during ipsiversive saccades and extending off-direction pauses during contraversive saccades. We conclude that cFN output keeps saccades accurate by controlling when ABD on-direction bursts and off-direction pauses end.This result has been published in the Journal of Neurophysiology (2014, 111: 1553-63).

**Publications associated with this project**

Excluded by Requester Cerebellar fastigial nucleus influence on ipsilateral abducens activity during saccades. J Neurophysiol. 2014 111(8):1553-63.

**Funding Sources**

NIH, Excluded by Requester $445,000, EY023277

**Project Title:** Can sustained neurotrophic treatment in a single extraocular muscle induce strabismus?

**IACUC#:** 4221-01 **Expiration:** 6/11/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthalmology, University of Minnesota, MN

**Principal Core Scientist:** Excluded by Requester PhD, Ophthalmology, WaNPRC
Excluded by Requester PhD, WaNPRC

**Project Description**
Developmental Strabismus (misaligned eyes) is a common problem affecting at least 3% of children born in the United States. Eye misalignment can lead to profound deficits in visual function including loss of stereovision and visual acuity (amblyopia). Although the etiology of strabismus is usually unknown, treatment must be applied early in life to preserve vision. Treatment often involves surgical manipulation of extraocular eye muscle insertions to realign the eyes as close to optimal as possible. Successful surgical correction of potentially under- or over-acting eye muscles is often the treatment of choice to allow development of binocular vision to proceed. Our studies seek to provide additional treatments for eye muscle impairments by applying slow-release (3 month) growth factors directly to specific eye muscles.

**Project Progress**
Infant monkeys were treated unilaterally with insulin-like growth factor-1 for 3 months via implantation of a sustained release pellet. All four monkeys developed strabismus, and it appears that the major adaptation was the significant hypertrophy of the treated muscles fibers as well as a coordinated increase in the myofiber size in the lateral rectus muscle of the same orbit. Mechanistically it appears that the IGF-1 treatment resulted in a maintenance of the exotropia seen in infant monkeys; prevention of adaptation to the visual world by perturbing muscle size and strength in the periphery is sufficient to disrupt the normal development of binocularity in these infant monkeys. This part of the study is ready to be submitted as a manuscript. We continue to analyze potential changes in the motor neurons caused by these treatments.

A second set of 2 infants received bilateral sustained treatment with brain derived neurotrophic factor. Neither monkey developed strabismus. Analysis of the muscles showed that the treated muscles developed a pronounced increase in slow myofiber cross-sectional area with a concomitant increase in neuromuscular junctional area. This would be predicted to alter muscle shortening velocity and potentially increase the sustained part of muscle contraction. Further studies are needed to determine if these changes have occurred. The data of the first part of this analysis is being prepared as a manuscript.

A third set of 2 infants received unilateral treatment with glial derived neurotrophic factor. These infant monkeys developed a significant strabismus. The collected tissues are in the process of being analyzed for the potential mechanism behind the development of their strabismus.

**Funding Sources**

| Funding Source | Primary Investigator | Total award amount | Funding ID |
|---|---|---|---|
| NIH | Excluded by Requester PhD, Excluded by Requester PhD | $530,421 | 5R01EY015313-10 |

**Project Title:** Neural Mechanisms of Visual-Vestibular Behavior

**IACUC#:** 4221-01 **Expiration:** 6/11/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthalmology, WaNPRC

**Principal Core Scientist:** Excluded by Requester PhD, Ophthalmology, WaNPRC
Excluded by Requester PhD, WaNPRC

**Other affiliate scientists:** Excluded by Requester PhD, Ophthalmology, University of Washington
Excluded by Requester PhD, Ophthalmology, University of Washington

**Project Description**

Our visual system is specialized for central vision, which is served by the region of the retina known as the fovea. High-acuity vision is possible only when the visual world is kept relatively stable on the retina. Visual image stability is preserved during head movements by the compensatory action of the vestibular ocular (VOR) and optokinetic reflexes (OKR). When an object of interest moves relative to the head, the VOR needs to be adjusted to maintain tracking. This adjustment is accomplished, in part, by the smooth pursuit (SP) system. SP is a volitional behavior, which depends on processing of visual and eye movement information in cerebral cortex, brainstem and cerebellum. There are multiple pathways leaving frontal and parietal cortical areas, which contribute differentially to SP and visual-vestibular behavior. The long-term goal of our studies is to determine the specific SP-related information represented in parallel frontal- and parietal-brainstem pathways. Our proposed studies are designed to determine neural mechanisms responsible for converting visual motion information into commands for eye movements during different behaviors. Our overarching hypothesis is that the information processed in each parallel cortical-brainstem pathway supports different aspects of SP including prediction, initiation, maintenance, gain control and adaptive modification. We have made progress in localizing the rostral pole of the SC for delivery of micro-stimulation while recording in FEF. We will now be able to examine the information carried in the FEF-SC pathway. The significance of our work is that SP is compromised in different developmental or disease processes and specific deficits may be attributable to different pathways. Therefore, our studies will aid in the diagnosis and potential treatment of disorders associated with strabismus, neurodegenerative disease, brain injury and stroke.

**Project Progress:**

We have discovered that the FEF-rSC pathway carries signals related to eye motion, including eye acceleration. We used antidromic activation of FEF neurons from rSC to uncover signals in this specific pathway. We are testing the hypothesis that signals the FEF sends different information to different brainstem centers to contribute to context specific gaze behavior. Similarly, we are defining the information carried in FEF-MST circuits during different visual-oculomotor and gaze behaviors. We predict that cortical-cortical signaling would carry different information from that in cortical-brainstem pathways related to eye movement production. We have developed a novel paradigm to examine the response of FEF neurons during volitional smooth pursuit. We deliver micro stimulation in the rSC to evoke a small saccade during pursuit according to the site stimulated on the SC saccade map. The evoked saccade creates a known offset between target position and eye position during ongoing pursuit. This then allows us to determine the sensitivity of neurons to eye motion, *per se*, compared to visual motion or error position with respect to the fovea. So far using this paradigm, we have found at least two classes of FEF neurons during. One type of neuron appears to code eye motion during pursuit regardless of the position error associated with the evoked saccade. The other type of neuron shows a large decrement in neuronal response in association with the evoked saccade.

**Funding Sources**

| Funding Source | Primary Investigator | Total award amount | Funding ID |
|---|---|---|---|
| NIH | Excluded by Requester | $393,480 | 2R01EY006069-28 |

**Project Title:** Visual Processing and Smooth Eye Movements

**IACUC#:** 4221-01 **Expiration:** 6/11/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthalmology, WaNPRC

**Principal Core Scientist:** Excluded by Requester PhD, Ophthalmology, WaNPRC

Excluded by Requester PhD, WaNPRC

**Other affiliate scientists:** Excluded by Requester PhD, Ophthalmology, University of Washington

**Project Description**

Primates make extensive use of binocular, frontal vision in their daily behavior. Much of primate visual function is dedicated to central vision where retinal ganglion cell density and associated cortical magnification factor are highest. To examine an object in detail its image must be kept relatively stable on the fovea. This is accomplished by foveating (e.g., smooth pursuit and saccades) and stabilizing (e.g., optokinetic and vestibular ocular) eye movement systems. The visual and oculomotor systems of human and nonhuman primates are immature at birth and sensitive to injury. The long-term goal of this project is to determine neural mechanisms that support visual motion processing in cerebral cortex for smooth pursuit, optokinetic and ocular following eye movements of normal and strabismic macaques. Our studies seek to understand the alterations in neural circuits associated with different components of infantile strabismus syndromes. Our overarching hypothesis is that different regions of the cortical pursuit system and their targets contribute differentially to defective gaze-holding, eye misalignment, defective eye movements and impaired visual function.

**Project Progress** In previous studies we have shown that horizontal saccades are disconjugate in monkeys with strabismus. In our recent studies (Walton et al. 2014), we show similar results for vertical and oblique saccades. We expect to report similar findings for other eye movements including smooth pursuit. We recorded eye movements from both eyes simultaneously using electromagnetic methods and precise calibration to assess the conjugacy in terms of both amplitude and direction. Our study compared esotropic, exotropic and normal juvenile macaques. We created the strabismic animals using either surgical approaches or prism rearing during the first weeks of life. Prism rearing during the first 3 months of life produced a permanent strabismus, as did medial rectus muscle tenotomy during the first 2 weeks of life. We trained macaques to track visual targets moving either in stepped or smooth trajectories. We then determined the conjugacy of saccades in various directions by comparing both amplitude and direction. We found that strabismic monkeys were disconjugate (both amplitude and direction). These effects were as large for vertical and oblique saccades as for horizontal ones. However, the pattern of disconjugacy often varied as a function of saccade direction. In some cases, saccades that appeared to be conjugate in terms of amplitude differed substantially when direction was taken into account. These data indicate that the assessment of saccade disconjugacy in strabismus may yield misleading results if direction is not considered. The complex pattern of disconjugacy suggests that strabismus is associated with substantial abnormalities within the circuitry controlling saccades. We are conducting neurophysiological studies to identify the specific neural substrates for these behavioral effects.

**Funding Sources**

| Funding Source | Primary Investigator | Total award amount | Funding ID |
|---|---|---|---|
| NIH | Excluded by Requester PhD | $393,480 | 2R01EY006069-28 |

**Project Title:** In vivo directed evolution of AAV vectors for cone based diseases

**IACUC #** 4205-04 **IACUC Expiration:** 9/18/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthalmology, U. of Washington, WA
Excluded by Requester PhD, Ophthalmology, U. of Washington, WA

**Principal Core Scientist:** n/a
**Other affiliate scientists:** n/a

**Project Description/Progress**
We are in the process of making viral libraries for injection for these experiments.

**Publications associated with this project:** n/a

**Funding Sources**
Private Source Excluded by Requester PI, $52,757, Private Source

**Project Title:** Genes and photopigments of red green colorvision: exploring circuitry with fMRI

**IACUC #** 4205-04 **IACUC Expiration:** 9/18/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthalmology, U. of Washington, WA

**Other affiliate scientists:**

Excluded by PhD, Ophthalmology, U. of Washington, WA
Excluded by Requester PhD, Ophthalmology, U. of Washington, WA
Excluded by Requester PhD, Ophthalmology, U. of Washington, WA
Excluded by Requester PhD, Ophthalmology, U. of Washington, WA
Excluded by Requester PhD, Ophthalmology, U. of Washington, WA

**Project Description/Progress**

We performed functional analyses of broad thorny ganglion cells in macaque retina, broad thorny cells. The functional characteristics we observed make a direct cross-species comparison of putative homologs possible for the first time. Broad thorny ganglion cells have been proposed to be homologs of rabbit local edge detector ganglion cells but our data shows that broad thorny cells do not share all physiological key features with rabbit local edge detectors. The differences could have resulted from evolutionary adaptations that have occurred since rabbits and primates diverged or, they may indicate that the two cell types are not homologs.

We developed and validated an S-cone isolating electroretinogram protocol for Old World primates to be used in experiments to study the circuitry of S cone pathways.

The distribution of the soluble NSF-attachment protein receptor protein syntaxin-4 and the Na-K-Cl cotransporter were investigated in the outer plexiform layer of human retina using immunohistochemistry. Both proteins, which are proposed to be components of a gamma-aminobutyric acid mediated feed-forward circuit from horizontal cells directly to bipolar cells, were enriched beneath S-cones. The expression pattern of syntaxin-4 was further analyzed in baboon and marmoset to determine if the synaptic specialization is common to primates. Syntaxin-4 was enriched beneath S-cones in both species, which together with the human results indicates that this specialization may have evolved for the purpose of mediating unique color vision capacities that are exclusive to primates.

**Publications associated with this project**

Excluded by Requester Cone-isolating ON-OFF electroretinogram for studying chromatic pathways in the retina. J Opt Soc Am AOpt Image Sci Vis. 2014 Apr 1;31(4):A208-13. doi: 10.1364/JOSAA.31.00A208. PubMed PMID: 24695171; PubMed Central PMCID: PMC4143118.

Excluded by Requester Specialized synaptic pathway for chromatic signals beneath S-cone photoreceptors is common to human, Old and New World primates. J Opt Soc Am A Opt Image Sci Vis. 2014 Apr 1;31(4):A189-94. doi: 10.1364/JOSAA.31.00A189. PubMed PMID: 24695169; PubMed Central PMCID: PMC4282935.

Excluded by Requester Synaptic elements for GABAergic feed-forward signaling between HII horizontal cells and blue cone bipolar cells are enriched beneath primate S-cones. PLoS One. 2014 Feb 20;9(2):e88963. doi: 10.1371/journal.pone.0088963. eCollection 2014. PMID: 24586460; PMC3930591.

**Funding Sources**

NIH Excluded by PhD NIH R01EY09303 (no cost extension)
Private Source Excluded by Phd
Private Source Excluded by Requester
NIH, Excluded by Requester PhD, F32EY024507, $46,092

**Project Title:** Exploring plasticity in the adult visual system using viral gene delivery

**IACUC #** 4205-01 **IACUC Expiration:** 12/2/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthamology, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:**
Excluded by Requester PhD, Ophthamology, U. of Washington, WA
Excluded by Requester PhD, Ophthalmology, U. of Washington, WA

**Project Description/Progress**
We have made substantial progress towards optimizing the AAV2 vector for cone-specific expression when injected into the vitreous. We have done two sets of experiments, the first aimed at determining whether placement of the injection within the vitreous matters with regard to final distribution of transfected cells, the second aimed at optimizing our vector to get better cone-specific expression of the passenger gene. Results from the first set of experiments showed very clearly that the location of the injection within the vitreous does not alter the distribution of transfected cells. In the second set of experiments, we have successfully developed an optimized set of cone-specific regulatory elements that give high level cone types specific expression. Using an AAV2 virus with the 7m8 capsid and the gene for GFP under control of our newly optimized regulatory elements, nearly all L and M cones in the fovea were transduced, and scattered cones in the peripheral retina were also transduced. We are in the process of transitioning the color vision gene therapy experiments to Old World primates. We plan to perform an intravitreal injection in the near future with the newly optimized cone-specific regulatory elements driving expression of a cone opsin gene the has a peak sensitivity that is well separated from the endogenous macaque cones.

**Publications associated with this project:** n/a

**Funding Sources**
NIH, PI Excluded by Requester $250,000, R01EY016861
Private Source
Private Source

**Project Title:** Neural Mechanisms for smooth pursuit adaptation

**IACUC #** 4245-01 **IACUC Expiration:** 11/30/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Ophthalmology, U. of Washington

**Principal Core Scientist:** Excluded by Requester Ph.D., WaNPRC, U. of Washington

**Other affiliate scientists:**
Excluded by Requester Ph.D., Department of Ophthalmology, U. of Washington
Excluded by Requester Ph.D., College of Optometry, U. of Houston, TX

**Project Description**
Smooth pursuit systems provide an ideal behavior model to study neuronal mechanisms for plasticity in visuomotor control. Smooth pursuit eye movements are required to maintain the image of the visual world or a selected target stable on the retina. The main goals of this project are to determine the neuronal mechanisms supporting adaptive plasticity in the smooth pursuit system. Our studies are directed at structures that form important parts of the afferent limb for smooth pursuit. These structures include cortical-pontine and cortical-pretectal pathways that provide visual- and eye-motion signals to the cerebellum for smooth pursuit. It is known that neurons in the MSTl/MT are sensitive to retinal motion during smooth pursuit.

**Project Progress**
Our initial hypothesis was that foveal/parafoveal motion related neurons in MSTl/ MT show changes in response modulation following smooth pursuit adaptation. Our results indicate that some MSTl neurons show differential changes in response modulation for gain-increase or gain-decrease adaptation paradigms. Therefore, we suggested that smooth pursuit adaptation could be associated with changes in visual sensitivity of neurons in cortical areas MT/MST. There might be different visuomotor mechanisms for pursuit adaptation associated with gain-increase and decrease paradigms. Furthermore, we attempted to define how the cortical visuomotor systems are involved in the gain modulation due to pursuit adaptation. We applied a brief target perturbation (sinusoidal motion) to characterize the properties of the gain modulation of visuomotor transmission. Our results demonstrated that pursuit adaptation had a significant effect on the perturbation response that was specific to the adapted direction. Therefore, it is suggested that pursuit adaptation could affect the dynamic regulation of the visuomotor gain.

**Publications associated with this project**
In Press

**Funding Sources**
NIH, PI: Excluded by Requester PhD, $401,782, 5R01EY019266-06

**Project Title:** Neural basis of visual shape representation and recognition

**IACUC #** 4133-01 **IACUC Expiration:** 6/6/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, WaNPRC, University of Washington

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, University of Washington

**Other affiliate scientists:**

Excluded by Requester BS, Graduate Student, Dept of Biological Structure, U. of Washington, WA
Excluded by Requester PhD, Postdoctoral Fellow, Dept of Biological Structure, U. of Washington, WA
Excluded by Requester MS, Graduate Student, Applied Math, U. of Washington, WA

**Project Description**

The primate brain successfully recognizes objects even when they are partially occluded. Visual area V4 and the prefrontal cortex likely play an important role in this perceptual capacity but their relative roles are unknown. Over the last year, we have studied the responses of neurons in V4 and the ventrolateral prefrontal cortex (vlPFC) while monkeys discriminated pairs of shapes under varying degrees of occlusion. For most V4 neurons, we found that partial occlusion caused a weakening of early (40-70 ms latency) shape selective responses, but over time selectivity gradually increased and peaked around 200 ms after stimulus onset. This delayed emergence of selectivity under occlusion was also recently observed in human inferotemporal cortex (ITC). In striking contrast, neurons in vlPFC, which receive visual form information primarily from V4 and ITC, showed the opposite trend—responses increased with increasing occlusion. Across the vlPFC population, this response pattern had the effect of amplifying responses and selectivity to the most occluded stimuli; because signals in vlPFC peaked ~150 ms after stimulus onset, they are appropriately timed to serve as the feedback modulation that facilitates the gradual increase in shape selectivity in V4. We implement a V4-PFC network model, wherein vlPFC responses are derived by gain-modulating the occluded shape signals from V4 by the level of occlusion also derived from V4 responses; vlPFC responses are then fed back to V4, facilitating an increase in responses and selectivity for the most occluded stimuli.

**Project Progress**

Our experimental results and model provide the first elaboration of how PFC circuits can selectively augment impoverished shape information in feedforward signals and contribute to enhanced shape selectivity in visual cortex and to the successful discrimination of partially occluded shapes.

**Publications associated with this project**

Excluded by Requester (2014) The role of area V4 in the discrimination of partially occluded shapes. JNeurosci 34:8570-84.

In Press

**Funding Sources**

Excluded by Requester RCNS: PI: Co-PI: Excluded by Requester $230,488 FA97215/A80404
Excluded by Requester no-cost extension R01EY018839
Private Source PI: Excluded by Requester $65,000

**Project Title:** Functional Organization of Cervical Spinal Interneurons

**IACUC #** 4187-03 **IACUC Expiration:** 11/8/2015

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Physiology & Biophysics, U. of Washington, WA

**Principal Core Scientist:** Excluded by Requester PhD, WaNPRC, Physiology & Biophysics, U. of Washington, WA

**Other affiliate scientists:** Excluded by Requester BS, Physiology & Biophysics, U. of Washington, WA

**Project Description**

We investigated the use of paired associative stimulation to induce synaptic plasticity in cerebral cortical circuits. Connected sites in the sensorimotor cortex in one hemisphere were identified by stimulus-evoked potentials recorded with implanted electrodes. For example, if stimulation at site A evoked a response at site B, we concluded that site A projected synaptically to site B. We attempted to modify the strength of this synaptic connection by delivering time-locked stimulation to the two sites, with the stimulation at site A preceding the stimulation at site B. This protocol was chosen to activate the neurons at sites A and B in a causal sequence, consistent with the synaptic connection A-to-B. The inter-stimulus delay was chosen so that neurons at site B would be activated slightly after action potentials arrived at the axon terminals of neurons at site A. After 3-24 hours of stimulation, the evoked potential recorded at site B after stimulation at site A was measured to detect changes in response size. We have found that this paired stimulation protocol can induce changes in synaptic strength in cortico-cortical connections. We are now characterizing the stimulation parameters needed to induce this effect, and the nature of the cortical connections that can be modified.

**Publications associated with this project**

Excluded by Requester (2014) High-voltage compliant, capacitative-load invariant neural stimulation electronics compatible with standard bulk-CMOS integration. Biomedical Circuits and Systems Conference, IEEE, pgs. 260-263

**Funding Sources**

| | | | |
|---|---|---|---|
| NINDS | Excluded by Requester | $714,689 | R01NS12542 |
| University of Washington | | $50,000 | Bridge Award |

**Project Title:** Electrical stimulation for the vestibular nerve

**IACUC #** 4146-01 **IACUC Expiration:** 11/4/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester Ph.D., Oto-HNS, Univ. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:**

Excluded by Ph.D., Oto-HNS, Univ. of Washington, WA
Excluded by Requester Ph.D., Biostructure, Univ. of Washington, WA, USA
Excluded by Requester Ph.D., Oto-HNS, Univ. of Washington, WA
Excluded by Requester M.D., Ph.D., Oto-HNS, Univ. of Washington, WA

**Project Description**

Our group is working on a fully implantable vestibular prosthesis to treat vestibular loss in human patients. To date, we have implanted both monkeys (12) and human subjects (4) as part of a combined basic scientific and human therapeutic trial. We tested the unmodified human device in monkeys before implanting it in patients with vestibular and hearing loss, and intermittent attacks of extreme vertigo. The device works well over long durations in monkey subjects, and works comparably in human subjects over shorter period of time. The efficacy of the device in driving vestibular responses changes longitudinally in humans. These changes may be due to changes in the stimulated nerve due to the underlying pathology, or to the consequences of stimulation.

Our current studies involve longitudinal testing in intact monkeys and animals with ototoxic lesions to reduce or eliminate hair cell function. Our current device has 3 leads which are implanted in the vestibular end organ, and one lead with multiple stimulation sites to be implanted either into the otolith organs or the cochlea, depending on the application.

**Project Progress**

This past year we have been studying the underlying mechanisms of vestibular control by substituting vestibular input provided by the prosthesis for natural input, and recording from vestibular afferents and brainstem neurons that process vestibular information.

**Publications**

Excluded by Requester

Excluded by Requester Prosthetic implantation of the human vestibular system. Otol Neurotol. 2014 Jan;35(1):136-47.

Excluded by Requester Longitudinal performance of an implantable vestibular prosthesis. Hear Res. 2014 Sep 22. pii: S0378-5955(14)00148-8. doi: 10.1016/j.heares.2014.09.003. [Epub ahead of print]

In Press

**Funding Sources**

NIH, Excluded by Requester P.I., Excluded by Requester Co.I., NIDCD $382,976, R01 DC014002-01

**Project Title:** Role of Cerebellar Nuclei in Eye Movement Control and Adaptation

**IACUC #** 2340-01 **IACUC Expiration:** 12/5/2014

**Unit:** Neuroscience

**Type of Project:** Research

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Biological Structure, U. Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:**

Excluded by Requester PhD, Physiology & Biophysics, U. Washington, WA
Excluded by Requester PhD, Physiology & Biophysics, U. Washington, WA
PhD, Physiology & Biophysics, U. Washington, WA
Excluded by Requester PhD, Physiology & Biophysics, U. Washington, WA

**Project Description**

We are characterizing the distribution of perineuronal nets (PNNs) around neurons in many parts of the monkey brain. One manuscript currently in revision documents that the cerebellar nuclei contain a higher proportion of neurons (93%) surrounded by PNNs that any other region in the CNS (e.g., all regions of the cerebral cortex, <10%). In an article published in 2014 in PLOS 1 we show that dissolving PNNs in the saccade-related part of the cerebellar nuclei does not change the size, rate, or persistence of motor learning in saccades and does not alter the function of neurons in the cerebellar nuclei enough to impair saccades. Our future work will describe what PNNs do in the cerebellar nuclei.

We also finished measuring the effect of cerebellar output on abducens neurons. Output from one side of the cerebellum normally suppresses activity at the end of saccade-related bursts in the ipsilateral abducens nucleus. It also normally increases the duration and depth of the pause in the ipsilateral abducens nucleus during contralateral saccades. In summary, our data show that CFN activity controls the end of agonist abducens bursts and the amount of antagonist resistance to saccades.

Finally analysis of saccades after approximately sagittal cuts through the saccade-related part of the cerebellar cortex confirms our earlier finding that parallel fibers crossing the midline are not necessary for normal saccade deceleration. Saccade abnormalities after these cuts almost certainly result from damage to a parasagittal region of the cerebellar cortex. We found that cuts more than 1.4 mm lateral to the midline disrupt saccades very little. This indicates that neurosurgeons may be able to remove tumors from the IVth ventricle (the most common type of pediatric brain tumor) without damaging a patient's eye movements by cutting through the cerebellum slightly lateral to the midline.

**Publications associated with this project**

Excluded by Requester (2014) N-acetylgalactosamine positive perineuronal nets in the saccade-related-part of the cerebellar fastigial nucleus do not maintain saccade gain. **PLOS ONE**, 9(3): e86154. doi:10.1371/journal.pone.0086154.

Excluded by Requester (2014) Cerebellar fastigial nucleus influence on ipsilateral abducens activity during saccades. ***Journal of Neurophysiology***, 111:1553-1563.

**Project Title:** Neurophysiology of Saccade Adaptation

**IACUC #** 4208-01 **IACUC Expiration:** 1/10/2015

**Unit:** Neuroscience

**Type of Project:** Research project

**Percent P51 dollars:** 0%

**AIDS?** No

**PI:** Excluded by Requester PhD, Physiology & Biophysics, U. of Washington, WA

**Principal Core Scientist:** n/a

**Other affiliate scientists:** n/a

**Project Description/Progress**

Adaptation of saccade is necessary so that its accuracy can be maintained throughout life despite the changes caused by development, aging and trauma. The long-term objective of this grant is to study the possible role of cerebellar oculomotor vermis (OMV) in the adaptation process. We will approach this objective with 3 sets of experiments. In the first, we will inactivate the OMV pharmacologically and determine the deficit in the behavioral adaptation of saccades to an intra-saccadic target step, which causes saccades to appear inaccurate. In the second, we will examine the behavior of simple spike activity in the Purkinje cells of the oculomotor vermis to determine how it changes during this behavioral adaptation. Finally, we will activate the putative error signal pathway that drives adaptation by stimulating the superior colliculus, which is the likely source of the error-related climbing fiber activity to the OMV. Because of the similarities of simian and human saccade behavior, the results of this project should have considerable relevance in the diagnosis, treatment and rehabilitation of patients with saccade disorders.

Our significant findings: 1) OMV activity has differential effects on amplitude decrease and increase adaptation. OMV inactivation abolishes amplitude increase adaptation, whereas disinhibition both impairs amplitude decrease adaptation and facilitates amplitude increase adaptation. 2) During targeting-saccade adaptation, half of OMV P-cells exhibit changes in activity that is specific to the adapted saccades. 3) OMV P-cell SS activity does not differ for different types of saccade. 4) GABAergic inhibitory processes control the characteristics of normal ipsiversive saccades. 5) The SC provides a vector error signal that drives targeting-saccade adaptation. We are currently confirming that this error signal traverses the SC-Medial Accessory Olive-OMV pathway with microstimulation in the SC and simultaneous CS recording in the OMV.

**Publications associated with this project**

Excluded by Requester (2014) Cerebellar fastigial nucleus influence on ipsilateral abducens activity during saccades. J Neurophysiol. Apr;111(8):1553-63

**Funding Sources**

NIH, PI: Excluded by Requester $395,010 , EY019258

B.4 (Please_refer_to_individual_components_for_details.pdf)

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

Please refer to individual components for details

## 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 |
|---|---|
| Complete | Excluded by Requester<br>Excluded by Requester Choriodecidual group B streptococcal inoculation induces fetal lung injury without intra-amniotic infection and preterm labor in Macaca nemestrina. PLoS One. 2011;6(12):e28972. PubMed PMID: 22216148; PubMed Central PMCID: PMC3244436. |
| Complete | Excluded by Requester<br>Excluded by Requester Long-term programming of antigen-specific immunity from gene expression signatures in the PBMC of rhesus macaques immunized with an SIV DNA vaccine. PLoS One. 2011;6(6):e19681. PubMed PMID: 21701683; PubMed Central PMCID: PMC3119060. |
| Complete | Excluded by Requester Nonhuman primate models used to study pelvic inflammatory disease caused by Chlamydia trachomatis. Infect Dis Obstet Gynecol. 2011;2011:675360. PubMed PMID: 21869858; PubMed Central PMCID: PMC3160047. |
| Complete | Excluded by Requester An information-theoretic approach for evaluating probabilistic tuning functions of single neurons. Front Comput Neurosci. 2011;5:15. PubMed PMID: 21503137; PubMed Central PMCID: PMC3071493. |
| Complete | Excluded by Requester Next-generation sequencing reveals HIV-1-mediated suppression of T cell activation and RNA processing and regulation of noncoding RNA expression in a CD4+ T cell line. MBio. 2011;2(5)PubMed PMID: 21933919; PubMed Central PMCID: PMC3175625. |
| Complete | Excluded by Requester Perinatal asphyxia in a nonhuman primate model. Dev Neurosci. 2011;33(3-4):210-21. PubMed PMID: 21659720; PubMed Central PMCID: PMC3225245. |
| Complete | Excluded by Requester<br>Vaccination against heterologous R5 clade C SHIV: prevention of infection and correlates of protection. PLoS One. 2011;6(7):e22010. PubMed PMID: 21799765; PubMed Central PMCID: PMC3140488. |
| Complete | Excluded by Requester Genomic analysis reveals pre- and postchallenge differences in a rhesus macaque AIDS vaccine trial: insights into mechanisms of vaccine efficacy. J Virol. 2011 Jan;85(2):1099-116. PubMed PMID: 21068249; PubMed Central PMCID: PMC3020003. |
| Complete | Excluded by Requester<br>Integrative deep sequencing of the mouse lung transcriptome reveals differential expression of diverse classes of small RNAs in response to respiratory virus infection. MBio. 2011;2(6)PubMed PMID: 22086488; PubMed Central PMCID: PMC3221602. |

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| Complete | Excluded by Requester<br>Excluded by Requester Primary hepatic Mycobacterium tuberculosis complex infection with terminal dissemination in a pig-tailed macaque (Macaca nemestrina). J Am Assoc Lab Anim Sci. 2011 Mar;50(2):258-62. PubMed PMID: 21439222; PubMed Central PMCID: PMC3061429. |
| Complete | Excluded by Requester Diagnosis and treatment of degenerative joint disease in a captive male chimpanzee (Pan troglodytes). J Am Assoc Lab Anim Sci. 2011 Mar;50(2):263-6. PubMed PMID: 21439223; PubMed Central PMCID: PMC3061430. |
| Complete | Excluded by Requester Pair housing for female longtailed and rhesus macaques in the laboratory: behavior in protected contact versus full contact. J Appl Anim Welf Sci. 2012;15(2):126-43. PubMed PMID: 22458874; PubMed Central PMCID: PMC3994748. |
| Complete | Excluded by Requester N-acetylgalactosamine positive perineuronal nets in the saccade-related-part of the cerebellar fastigial nucleus do not maintain saccade gain. PLoS One. 2014;9(3):e86154. PubMed PMID: 24603437; PubMed Central PMCID: PMC3945643. |
| Complete | Excluded by Requester Closed-loop neuroscience and neuroengineering. Front Neural Circuits. 2014;8:115. PubMed PMID: 25294988; PubMed Central PMCID: PMC4171982. |
| Complete | Excluded by Requester Distinct synaptic mechanisms create parallel S-ON and S-OFF color opponent pathways in the primate retina. Vis Neurosci. 2014 Mar;31(2):139-51. PubMed PMID: 23895762; PubMed Central PMCID: PMC4309572. |
| Complete | Excluded by Requester<br>Excluded by Requester Adoptive therapy with chimeric antigen receptor-modified T cells of defined subset composition. Cancer J. 2014 Mar-Apr;20(2):141-4. PubMed PMID: 24667960; PubMed Central PMCID: PMC4149222. |
| Complete | Excluded by Requester<br>Excluded by Group B streptococcal infection of the choriodecidua induces dysfunction of the cytokeratin network in amniotic epithelium: a pathway to membrane weakening. PLoS Pathog. 2014 Mar;10(3):e1003920. PubMed PMID: 24603861; PubMed Central PMCID: PMC3946355. |
| Complete | Excluded by Requester<br>Excluded by Requester Advancing the high throughput identification of liver fibrosis protein signatures using multiplexed ion mobility spectrometry. Mol Cell Proteomics. 2014 Apr;13(4):1119-27. PubMed PMID: 24403597; PubMed Central PMCID: PMC3977189. |
| Complete | Excluded by Requester Comparison of the Richmond HRR 4th edition and Farnsworth-Munsell 100 Hue Test for quantitative assessment of tritan color deficiencies. J Opt Soc Am A Opt Image Sci Vis. 2014 Apr 1;31(4):A186-8. PubMed PMID: 24695168; PubMed Central PMCID: PMC4282932. |
| Complete | Excluded by Requester Cerebellar fastigial nucleus influence on ipsilateral abducens activity during saccades. J Neurophysiol. 2014 Apr;111(8):1553-63. PubMed PMID: 24478158; PubMed Central PMCID: PMC4035777. |
| Complete | Excluded by Requester Alopecia in three macaque |

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| | | species housed in a laboratory environment. Am J Primatol. 2014 Apr;76(4):325-34. PubMed PMID: 24243351; PubMed Central PMCID: PMC4066655. |
| | Complete | Excluded by Requester Cone-isolating ON-OFF electroretinogram for studying chromatic pathways in the retina. J Opt Soc Am A Opt Image Sci Vis. 2014 Apr 1;31(4):A208-13. PubMed PMID: 24695171; PubMed Central PMCID: PMC4143118. |
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| | Complete | Excluded by Requester<br>Excluded by Requester Human embryonic-stem-cell-derived cardiomyocytes regenerate non-human primate hearts. Nature. 2014 Jun 12;510(7504):273-7. PubMed PMID: 24776797; PubMed Central PMCID: PMC4154594. |
| | Complete | Excluded by Requester The role of visual area V4 in the discrimination of partially occluded shapes. J Neurosci. 2014 Jun 18;34(25):8570-84. PubMed PMID: 24948811; PubMed Central PMCID: PMC4061394. |
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| Complete | Excluded by Requester<br>Excluded by Requester Infection with MERS-CoV causes lethal pneumonia in the common marmoset. PLoS Pathog. 2014 Aug;10(8):e1004250. PubMed PMID: 25144235; PubMed Central PMCID: PMC4140844. |
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| Complete | Excluded by Requester<br>Influenza virus A/Anhui/1/2013 (H7N9) replicates efficiently in the upper and lower respiratory tracts of cynomolgus macaques. MBio. 2014 Aug 12;5(4)PubMed PMID: 25118237; PubMed Central PMCID: PMC4145683. |
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| PMC Journal - In process | Excluded by Requester Eschenbach DA, Gravett MG, Adams Waldorf KM. Synergy and interactions among biological pathways leading to preterm premature rupture of membranes. Reprod Sci. 2014 Oct;21(10):1215-27. PubMed PMID: 24840939. |
| Complete | Excluded by Requester<br>Excluded by Requester Assessment and improvement of Indian-origin rhesus macaque and Mauritian-origin cynomolgus macaque genome annotations using deep transcriptome sequencing data. J Med Primatol. 2014 Oct;43(5):317-28. PubMed PMID: 24810475; PubMed Central PMCID: PMC4176519. |
| Complete | Excluded by Requester Erythropoietin: emerging role of erythropoietin in neonatal neuroprotection. Pediatr Neurol. 2014 Oct;51(4):481-8. PubMed PMID: 25266611; PubMed Central PMCID: PMC4180944. |

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| | Complete | Excluded by Requester<br>Excluded by Requester Increased susceptibility to vaginal simian/human immunodeficiency virus transmission in pig-tailed macaques coinfected with Chlamydia trachomatis and Trichomonas vaginalis. J Infect Dis. 2014 Oct 15;210(8):1239-47. PubMed PMID: 24755433; PubMed Central PMCID: PMC4271071. |
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| | Complete | Excluded by Requester et al regarding article, "Embryonic stem cell-derived cardiac myocytes are not ready for human trials". Circ Res. 2014 Oct 24;115(10):e28-9. PubMed PMID: 25342771; PubMed Central PMCID: PMC4209407. |
| Excluded by Requester | mplete | Cardiac regeneration using pluripotent stem cells--progression to large animal models. Stem Cell Res. 2014 Nov;13(3 Pt B):654-65. PubMed PMID: 25087896; PubMed Central PMCID: PMC4253057. |
| | Complete | Excluded by Requester Early preservation of CXCR5+ PD-1+ helper T cells and B cell activation predict the breadth of neutralizing antibody responses in chronic HIV-1 infection. J Virol. 2014 Nov;88(22):13310-21. PubMed PMID: 25210168; PubMed Central PMCID: PMC4249103. |
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| | Complete | Excluded by Requester Expression and localization of p-glycoprotein, multidrug resistance protein 4, and breast cancer resistance protein in the female lower genital tract of human and pigtailed macaque. AIDS Res Hum Retroviruses. 2014 Nov;30(11):1106-16. PubMed PMID: 24803409; PubMed Central PMCID: PMC4212939. |
| | Complete | Excluded by Requester Abnormal activity of neurons in abducens nucleus of strabismic monkeys. Invest Ophthalmol Vis Sci. 2014 Nov 20;56(1):10-9. PubMed PMID: 25414191; PubMed Central PMCID: PMC4283474. |
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| | Complete | Excluded by Requester Modeling promising nonmyeloablative conditioning regimens in nonhuman primates. Hum Gene Ther. 2014 Dec;25(12):1013-22. PubMed PMID: 24937231; PubMed Central PMCID: PMC4270134. |
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| | Complete | Excluded by Requester<br>Excluded by Requester The |

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| | draft genome sequence of the ferret (Mustela putorius furo) facilitates study of human respiratory disease. Nat Biotechnol. 2014 Dec;32(12):1250-5. PubMed PMID: 25402615; PubMed Central PMCID: PMC4262547. |
| Complete | Excluded by Requester<br>Excluded by Requester Multiple low-dose challenges in a rhesus macaque AIDS vaccine trial result in an evolving host response that affects protective outcome. Clin Vaccine Immunol. 2014 Dec;21(12):1650-60. PubMed PMID: 25274805; PubMed Central PMCID: PMC4248781. |
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| PMC Journal - In process | Excluded by Requester<br>Excluded by Tissue-specific transcriptome sequencing analysis expands the non-human primate reference transcriptome resource (NHPRTR). Nucleic Acids Res. 2015 Jan 28;43(Database issue):D737-42. PubMed PMID: 25392405. |
| Complete | Excluded by Requester<br>Excluded by Requester Safety of Targeting ROR1 in Primates with Chimeric Antigen Receptor-Modified T Cells. Cancer Immunol Res. 2015 Feb;3(2):206-16. PubMed PMID: 25355068; PubMed Central PMCID: PMC4324006. |
| Complete | Excluded by Requester<br>Excluded by Requester Delaying BCG vaccination until 8 weeks of age results in robust BCG-specific T-cell responses in HIV-exposed infants. J Infect Dis. 2015 Feb 1;211(3):338-46. PubMed PMID: 25108027; PubMed Central PMCID: PMC4318913. |
| Complete | Excluded by Requester Isolation, characterization, and functional analysis of ferret lymphatic endothelial cells. Vet Immunol Immunopathol. 2015 Feb 15;163(3-4):134-45. PubMed PMID: 25540877; PubMed Central PMCID: PMC4323863. |
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**C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)**

The WaNPRC hosts a website that is publicly available at http://www.wanprc.org/ This site is updated on a regular basis to provide timely, relevant information to the public regarding research conducted at the WaNPRC and its application to current global health concerns. This website also serves as a means for those who are interested in learning more about research opportunities to contact the administrative offices at the Center.

**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**

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b Resource sharing**

File uploaded: WaNPRC_Overview_C5b.pdf

The resource sharing plans of the Washington National Primate Research Center are addressed in the relevant Divisional components.

## D. OVERALL PARTICIPANTS

### D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

| Commons ID | S/K | Name | SSN | DOB | Degree(s) | Role | Cal | Aca | Sum | Foreign Org | Component(s) | Country | SS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| eRA Commons User Name | Y | ANDERSON, DAVID M | SSN | DOB | BA,DVM | PD/PI | EFFORT | | | | | | NA |
| | N | Excluded by Requester | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-6089 (Bioengineer ing) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BA | Technician | | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 | | NA |

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| | | Excluded by Requester | SSN | DOB | | | EFFORT | | (Division of Primate Resour…lon y Services) | | |
| | N | | | | | Technician | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | BS | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS,DVM | Staff scientist (Doctoral level) | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BS | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS,MS, DVM | Staff scientist (Doctoral level) | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BS | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5932 (Division of Developmen tal …tive Sciences) | | NA |
| | N | | | | BA | Technician | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | | Non-Student Research Assistant | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BS | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of | | NA |

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| | | | | | | | | | | | Primate Resour…lon y Services) | | |
| | N | Excluded by Requester | SSN | DOB | | Technician | EFFORT | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5893 (Division of Primate Resources-Pathology) | | NA |
| | N | | | | | Technician | | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BA | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5893 (Division of Primate Resources-Pathology) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | DBS,PhD | Staff scientist (Doctoral level) | | | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BA | Technician | | | | | Core-5889 | | NA |

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| | | | | | | | | | | (Division of Primate Resour…lon y Services) | | |
| | N | Excluded by Requester | SSN | DOB | BA,MBA, PhD | Staff scientist (Doctoral level) | EFFORT | | | Core-6091 (Biostructure Technology Laboratory) | | NA |
| | N | | | | BA | Technician | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | | Technician | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | Core-5932 (Division of Developmen tal …tive Sciences) | | NA |
| | N | | | | | Technician | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BA,MA,P hD | Staff scientist (Doctoral level) | | | Private Source | Core-5933 (Division of Global Programs) | Excluded by Requester | NA |
| | N | | | | BS | Technician | | | | Core-5895 (Division of Primate Resour…me nt Services) | | NA |
| | N | | | | BA,MS, DVM | Staff scientist (Doctoral level) | | | | Core-5896 (Division of Primate Resour…por t Services) | | NA |
| | N | | | | BS | Technician | | | | Core-6089 (Bioengineer ing) | | NA |
| | N | | | | BS | Technician | | | | Core-5889 (Division of | | NA |

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| | | | | | | | | | | | Primate Resour…lon y Services) | | |
| | N | Excluded by Requester | SSN | DOB | BS | Technician | EFFORT | | | | Core-5895 (Division of Primate Resour…me nt Services) | | NA |
| | N | | | | BS,PhD | Staff scientist (Doctoral level) | | | | | Core-5924 (Neuroscien ce) | | NA |
| | N | | | | BA | Technician | | | | | Core-5932 (Division of Developmen tal …tive Sciences) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS,MS,P hD | Staff scientist (Doctoral level) | | | | | Core-5933 (Division of Global Programs) | | NA |
| | N | | | | BS,PhD | Staff scientist (Doctoral level) | | | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BS | Technician | | | | | Core-5895 (Division of Primate Resour…me nt Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | MS,PhD | Staff scientist (Doctoral level) | | | | | Core-5917 (AIDS/Virolo gy) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon | | NA |

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| | | | | | | | | | y Services) | | |
| | N | Excluded by Requester | SSN | DOB | | Technician | EFFORT | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5896 (Division of Primate Resour…por t Services) | | NA |
| | N | | | | BS | Technician | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5899 (Division of Primate Resour…es Laboratory) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS,MS,PhD | Staff scientist (Doctoral level) | | | Core-6089 (Bioengineering) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | Core-5932 (Division of Developmental …tive Sciences) | | NA |
| | N | | | | | Technician | | | Core-5919 | | NA |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Excluded by Requester | | | | | | | | | (NHP Systems Biology) | | |
| | N | | SSN | DOB | | Technician | EFFORT | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | PhD | Staff scientist (Doctoral level) | | | | | Core-5924 (Neuroscien ce) | | NA |
| | N | | | | MS | Technician | | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BS,MS,P hD | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5899 (Division of Primate Resour…es Laboratory) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BA | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5895 (Division of Primate Resour…me nt Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-6089 (Bioengineer ing) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate | | NA |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Resour…lon y Services) | | |
| | N | Excluded by Requester | SSN | DOB | BS | Technician | EFFORT | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5895 (Division of Primate Resour…me nt Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | DVM | Staff scientist (Doctoral level) | | | | | Core-5917 (AIDS/Virolo gy) | | NA |
| | N | | | | MS,B Vet Science | Staff scientist (Doctoral level) | | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | | Technician | | | | | Core-5917 (AIDS/Virolo gy) | | NA |
| | N | | | | BS,MS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS,BS,B A,DVM | Staff scientist (Doctoral level) | | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BA | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | | Technician | | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| eRA Commons User Name | Y | | | | PHD | Staff scientist (Doctoral level) | | | | | Core-5924 (Neuroscien ce) | | NA |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| eRA Commons User Name | N | Excluded by Requester | SSN | DOB | DVM | Staff scientist (Doctoral level) | EFFORT | | Core-5893 (Division of Primate Resources-Pathology) | | NA |
| | N | | | | BS,DVM,MPH,PhD | Staff scientist (Doctoral level) | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | DVM,PhD,AB,DVM,PhD | Staff scientist (Doctoral level) | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | PhD,BA | Staff scientist (Doctoral level) | | | Core-5924 (Neuroscience) | | NA |
| | Y | | | | BS,PhD | Staff scientist (Doctoral level) | | | Core-5924 (Neuroscience) | | NA |
| | Y | | | | BA,PhD | Staff scientist (Doctoral level) | | | Core-5924 (Neuroscience) | | NA |
| | N | | | | BS,MS,PhD | Staff scientist (Doctoral level) | | | Core-5932 (Division of Developmental …tive Sciences) | | NA |
| | N | | | | PHD,BA | Postdoctoral Scholar, Fellow, or Other Postdoctoral Position | | | Core-5919 (NHP Systems Biology) | | NA |
| | Y | | | | PhD | Staff scientist (Doctoral level) | | | Core-5917 (AIDS/Virology) | | NA |
| | Y | | | | BA,MS,PhD | Staff scientist (Doctoral level) | | | Core-5924 (Neuroscience) | | NA |
| | Y | | | | PhD,BA | Staff scientist (Doctoral level) | | | Core-5917 (AIDS/Virology) | | NA |
| | Y | | | | PhD,MA,BA | Staff scientist (Doctoral level) | | | Core-5932 (Division of Developmental …tive Sciences) | | NA |
| | Y | | | | BS,MS,DVM | Staff scientist (Doctoral | | | Admin Core-5880 (Director's | | NA |

| eRA Commons User Name | | Excluded by Requester | SSN | DOB | | level) | | | | Office) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | | | | PHD | Postdoctoral Scholar, Fellow, or Other Postdoctoral Position | EFFORT | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | PhD | Staff scientist (Doctoral level) | | | | | | NA |
| | N | | | | PhD | Staff scientist (Doctoral level) | | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | Y | | | | BA,PhD, MS | Staff scientist (Doctoral level) | | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | MS,PhD | Staff scientist (Doctoral level) | | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | PhD | Postdoctoral Scholar, Fellow, or Other Postdoctoral Position | | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | PhD | Postdoctoral Scholar, Fellow, or Other Postdoctoral Position | | | | Core-5917 (AIDS/Virology) | | NA |
| | Y | | | | PhD,BA, MA | Staff scientist (Doctoral level) | | | | Core-5933 (Division of Global Programs) | | NA |
| | N | | | | DVM,PhD | Staff scientist (Doctoral level) | | | | Core-5893 (Division of Primate Resources-Pathology) | | NA |
| | N | | | | BS,MS,PhD | Staff scientist (Doctoral level) | | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | PhD | Postdoctoral Scholar, Fellow, or Other Postdoctoral Position | | | | Core-5919 (NHP Systems Biology) | | NA |
| | Y | | | | PhD,PhD,BA | Staff scientist (Doctoral | | | | Core-5932 (Division of Developmen | | NA |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | level) | | | tal …tive Sciences) | | |
| eRA Commons User Name | N | Excluded by Requester | SSN | DOB | PhD,BA | Staff scientist (Doctoral level) | EFFORT | | Core-5895 (Division of Primate Resour…ment Services) | | NA |
| | N | | | | MS,MS, PhD,MS, BS | Staff scientist (Doctoral level) | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | | Scientist-non PhD | | | Core-5896 (Division of Primate Resour…port Services) | | NA |
| | N | | | | BS | Scientist-non PhD | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | MS | Scientist-non PhD | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BA | Scientist-non PhD | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | BA | Scientist-non PhD | | | Core-5895 (Division of Primate Resour…ment Services) | | NA |
| | N | | | | BA | Scientist-non PhD | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BA | Administrative | | | Admin Core-5882 (Center Programs) | | NA |
| | N | | | | BA,BS | Scientist-non PhD | | | Core-5898 (Division of Primate Resour…e and Surgery) | | NA |
| | N | | | | BA | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BA | Information Technology | | | Admin Core-5887 (Information Technology) | | NA |
| | N | | | | BA,MA | Administrative | | | Admin Core-5881 | | NA |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | (Finance and Administration) | | |
| | N | Excluded by Requester | SSN | DOB | | Administrative | EFFORT | | | | Core-5889 (Division of Primate Resour…lony Services) | | NA |
| | N | | | | | Scientist-non PhD | | | | | Core-5896 (Division of Primate Resour…port Services) | | NA |
| | N | | | | BS | Scientist-non PhD | | | | | Core-5932 (Division of Developmental …tive Sciences) | | NA |
| | N | | | | | Scientist-non PhD | | | | | Core-5896 (Division of Primate Resour…port Services) | | NA |
| | N | | | | BA | Administrative | | | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BA,MS | Scientist-non PhD | | | | | Core-5924 (Neuroscience) | | NA |
| | N | | | | BA | Scientist-non PhD | | | | | Core-5924 (Neuroscience) | | NA |
| | N | | | | MS | Scientist-non PhD | | | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | BA,MS | Scientist-non PhD | | | | | Core-5896 (Division of Primate Resour…port Services) | | NA |
| | N | | | | BA | Facilities and Maintenance | | | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | | Administrative | | | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | | Administrative | | | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | | Administrati | | | | | Core-5889 | | NA |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Excluded by Requester | | | | ve | | | | (Division of Primate Resour…lon y Services) | | |
| | N | | SSN | DOB | BA | Administrati ve | EFFORT | | | Admin Core-5881 (Finance and Administratio n) | | NA |
| | N | | | | | Administrati ve | | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BA | Administrati ve | | | | Admin Core-5881 (Finance and Administratio n) | | NA |
| | N | | | | BA | Administrati ve | | | | Core-5889 (Division of Primate Resour…lon y Services) | | NA |
| | N | | | | BS | Scientist-non PhD | | | | Core-5899 (Division of Primate Resour…es Laboratory) | | NA |
| | N | | | | BS | Information Technology | | | | Admin Core-5887 (Information Technology) | | NA |
| | N | | | | BA, PhD | Administrati ve | | | | Admin Core-5881 (Finance and Administratio n) | | NA |
| | N | | | | BS | Scientist-non PhD | | | | Core-5924 (Neuroscien ce) | | NA |
| | N | | | | BA,BS | Scientist-non PhD | | | | Core-6091 (Biostructure Technology Laboratory) | | NA |
| | N | | | | | Scientist-non PhD | | | | Core-5933 (Division of Global Programs) | | NA |
| | N | | | | BS | Administrati ve | | | | Admin Core-5882 (Center Programs) | | NA |
| | N | | | | | Administrati ve | | | | Admin Core-5881 (Finance and Administratio n) | | NA |
| | N | | | | BA | Scientist- | | | | Core-5889 | | NA |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Excluded by Requester | | | | non PhD | | | | (Division of Primate Resour…Ion y Services) | | |
| | N | | SSN | DOB | BS,MS, MS | Scientist-non PhD | EFFORT | | | Core-5917 (AIDS/Virolo gy) | | NA |
| | N | | | | BS | Scientist-non PhD | | | | Core-5917 (AIDS/Virolo gy) | | NA |
| | N | | | | | Facilities/M aintenance | | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | BA | Administrati ve | | | | Core-5889 (Division of Primate Resour…Ion y Services) | | NA |
| | N | | | | | Facilities/M aintenance | | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | BA,BS | Scientist-non PhD | | | | Core-5924 (Neuroscien ce) | | NA |
| | N | | | | BS | Scientist-non PhD | | | | Core-5894 (Division of Primate Resour…Ion y Services) | | NA |
| | N | | | | | Administrati ve | | | | Core-5896 (Division of Primate Resour…por t Services) | | NA |
| | N | | | | | Program Manager | | | | Core-5889 (Division of Primate Resour…Ion y Services) | | NA |
| | N | | | | MS | Scientist-non PhD | | | | Core-5924 (Neuroscien ce) | | NA |
| | N | | | | | Information Technology | | | | Admin Core-5887 (Information Technology) | | NA |
| | N | | | | BA | Facilities/M aintenance | | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | | Scientist-non PhD | | | | Core-5924 (Neuroscien ce) | | NA |
| | N | | | | | Facilities/M aintenance | | | | Admin Core-5886 (Facilities) | | NA |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Excluded by Requester | SSN | DOB | | Information Technology | EFFORT | | Admin Core-5887 (Information Technology) | | NA |
| | N | | | | | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BA | Administrative | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | BA | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BS | Scientist-non PhD | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | BS,MS | Scientist-non PhD | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | | Scientist-non PhD | | | Core-5896 (Division of Primate Resour…port Services) | | NA |
| | N | | | | BS | Scientist-non PhD | | | Core-5917 (AIDS/Virology) | | NA |
| | N | | | | BS,MS | Scientist-non PhD | | | Core-5899 (Division of Primate Resour…es Laboratory) | | NA |
| | N | | | | BS | Scientist-non PhD | | | Core-5889 (Division of Primate Resour…lony Services) | | NA |
| | N | | | | BS | Scientist-non PhD | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | | Administrative | | | Admin Core-5882 (Center Programs) | | NA |
| eRA Commons User Name | N | | | | BS | Scientist-non PhD | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BS,MS,PhD | Administrative | | | Admin Core-5882 (Center Programs) | | NA |

| eRA Commons User Name | | Excluded by Requester | SSN | DOB | | | EFFORT | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Y | | | | BA,BA | Asst Director, CPro | | | Admin Core-5882 (Center Programs) | | NA |
| | N | | | | BS | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | Y | | | | BA | Asst Director, Facilities and Planning | | | Admin Core-5886 (Facilities) | | NA |
| | N | | | | BA,MBA | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | | Administrative | | | Admin Core-5882 (Center Programs) | | NA |
| | N | | | | BA | Scientist-non PhD | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BA | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BA | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BA,MA | Assoc Director, Finance | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BS | Administrative | | | Admin Core-5882 (Center Programs) | | NA |
| | Y | | | | PhD,BA, MA | Director | | | Admin Core-5880 (Director's Office) | | NA |
| | N | | | | BA | Scientist-non PhD | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BA | Administrative | | | Admin Core-5881 (Finance and Administration) | | NA |
| | N | | | | BA,MA | Administrati | | | Admin Core- | | NA |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Excluded by Requester | | | | ve | | | | 5882 (Center Programs) | | |
| eRA Commons User Name | N | | SSN | DOB | BS | Scientist-non PhD | EFFORT | | | Core-5919 (NHP Systems Biology) | | NA |
| | N | | | | BA | Information Technology | | | | Admin Core-5887 (Information Technology) | | 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

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**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?**

NA

Excluded by Requester

## RPPR OTHER SUPPORT

ACTIVE

**R01 EY 006069** Excluded by Requester 01/01/14 – 12/31/17 EFFORT calendar
NIH/NEI $225,000
Visual Processing and Smooth Eye Movements

Human infantile strabismus syndrome is a common problem affecting at least 3% of children born in the United States. The abnormal gaze-holding, eye misalignment and asymmetric eye movements of infantile strabismus impairs vision. We have developed effective animal models (Macaca mulatta) for studying development of visual and oculomotor behavior and the underlying neural mechanisms associated with strabismus. Our research is important for improving understanding of clinically important disorders affecting children and developing new treatment options.

**R01 EY 013308** Excluded by Requester 2/1/2014 – 1/31/2017 EFFORT calendar
NIH/NEI $182,250
Neural Control of Visual-Vestibular Behavior

The purpose of this project is to consider the sources of motion information (eye, retinal error and head) essential for normal visual-vestibular and gaze behavior. Our long-range goal is to determine the information conveyed in FEF-rNRTP and MST-DLPN pathways that support visual-vestibular behavior. The basilar pontine nuclei provide FEF and MST cortex with access to different regions of the cerebellum essential for visually guided motor learning in the VOR and compensation following injury to the labyrinth.

**R01 EY 015313** Excluded by Requester 8/1/2014 - 7/31/2015 EFFORT calendar
NIH/NEI $145,021 (subcontract)
Novel Immunotoxin and IGF therapy for Strabismus

The goal of this project is to develop and evaluate novel agents, including growth factors and immunotoxins that could lead to improved treatment options for strabismus. These agents are delivered to extraocular muscle using pellets, which deliver a calibrated daily dose in a sustained release manner to improve overall muscle efficacy.

**R24 EY023937-01** Excluded by Requester 09/01/2014 – 08/31/2015 EFFORT calendar
NIH/NEI $1,108,654 (DC)
Photoswitchable channel blockers for treatment of blindness

The main goals of this study are to determine the relative efficacy of DENAQ and PhENAQ in vision restoration in multiple animal models, determine the effect of DENAQ and PhENAQ on primate ganglion cell activity, and to establish the safety profile of ocular administration of DENAQ and PhENAQ in multiple animal models.

Project Number **U42OD011123** Dates of Approved Project Person Months
(PI) Excluded by Requester 9/3/14 – 5/31/15 EFFORT (Cal)
Source NIH/ORIP Annual Direct Costs $1,786,487
Title of Project **WaNPRC Macaca nemestrina SPF Breeding Colony**

The major goals of this project are to increase animal resources available to meet the ongoing needs of AIDS-related research efforts for vaccine development, therapeutic agent discovery and pathogenesis. The Macaca nemestrina (Mn) is used extensively in primate AIDS studies, and is the primary species in use at the WaNPRC. Thus, the WaNPRC continues to expand the size of its existing SPF Mn breeding colony to provide a significant increase in the long-term availability of appropriate nonhuman primates for AIDS research. Excluded by Requester is the Principal Investigator.

PENDING: None

OVERLAP: None

## 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?**

NOTHING TO REPORT

**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

NOTHING TO REPORT

### 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:** Washington National Primate Research Center | 605799469 | WA-007 | 1705 NE Pacific St.<br>Box 357330<br>Seattle WA 981957330 |
| University of Washington | 605799469 | WA-007 | Office of Sponsored Programs<br>4333 Brooklyn Ave NE; Box 359472<br>Seattle WA 981959472 |
| WaNPRC Arizona Breeding Colony | 605799469 | AZ-006 | PO Box 20836<br>Mesa AZ 852770836 |
| Shin Nippon Biomedical | 187770821 | TX-015 | 2103 Fm 625 |

| | | | |
|---|---|---|---|
| Laboratory-Scientific Research Center | | | Alice TX 783327471 |
| New Iberia Research Center | 799451273 | LA-003 | PO Box 13610<br>New Iberia LA 705623610 |

**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) |
|---|---|
| 3900000 | Animal use fees, per diem, procedures |

**G.12 F&A COSTS**

Not Applicable

Composite Application Budget Summary

| Categories | Budget Period |
|---|---|
| Salary, Wages and Fringe Benefits | 6,381,105 |
| Equipment | 10,000 |
| Travel | 141,298 |
| Participant/Trainee Support Costs | 0 |
| Other Direct Costs (excluding Consortium) | 2,437,583 |
| Consortium Costs | 130,042 |
| Direct Costs | 9,100,028 |
| Indirect Costs | 3,695,476 |
| Total Direct and Indirect Costs | 12,795,504 |

Component Budget Summary

| Components | Categories | Budget Period |
|---|---|---|
| 5882-001 (Admin Core) | Salary, Wages and Fringe Benefits | 182,090 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 30,259 |
| | Consortium Costs | 0 |
| | Direct Costs | 212,349 |
| | Indirect Costs | 89,187 |
| TOTALS | Total Direct and Indirect Costs | 301,536 |
| 5881-002 (Admin Core) | Salary, Wages and Fringe Benefits | 264,046 |
| | Equipment | 0 |
| | Travel | 11,000 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 66,696 |
| | Consortium Costs | 0 |
| | Direct Costs | 341,742 |
| | Indirect Costs | 143,532 |
| TOTALS | Total Direct and Indirect Costs | 485,274 |
| 5880-003 (Admin Core) | Salary, Wages and Fringe Benefits | 67,732 |
| | Equipment | 0 |
| | Travel | 25,000 |

| | | |
|---|---|---|
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 19,940 |
| | Consortium Costs | 0 |
| | Direct Costs | 112,672 |
| | Indirect Costs | 47,322 |
| TOTALS | Total Direct and Indirect Costs | 159,994 |
| 5886-004 (Admin Core) | Salary, Wages and Fringe Benefits | 35,144 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 0 |
| | Consortium Costs | 0 |
| | Direct Costs | 35,144 |
| | Indirect Costs | 14,760 |
| TOTALS | Total Direct and Indirect Costs | 49,904 |
| 5887-005 (Admin Core) | Salary, Wages and Fringe Benefits | 159,588 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 47,949 |
| | Consortium Costs | 0 |
| | Direct Costs | 207,537 |
| | Indirect Costs | 87,166 |
| TOTALS | Total Direct and Indirect Costs | 294,703 |

| | | |
|---|---|---|
| 6091-001 (Core) | Salary, Wages and Fringe Benefits | 93,714 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 900 |
| | Consortium Costs | 0 |
| | Direct Costs | 94,614 |
| | Indirect Costs | 39,738 |
| TOTALS | Total Direct and Indirect Costs | 134,352 |
| 6093-002 (Core) | Salary, Wages and Fringe Benefits | 152,386 |
| | Equipment | 0 |
| | Travel | 14,162 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 1,856 |
| | Consortium Costs | 0 |
| | Direct Costs | 168,404 |
| | Indirect Costs | 70,730 |
| TOTALS | Total Direct and Indirect Costs | 239,134 |
| 5933-003 (Core) | Salary, Wages and Fringe Benefits | 211,506 |
| | Equipment | 0 |
| | Travel | 27,050 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 9,646 |
| | Consortium Costs | 0 |

| | | |
|---|---|---|
| | Direct Costs | 248,202 |
| | Indirect Costs | 104,245 |
| **TOTALS** | Total Direct and Indirect Costs | 352,447 |
| 5932-004 (Core) | Salary, Wages and Fringe Benefits | 136,354 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 4,545 |
| | Consortium Costs | 0 |
| | Direct Costs | 140,899 |
| | Indirect Costs | 59,178 |
| **TOTALS** | Total Direct and Indirect Costs | 200,077 |
| 6089-005 (Core) | Salary, Wages and Fringe Benefits | 211,367 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 0 |
| | Consortium Costs | 0 |
| | Direct Costs | 211,367 |
| | Indirect Costs | 88,774 |
| **TOTALS** | Total Direct and Indirect Costs | 300,141 |
| 5898-006 (Core) | Salary, Wages and Fringe Benefits | 968,637 |
| | Equipment | 0 |
| | Travel | 6,000 |

| | | |
|---|---|---|
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 17,538 |
| | Consortium Costs | 0 |
| | Direct Costs | 992,175 |
| | Indirect Costs | 416,714 |
| **TOTALS** | Total Direct and Indirect Costs | 1,408,889 |
| 5900-007 (Core) | Salary, Wages and Fringe Benefits | 0 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 0 |
| | Consortium Costs | 130,042 |
| | Direct Costs | 130,042 |
| | Indirect Costs | 0 |
| **TOTALS** | Total Direct and Indirect Costs | 130,042 |
| 5899-008 (Core) | Salary, Wages and Fringe Benefits | 211,855 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 24,739 |
| | Consortium Costs | 0 |
| | Direct Costs | 236,594 |
| | Indirect Costs | 99,369 |
| **TOTALS** | Total Direct and Indirect Costs | 335,963 |

| | | |
|---|---|---|
| 5894-009 (Core) | Salary, Wages and Fringe Benefits | 191,838 |
| | Equipment | 0 |
| | Travel | 2,357 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 0 |
| | Consortium Costs | 0 |
| | Direct Costs | 194,195 |
| | Indirect Costs | 81,562 |
| TOTALS | Total Direct and Indirect Costs | 275,757 |
| 5895-010 (Core) | Salary, Wages and Fringe Benefits | 489,246 |
| | Equipment | 0 |
| | Travel | 6,000 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 16,447 |
| | Consortium Costs | 0 |
| | Direct Costs | 511,693 |
| | Indirect Costs | 214,911 |
| TOTALS | Total Direct and Indirect Costs | 726,604 |
| 5896-011 (Core) | Salary, Wages and Fringe Benefits | 152,410 |
| | Equipment | 0 |
| | Travel | 2,115 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 0 |
| | Consortium Costs | 0 |

| | | |
|---|---|---|
| | Direct Costs | 154,525 |
| | Indirect Costs | 64,901 |
| **TOTALS** | Total Direct and Indirect Costs | 219,426 |
| 5924-012 (Core) | Salary, Wages and Fringe Benefits | 353,486 |
| | Equipment | 0 |
| | Travel | 25,000 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 173,800 |
| | Consortium Costs | 0 |
| | Direct Costs | 552,286 |
| | Indirect Costs | 231,960 |
| **TOTALS** | Total Direct and Indirect Costs | 784,246 |
| 5919-013 (Core) | Salary, Wages and Fringe Benefits | 214,692 |
| | Equipment | 0 |
| | Travel | 6,000 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 13,108 |
| | Consortium Costs | 0 |
| | Direct Costs | 233,800 |
| | Indirect Costs | 98,196 |
| **TOTALS** | Total Direct and Indirect Costs | 331,996 |
| 5893-014 (Core) | Salary, Wages and Fringe Benefits | 307,153 |
| | Equipment | 0 |
| | Travel | 3,000 |

| | | |
|---|---|---|
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 31,239 |
| | Consortium Costs | 0 |
| | Direct Costs | 341,392 |
| | Indirect Costs | 143,385 |
| TOTALS | Total Direct and Indirect Costs | 484,777 |
| 5917-015 (Core) | Salary, Wages and Fringe Benefits | 245,850 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 167,106 |
| | Consortium Costs | 0 |
| | Direct Costs | 412,956 |
| | Indirect Costs | 173,442 |
| TOTALS | Total Direct and Indirect Costs | 586,398 |
| 7463-016 (Core) | Salary, Wages and Fringe Benefits | 126,516 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 4,537 |
| | Consortium Costs | 0 |
| | Direct Costs | 131,053 |
| | Indirect Costs | 55,042 |
| TOTALS | Total Direct and Indirect Costs | 186,095 |

| | | |
|---|---|---|
| 7462-017 (Core) | Salary, Wages and Fringe Benefits | 197,490 |
| | Equipment | 10,000 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 61,857 |
| | Consortium Costs | 0 |
| | Direct Costs | 269,347 |
| | Indirect Costs | 108,926 |
| TOTALS | Total Direct and Indirect Costs | 378,273 |
| 5889-018 (Core) | Salary, Wages and Fringe Benefits | 1,408,005 |
| | Equipment | 0 |
| | Travel | 6,000 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 1,019,903 |
| | Consortium Costs | 0 |
| | Direct Costs | 2,433,908 |
| | Indirect Costs | 1,022,241 |
| TOTALS | Total Direct and Indirect Costs | 3,456,149 |
| 5888-001 (Other) | Salary, Wages and Fringe Benefits | 0 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 499,168 |
| | Consortium Costs | 0 |

| | | |
|---|---|---|
| | Direct Costs | 499,168 |
| | Indirect Costs | 141,930 |
| **TOTALS** | Total Direct and Indirect Costs | 641,098 |
| 7353-002 (Other) | Salary, Wages and Fringe Benefits | 0 |
| | Equipment | 0 |
| | Travel | 7,614 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 1,350 |
| | Consortium Costs | 0 |
| | Direct Costs | 8,964 |
| | Indirect Costs | 3,765 |
| **TOTALS** | Total Direct and Indirect Costs | 12,729 |
| 5940-001 (Project) | Salary, Wages and Fringe Benefits | 0 |
| | Equipment | 0 |
| | Travel | 0 |
| | Participant/Trainee Support Costs | 0 |
| | Other Direct Costs (excluding Consortium) | 225,000 |
| | Consortium Costs | 0 |
| | Direct Costs | 225,000 |
| | Indirect Costs | 94,500 |
| **TOTALS** | Total Direct and Indirect Costs | 319,500 |
| **TOTALS** | | **12,795,504** |

Categories Budget Summary

| Categories | Components | Budget Period |
|---|---|---|
| R&R Budget - Senior/Key Person Funds Requested | 5882-001 (Admin Core) | 19,482 |
| | 5881-002 (Admin Core) | 44,673 |
| | 5880-003 (Admin Core) | 60,579 |
| | 5886-004 (Admin Core) | 35,144 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 20,060 |
| | 6093-002 (Core) | 152,386 |
| | 5933-003 (Core) | 118,580 |
| | 5932-004 (Core) | 26,993 |
| | 6089-005 (Core) | 99,757 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 23,444 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 232,359 |
| | 5919-013 (Core) | 16,050 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 165,537 |
| | 7463-016 (Core) | 9,880 |

| | | |
|---|---|---|
| | 7462-017 (Core) | 9,880 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 1,034,804 |
| R&R Budget - Other Personnel Funds Requested | 5882-001 (Admin Core) | 162,608 |
| | 5881-002 (Admin Core) | 219,373 |
| | 5880-003 (Admin Core) | 7,153 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 159,588 |
| | 6091-001 (Core) | 73,654 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 92,926 |
| | 5932-004 (Core) | 109,361 |
| | 6089-005 (Core) | 111,610 |
| | 5898-006 (Core) | 968,637 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 211,855 |
| | 5894-009 (Core) | 168,394 |
| | 5895-010 (Core) | 489,246 |
| | 5896-011 (Core) | 152,410 |
| | 5924-012 (Core) | 121,127 |
| | 5919-013 (Core) | 198,642 |

| | | |
|---|---|---|
| | 5893-014 (Core) | 307,153 |
| | 5917-015 (Core) | 80,313 |
| | 7463-016 (Core) | 116,636 |
| | 7462-017 (Core) | 187,610 |
| | 5889-018 (Core) | 1,408,005 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 5,346,301 |
| R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B) | 5882-001 (Admin Core) | 182,090 |
| | 5881-002 (Admin Core) | 264,046 |
| | 5880-003 (Admin Core) | 67,732 |
| | 5886-004 (Admin Core) | 35,144 |
| | 5887-005 (Admin Core) | 159,588 |
| | 6091-001 (Core) | 93,714 |
| | 6093-002 (Core) | 152,386 |
| | 5933-003 (Core) | 211,506 |
| | 5932-004 (Core) | 136,354 |
| | 6089-005 (Core) | 211,367 |
| | 5898-006 (Core) | 968,637 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 211,855 |
| | 5894-009 (Core) | 191,838 |

| | | |
|---|---|---|
| | 5895-010 (Core) | 489,246 |
| | 5896-011 (Core) | 152,410 |
| | 5924-012 (Core) | 353,486 |
| | 5919-013 (Core) | 214,692 |
| | 5893-014 (Core) | 307,153 |
| | 5917-015 (Core) | 245,850 |
| | 7463-016 (Core) | 126,516 |
| | 7462-017 (Core) | 197,490 |
| | 5889-018 (Core) | 1,408,005 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 6,381,105 |
| R&R Budget - Section C. Total Equipment | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |

| | | |
|---|---|---|
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 10,000 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 10,000 |
| R&R Budget - Domestic Travel | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 7,000 |
| | 5880-003 (Admin Core) | 21,000 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 14,162 |
| | 5933-003 (Core) | 1,500 |

| | | |
|---|---|---|
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 6,000 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 2,357 |
| | 5895-010 (Core) | 6,000 |
| | 5896-011 (Core) | 2,115 |
| | 5924-012 (Core) | 20,000 |
| | 5919-013 (Core) | 3,000 |
| | 5893-014 (Core) | 3,000 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 6,000 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 7,614 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 99,748 |
| R&R Budget - Foreign Travel | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 4,000 |
| | 5880-003 (Admin Core) | 4,000 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |

| | | |
|---|---|---|
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 25,550 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 5,000 |
| | 5919-013 (Core) | 3,000 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 41,550 |
| R&R Budget - Section D. Total Travel | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 11,000 |

| | | |
|---|---|---|
| | 5880-003 (Admin Core) | 25,000 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 14,162 |
| | 5933-003 (Core) | 27,050 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 6,000 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 2,357 |
| | 5895-010 (Core) | 6,000 |
| | 5896-011 (Core) | 2,115 |
| | 5924-012 (Core) | 25,000 |
| | 5919-013 (Core) | 6,000 |
| | 5893-014 (Core) | 3,000 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 6,000 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 7,614 |
| | 5940-001 (Project) | 0 |

| TOTALS | | 141,298 |
|---|---|---|
| R&R Budget - Tuition/Fees/Health Insurance | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |

| | | |
|---|---|---|
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Stipends | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |

| | | |
|---|---|---|
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Trainee Travel | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |

| | | |
|---|---|---|
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Subsistence | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |

| | | |
|---|---|---|
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Other Participants/Trainee Support Costs | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |

| | | |
|---|---|---|
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Section E. Total Participants/Trainee Support Costs | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |

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|---|---|---|
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Materials and Supplies | 5882-001 (Admin Core) | 30,259 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 2,213 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |

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|---|---|---|
| | 6091-001 (Core) | 900 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 6,500 |
| | 5932-004 (Core) | 4,545 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 82,396 |
| | 5919-013 (Core) | 10,883 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 121,634 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 39,801 |
| | 5889-018 (Core) | 723,305 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 1,350 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 1,023,786 |
| R&R Budget - Publication Costs | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |

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|---|---|---|
| | 5880-003 (Admin Core) | 1,787 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 1,000 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 797 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |

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|---|---|---|
| TOTALS | | 3,584 |
| R&R Budget - Consultant Services | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 8,000 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |

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|---|---|---|
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 8,000 |
| R&R Budget - ADP/Computer Services | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |

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|---|---|---|
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Subawards/Consortium/Contractual Costs | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 130,042 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |

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|---|---|---|
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 130,042 |
| R&R Budget - Equipment or Facility Rental User Fees | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |

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|---|---|---|
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Alterations and Renovations | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 0 |
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 0 |

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|---|---|---|
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 0 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 0 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 0 |
| TOTALS | | 0 |
| R&R Budget - Other Direct Cost 1 | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 33,816 |
| | 5880-003 (Admin Core) | 6,000 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 35,000 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 1,856 |
| | 5933-003 (Core) | 1,256 |

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|---|---|---|
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 8,000 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 8,500 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 14,150 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 58,404 |
| | 5919-013 (Core) | 2,225 |
| | 5893-014 (Core) | 21,913 |
| | 5917-015 (Core) | 45,472 |
| | 7463-016 (Core) | 4,537 |
| | 7462-017 (Core) | 19,556 |
| | 5889-018 (Core) | 296,598 |
| | 5888-001 (Other) | 157,203 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 75,000 |
| TOTALS | | 789,486 |
| R&R Budget - Other Direct Cost 2 | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 25,000 |
| | 5880-003 (Admin Core) | 9,940 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 12,949 |

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|---|---|---|
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 1,890 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 7,538 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 5,600 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 1,500 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 25,000 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 9,326 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 2,500 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 161,240 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 75,000 |
| TOTALS | | 337,483 |
| R&R Budget - Other Direct Cost 3 | 5882-001 (Admin Core) | 0 |
| | 5881-002 (Admin Core) | 7,880 |

| | | |
|---|---|---|
| | 5880-003 (Admin Core) | 0 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 0 |
| | 6091-001 (Core) | 0 |
| | 6093-002 (Core) | 0 |
| | 5933-003 (Core) | 0 |
| | 5932-004 (Core) | 0 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 1,000 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 10,639 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 0 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 0 |
| | 5919-013 (Core) | 0 |
| | 5893-014 (Core) | 0 |
| | 5917-015 (Core) | 0 |
| | 7463-016 (Core) | 0 |
| | 7462-017 (Core) | 0 |
| | 5889-018 (Core) | 0 |
| | 5888-001 (Other) | 180,725 |
| | 7353-002 (Other) | 0 |
| | 5940-001 (Project) | 75,000 |

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|---|---|---|
| TOTALS | | 275,244 |
| R&R Budget - Section F. Total Other Direct Cost | 5882-001 (Admin Core) | 30,259 |
| | 5881-002 (Admin Core) | 66,696 |
| | 5880-003 (Admin Core) | 19,940 |
| | 5886-004 (Admin Core) | 0 |
| | 5887-005 (Admin Core) | 47,949 |
| | 6091-001 (Core) | 900 |
| | 6093-002 (Core) | 1,856 |
| | 5933-003 (Core) | 9,646 |
| | 5932-004 (Core) | 4,545 |
| | 6089-005 (Core) | 0 |
| | 5898-006 (Core) | 17,538 |
| | 5900-007 (Core) | 130,042 |
| | 5899-008 (Core) | 24,739 |
| | 5894-009 (Core) | 0 |
| | 5895-010 (Core) | 16,447 |
| | 5896-011 (Core) | 0 |
| | 5924-012 (Core) | 173,800 |
| | 5919-013 (Core) | 13,108 |
| | 5893-014 (Core) | 31,239 |
| | 5917-015 (Core) | 167,106 |
| | 7463-016 (Core) | 4,537 |
| | 7462-017 (Core) | 61,857 |
| | 5889-018 (Core) | 1,019,903 |

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|---|---|---|
| | 5888-001 (Other) | 499,168 |
| | 7353-002 (Other) | 1,350 |
| | 5940-001 (Project) | 225,000 |
| TOTALS | | 2,567,625 |
| R&R Budget - Section G. Total Direct Cost (A thru F) | 5882-001 (Admin Core) | 212,349 |
| | 5881-002 (Admin Core) | 341,742 |
| | 5880-003 (Admin Core) | 112,672 |
| | 5886-004 (Admin Core) | 35,144 |
| | 5887-005 (Admin Core) | 207,537 |
| | 6091-001 (Core) | 94,614 |
| | 6093-002 (Core) | 168,404 |
| | 5933-003 (Core) | 248,202 |
| | 5932-004 (Core) | 140,899 |
| | 6089-005 (Core) | 211,367 |
| | 5898-006 (Core) | 992,175 |
| | 5900-007 (Core) | 130,042 |
| | 5899-008 (Core) | 236,594 |
| | 5894-009 (Core) | 194,195 |
| | 5895-010 (Core) | 511,693 |
| | 5896-011 (Core) | 154,525 |
| | 5924-012 (Core) | 552,286 |
| | 5919-013 (Core) | 233,800 |
| | 5893-014 (Core) | 341,392 |
| | 5917-015 (Core) | 412,956 |

| | | |
|---|---|---|
| | 7463-016 (Core) | 131,053 |
| | 7462-017 (Core) | 269,347 |
| | 5889-018 (Core) | 2,433,908 |
| | 5888-001 (Other) | 499,168 |
| | 7353-002 (Other) | 8,964 |
| | 5940-001 (Project) | 225,000 |
| TOTALS | | 9,100,028 |
| R&R Budget - Section H. Indirect Costs | 5882-001 (Admin Core) | 89,187 |
| | 5881-002 (Admin Core) | 143,532 |
| | 5880-003 (Admin Core) | 47,322 |
| | 5886-004 (Admin Core) | 14,760 |
| | 5887-005 (Admin Core) | 87,166 |
| | 6091-001 (Core) | 39,738 |
| | 6093-002 (Core) | 70,730 |
| | 5933-003 (Core) | 104,245 |
| | 5932-004 (Core) | 59,178 |
| | 6089-005 (Core) | 88,774 |
| | 5898-006 (Core) | 416,714 |
| | 5900-007 (Core) | 0 |
| | 5899-008 (Core) | 99,369 |
| | 5894-009 (Core) | 81,562 |
| | 5895-010 (Core) | 214,911 |
| | 5896-011 (Core) | 64,901 |
| | 5924-012 (Core) | 231,960 |

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|---|---|---|
| | 5919-013 (Core) | 98,196 |
| | 5893-014 (Core) | 143,385 |
| | 5917-015 (Core) | 173,442 |
| | 7463-016 (Core) | 55,042 |
| | 7462-017 (Core) | 108,926 |
| | 5889-018 (Core) | 1,022,241 |
| | 5888-001 (Other) | 141,930 |
| | 7353-002 (Other) | 3,765 |
| | 5940-001 (Project) | 94,500 |
| TOTALS | | 3,695,476 |
| R&R Budget - Section I. Total Direct and Indirect Costs (G +H) | 5882-001 (Admin Core) | 301,536 |
| | 5881-002 (Admin Core) | 485,274 |
| | 5880-003 (Admin Core) | 159,994 |
| | 5886-004 (Admin Core) | 49,904 |
| | 5887-005 (Admin Core) | 294,703 |
| | 6091-001 (Core) | 134,352 |
| | 6093-002 (Core) | 239,134 |
| | 5933-003 (Core) | 352,447 |
| | 5932-004 (Core) | 200,077 |
| | 6089-005 (Core) | 300,141 |
| | 5898-006 (Core) | 1,408,889 |
| | 5900-007 (Core) | 130,042 |
| | 5899-008 (Core) | 335,963 |
| | 5894-009 (Core) | 275,757 |

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|---|---|---|
| | 5895-010 (Core) | 726,604 |
| | 5896-011 (Core) | 219,426 |
| | 5924-012 (Core) | 784,246 |
| | 5919-013 (Core) | 331,996 |
| | 5893-014 (Core) | 484,777 |
| | 5917-015 (Core) | 586,398 |
| | 7463-016 (Core) | 186,095 |
| | 7462-017 (Core) | 378,273 |
| | 5889-018 (Core) | 3,456,149 |
| | 5888-001 (Other) | 641,098 |
| | 7353-002 (Other) | 12,729 |
| | 5940-001 (Project) | 319,500 |
| TOTALS | | 12,795,504 |

## 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?

Scientific Divisions (Research):

1.Recruit new Core Staff and Affiliate Scientists to leverage the best science
2.Expand the Ignition Pilot Program to foster work using nonhuman primates

Primate Resources Division:
1.To support expansion of the M. nemestrina (pigtail) breeding colony
2.To support an outstanding animal care and biology program with particular emphasis on socialization
Division of Finance and Administration:
1.Continue and expand emphasis on efficiency and operational improvement
2.To represent the WaNPRC interests in the UW conversion to Activity-Based Budgeting
3.Pursue efforts to expand and diversify the funding portfolio
Facilities & Planning Division
1.Expand the central UW commitment for financial support for proactive maintenance
2.Continue efforts to provide opportunities for WaNPRC expansion
C. Consortium Activities with other NPRCs
1.Expansion of ARMS initiative in both scope and participation
2.Expansion of consortium activities to include specific research 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?

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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?

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?

Strategic Planning: Preparation of the competing renewal of our P51has begun. As part of this process, we will include a major assessment of all programs for productivity and consistency with our resource and scientific missions. Our National Scientific Advisory Board (NSAB) will provide objective external advice during this process. With approval from ORIP, we organized our NSAB meeting into two components. First, we will hold teleconferences in early March, 2015 between Division Chiefs and their advisors to discuss achievements and future plans. Next, we will hold an in person NSAB meeting in September, 2015 to review aspects of our P51 competitive renewal. This format will provide us with timely feedback to address strengths and opportunities consistent with our commitment to maintain and advance our Center as a leading research center.

Scientific Divisions: Our scientific divisions are strong and have plans for growth and new initiatives going forward. We plan to recruit new Core and Affiliate Scientists. For example, we will need to replace faculty who plan to retire in 2015-2020. We also seek to expand the scope of research supported in our Center. [redacted] works with basic science and clinical department chairs to enlarge the WaNPRC' s research presence. This will be a major focus of his efforts in 2015. Our Center has a tradition of applying basic science results to clinical application (e.g., cochlear implant, HIV antivirals). Part of our strategic plan is to recruit investigators in emerging areas of research with high potential for advancing basic and applied science to conquer diseases. We have an opportunity to optimize and add further laboratory space in our Center to support the growth of such programs such as stem-cell therapies, neural engineering, HIV treatments, microbicides and neuroscience .

Scientific Initiatives: Another goal is to encourage further collaborations within and across divisions. Core and affiliate faculty at WaNPRC have demonstrated success in bringing together basic scientists and clinicians in teams to target specific diseases. For example, Dr.

Excluded by Requester (Ophthalmology) received funds to develop cures for macular degeneration. This project involves Core and affiliate faculty in the WaNPRC and other national and international centers. Similarly [redacted] (WaNPRC, Physiology & Biophysics) received funds from DARPA for improving memory function associated with mild cognitive impairment, Alzheimer's Disease and traumatic brain injury. The research team includes PIs from clinical and basic science departments, and plans include studies in nonhuman primates and humans. Excluded by Requester

WaNPRC and UW relations Excluded by Requester will continue to work closely with Dr. David M. Anderson (Health Sciences Administration, P51OD010425 PI) to meet the needs of a growing research center. An example of this activity can be seen in the development of the new Animal Resource Facility (ARCF), which will house an additional 300-400 nonhuman primates and provide new procedure space. Groundbreaking for construction of the ARCF occurred in February, 2015, with occupancy expected in 2017. The ARCF will provide significant resources in support of WaNPRC's resource and research efforts. We also work in close partnership with the UW Office of Animal Welfare, our IACUC and Office of Environmental Health and Safety to ensure best practices across Center functions. Excluded by Requester has focused on open communications and partnerships with all UW offices.

Division of Primate Resources (DPR): Excluded by Requester Assoc Director of DPR, will continue work with Excluded by Request to address challenges and opportunities in expanding our animal housing and research capacity Excluded by provides critical leadership to our veterinary team, addressing clinical care for all of our nonhuman primates. He will also spearhead our SPF colony management with support from our veterinary and diagnostics teams. Excluded by Requester [redacted] heads the Research Advisory Committee, which meets monthly to evaluate resource allocations and provides advice to the Director.

Finance: Our Assoc. Director of Finance, Personal Info at the end of 2014. [redacted] leads a search committee to recruit a new Associate Director of Finance. Our search team has completed initial screening of applicants and we expect to be able to fill this position in March-April, 2015. During the interim period our Finance team has received guidance from [redacted] Director of Finance & Administration from Health Sciences Administration. Our current team of financial specialists, including Excluded by Requester provides excellent service across the financial affairs of our Center. Excluded by Requester Excluded by Requester

Facilities: Excluded by Requester (Asst. Director Facilities) leads our Facilities group and serves as a member of our SMT. Excluded by Requester works closely with [redacted] to address modernization of our research facilities in the I-Wing. With the completion of renovation of our Western facility, we are moving towards modernization of 4 floors in the I-Wing to increase housing space and ensure best practices in BSL-2 laboratories. We will continue working with an experienced engineering firm [redacted] to develop contingency plans for this modernization effort. Excluded by Requester Specific Private Vendor

Center Programs: Excluded by Requester (Asst. Director, Center Programs) leads our CPro group and serves as a member of our SMT. Excluded by Requester Excluded by Requester plays an important role in advancing the culture of excellence across our Center and in support of Consortium efforts. This includes direction and supervision of our Public Relations efforts, Training Program, direct Assistance to the Director and liaison with UW Government Relations office, UW public affairs office and UW-HR. For example Excluded has been highly involved in a number of Director's Office projects, including the hiring of new senior personnel (AD-DPR, AD-Finance) using our Best Practices Hiring model. Center Programs achieved a number of milestones during this reporting period. Phase II of the Center's training database was completed. We can now track employee training and send alerts when an employee is nearing or out of compliance on essential trainings. Excluded by Request is working on rebuilding our Center's external website. We are focusing on proactively releasing positive news to local and national organizations. We recently released the first edition of the "BioBulletin," our semi-annual newsletter featuring people, events, and scientific achievements across the center. Our Program Coordinator Excluded by Req plays a significant role in organization and support of our next P51 submission. Emergency Preparedness continues to be a major focus with updates to our Emergency Call Plan and disaster response, as well as the appointment of Excluded by Reque to the Health Sciences Administration "Unit Response Committee."

Consortium: We will continue our consortium efforts with other NPRC working groups. [redacted] (AD-DPR) will play a leading role in our consortium efforts directed at improving colony management. Consortium efforts in the Breeding Colony Management group will remain a major commitment. Behavior Management will continue to receive significant support to ensure animal health and well-being. We are just starting the process of refocusing our Outreach efforts to improve the national and international awareness of our research success. Local outreach will continue to help provide a proper perspective about the role played by our Center in the culture of science in the U.S. and around the world. We are well served by our Occupational and Health officer and Pathology group. Excluded by Requester

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

We have made progress on all of our aims and are enthusiastically pursuing further advances. We provide a detailed account of accomplishments under each Division's progress report. Some representative major areas of achievement and endeavor are indicated here.

1. Major activities:
    i. Core and affiliate investigators have developed new projects and been awarded new grants (C06, G20, K08, K22, N01, P01, P30, P40, P41, P50, P51, P60, R01, R03, R13, R21, R24, U01, U19, U10, DARPA, Private Source). We have new teams formed that bring together basic and clinical scientists to address unmet needs in research and its application.
    ii. Our Research Support Services group plays a major role in supporting NIH funded investigators
    iii. Our Core and affiliated faculty have established programs with multiple NIH institutes (NIAID, NIDA, NLM, NIDCR, NICHD, NHLBI, NIMH, NINDS, NEI, NCI, NIGMS, NIDDK, DPCPSI, OAR).
    iv. WaNPRC plays a major role in the scientific culture of the University of Washington. We currently have active relationships with more than 20 basic science and clinical departments at the University of Washington. Similarly, we have significant research with Fred Hutchinson Cancer Research Center, Seattle Children's Hospital, Seattle Children's Research Institute, Seattle Biomedical Research institute and Center on Human Development and Disability.
    v. WaNPRC scientists have been productive including recent high-impact publications related to HIV, Ebola, safety of the measles (MMR) vaccination, neural development, stem-cell treatment of cardiac ischemic injury, prevention of premature birth, treatment of ischemic injury associated with cerebral palsy, neural prosthetics, vestibular prosthetics, prevention of blindness, treatment of memory disorders and more.
    vi. Senior staff recruitments: We recruited Excluded by Requester as our new Associate Director of Primate Resources Excluded by Requester is a highly accomplished veterinarian who has more than a decade of experience working in support of nonhuman primate care and research at major research centers, most recently at the National Cancer Institute. He is working with the Director and other senior management personnel to improve our Center's capacity and efficiency in support of our NIH mission.
    vii. We have recruited additional veterinarians for our Seattle and Arizona facilities to support our animal colony and increasing research portfolio.
    viii. Renovation of our Western facility to increase housing for nonhuman primates, and add procedure/surgical suites.

2) Specific objectives:
    i. To increase our housing and support for expanding research needs.
    ii. Begin renovation of the I-Wing 3rd floor space to increase research laboratory space.

3) Significant results:
    i. Renovation of our Western facility is virtually complete and should be ready for full occupancy in March 2015.
    ii. We have improved local infrastructure to support our expanding research portfolio. To accomplish this we renovated existing space in the Western facility and in the I-Wing, resulting in increased space for housing nonhuman primates and additional procedure and surgical suite capacity.

4) Key outcomes or other achievements
    i. Completion of the renovation of the Western Facility on time.
    ii. Initial renovation of lab space on the 3rd floor of the I-Wing to build 2 new laboratories.
    iii. Developed architectural plans for complete and partial renovation of I-Wing floors 3, 4 and 5.
    iv. Outstanding record of publications in top journals.
    v. Strong growth in new funding for junior and established scientists.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | | Director | Institutional Base Salary | EFFORT | | | 37,210.00 | 10,382.00 | 47,592.00 |
| 2. | | | | | | Assistant Director | | | | | 10,154.00 | 2,833.00 | 12,987.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **60,579.00**

## B. Other Personnel

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 1 | Other | 1.13 | | | 5,593.00 | 1,560.00 | 7,153.00 |
| **1** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **7,153.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **67,732.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 21,000.00 |
| 2. Foreign Travel Costs | 4,000.00 |
| **Total Travel Cost** | **25,000.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 2,213.00 |
| 2. Publication Costs | 1,787.00 |
| 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. Community Outreach(educational support, web support, Mailing and printing, rental space for community outreach) | 6,000.00 |
| 9. Training and Career Development, Recognition, Safety training, Visiting Scholars Visa | 9,940.00 |
| **Total Other Direct Costs** | **19,940.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **112,672.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Costs (MTDC) | 42.0 | 112,672.00 | 47,322.00 |
| | | **Total Indirect Costs** | **47,322.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center(PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **159,994.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Director's Office - 5880

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

## PERSONNEL:

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 1 | Information Specialist | 1.13 | 5,593 | 1,560 | 7,153 |
| **1** | **TOTAL OTHER:** | **1.13** | **5,593** | **1,560** | **7,153** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Finance and Administration

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The goals of the Division of Finance and Administration (The Division) are to provide customer support that:
•Enables the most effective use of fiscal and human capital assets in support of nonhuman primate research and resources,
•Leverages technology to enhance the organizational infrastructure platform, and
•Promotes business efficiencies through collaborative relationships and the incorporation of best business practices.

The Division consists of pre-award services, financial services, business services, and personnel & payroll services. The specific scope of these services are as follows:
•Pre-award and Research Liaison Services – This function is responsible for: formulating accurate budgets sufficient to see their projects to conclusion, with particular attention to the nonhuman primate study costs; application development and review; timely processing of grant applications; coordination of subcontracts, and; assuring all regulatory requirements regarding the use of nonhuman primates were documented and approved.
•Post Award/Financial Services – This function serves three overarching goals: complete post-award support and service; financial services which include regulatory and management accounting; and competitive and noncompetitive budget development for the Center's P51 grant. Performed in conjunction with the latter is service and maintenance of the Center's budget model.
•Business Services - This function is responsible for the following: program income billing for 8 cost centers, shipping and receiving, rate setting/pricelists, shuttle services, procurement, and imprest funds (petty cash/reimbursements). Routine duties include materials billing for all research projects conducted at the WaNPRC. This office also bills for outside sales of animals, assays, tissue, and similar products. Sales and shipping are global in scope, and shipping and receiving facilities are maintained at both the Health Sciences Building and Western facility
•Personnel & Payroll Services – This function is part of the administrative infrastructure and its primary goal is to provide quality personnel and payroll services to ensure minimum distraction to researchers, PIs, and their staff. This program also provides consultation and facilitation related to unfavorable personnel actions.

### 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: WaNPRC_Fin_And_Admin_B2.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?

Plans for Next Reporting Period:
Foremost in the Division's plans is to on-board a new Associate Director to replace the Personal Info. During and after this transition, we plan to continue progress towards our goals of providing effective use of assets, improved technology leverage, and efficient business processes for the best possible customer support, by implementing the following plans for each of the Division service areas:

Pre-Award and Research Liaison: We plan to continue our efforts to achieve timely, compliant, and successful pre-award submissions in line with Center resources. We will do so by effective 1:1 communication with investigators, consistent outreach throughout the Center, collaborations with other units especially the Division of Primate Resources, and continued integration of ARMS into work processes.

Post Award/Financial Services – We plan to maintain our high-level of customer service for post-award administration through continued training, daily stand-up meetings, and a disciplined approach to scheduling due dates and work items. We will continue our current practice of generating PI reports on a monthly basis, and soliciting frequent conversations with PIs, especially those with unsustainable financial burn-rates. Additionally, we plan on making significant progress on the following projects:
•Financial Reporting: Depending on the availability of IT resources, we plan on expanding our prototype of the automated report engine

in business objects. Regardless of IT resources, we will continue to refine our reports. We also plan on introducing an electronic dashboard for senior leadership to display key metrics.
•Program Income: Consistent with the Financial Reporting project described above, we will continue to refine our program income reports, and share findings with relevant partners in the center.
•Capital projects: In the coming year, this project will focus on the Arizona breeding colony capital development, providing financial analysis to assist Senior Leadership in planning.
•Financial Reconciliations: We have developed a scope of work to re-organize our filing system, with an eye towards easier and more timely archiving of old files, and to assist in the utilization of electronic record keeping. We will also continue to refine our LEAN methodologies for greater efficiency.

Business Services – Our plan is to continue to leverage technology for the automation of billing and procurement processes, eliminate or reduce paper-intensive systems and manual processes, and reduce overall process cycle times and costs. University investments in technology systems – particularly in Purchasing - will continue to provide benefits, and we plan on capitalizing on those investments through continued training, rapid adoption of the new tools, and matching redesign of internal processes.
Additionally, we plan on making significant progress on the following projects:
•Material Billing Program: ARMS has proven an effective tool for improving efficiencies, and we will continue to work with IT to expand its capacity to improve the billing cycle. We have also identified some opportunities to improve efficiencies by direct connections with various University databases; for example, to create a sub-table to identify expired budgets and thereby avoid rejected invoices.
•Procurement Services: The University is continuing its implementation of the eProcurement Ariba system, particularly in its recent transition of POs to BPOs (Blanket Purchase Orders), which allows for electronic submission of vendor invoices for payment. Business Services staff plan to take a middle-ground role, assisting UW eProcurement in vendor registration, and vendors in order processing and invoice transition. Our efforts will help ensure a quicker transition to efficient and effective vendor transactions.
•Imprest Funds: The University has transitioned from petty cash (Imprest funds) to an electronic eReimbursement system for processing of individual staff payments of University business expenses. We plan to continue the reduction of Imprest-fund and eReimbursement needs with the use of efficient just-in-time purchasing methods, inventory management, and supplies-order planning.
•Shipping and Receiving: We have recently developed several new tools to track and report on due dates of Center orders - and unplanned changes to orders – in real time during the delivery and receiving process. We plan to implement these tracking and reporting tools for quicker notification and correction of order changes.

Personnel & Payroll Services – We will continue to leverage the University investment in centralized systems and emphasize decision support for managers and supervisors in the center through effective reporting and trend analysis. Superior service will also be achieved through continued cooperation with Financial Services in the area of payroll.
Additionally, we plan on making significant progress on the following projects:
•Paperless Payroll System: The University of Washington (UW) is adopting a new personnel and payroll software system. Training of our staff and managers regarding the new systems will take place in November / December 2015 time frame.To ensure a smooth transition to the UW Workday system which includes position and work force management a systematic review of all staff job descriptions will be done.
•Payroll Disaster Recovery Plan: This item is removed from our planning as the UW is responsible for implementing its payroll disaster recovery plan, and these plans will change with the adoption of the Work Day system.
•On-line Forms Submission: With the UW moving to the Work Day system, on line forms submission is on hold pending the Work Day implantation in order to ensure Primate Center systems complement the UW systems, and not duplicate it.
•Personnel and Payroll Webpage: The Center Personnel web pages will be updated regarding personnel and payroll rules for Staff represented by several unions, Classified Civil Service Staff, and Professional Scientific and Management Staff. Web pages will also be set up to provide Primate Center Staff with training for the Work Day system.
•Recruitment/Hiring Process: We will continue training our staff in regards to the UW Hires system, with the view that in phase two of the Work Day system implementation a Talent Acquisition package will be adopted.
•Performance Evaluation: The Personnel Database will include tracking / follow-up features regarding personnel evaluations, to ensure all staff receive evaluations in accordance with UW policy.
•Personnel Database: development for storing performance evaluations in database records, replacing the current paper system of retaining performance evaluations.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

**Accomplishments:**

Pre-Award and Research Liaison: The Division has been successful in meeting its goals with respect to this unit. This success is demonstrated by zero submissions being rejected by the University's central Office of Sponsored Programs, successful training and knowledge sharing with other units within the Division and the Center, as well as the progress on the projects described below. Additionally, in support of the identified projects, the following outcomes were achieved:

The Project Review Process Improvement project:

- The *Project Review Process* has been fully shifted to the Division of Primate Resources. As part of her role with the RAC, the incumbent works along with the Research Facilitator to revise and update the forms required to request new projects to continue to improve and streamline that step of the process for the investigators.

Post Award/Financial Services – The Division has been successful in meeting its goals this year with respect to Post Award/Financial Services, demonstrated by smooth post award management of projects, as well as progress on the projects described below. The Division also assisted the University's office of Management Accounting and Analysis (MAA) with the federal rate negotiation process by providing data and support. More broadly, the Division has been working closely with various university departments to coordinate the management of grants to ensure indirect costs are properly distributed to the Center. Additionally, in support of the identified projects, the following outcomes were achieved:

The *Financial Reporting* project:

- The Project Forecasting Model was redesigned to be better in-line with an executive style report with critical metrics.
- As a result of clearer financial metrics, investigators have dramatically increased their engagement with the finance team, and budget management has improved.
- A monthly, comprehensive, dashboard-style report of all of the Center's financial operations was developed this year for senior leadership using the Master Budget Model as a data source.
- A prototype for automating some of the reports described above has been developed using Business Objects, the same system used for ARMS reporting.

The *Program Income Management* project:

- A new model was created to easily develop and compare the financial effects of different operational scenarios in the external breeding colonies to Center leadership.
- Accounts receivables collection this year has been 100% successful due to diligent follow-up and weekly reports to management.

The *Financial Reconciliations* project:

- A lean process methodology has been adopted within the Division. This has resulted in improved efficiencies, especially around reconciliation.

Business Services – The Division has been successful in meeting its goals with respect to Business Services this year. Consistent with our 5-year plan, technology was leveraged for the automation of processes, thereby reducing process cycle times, reducing paper intensive systems and manual processes, improving controls, and reducing process costs. This resulted in greater efficiencies that allowed improved services, with the same number of staff, despite increased workload and volumes. Additionally, in support of the identified projects, the following outcomes were achieved:

The *Procurement Services* project:

- Off the shelf technology systems, such as ARIBA (the enterprise wide integrated procurement system), were more fully utilized by the Center to reduce processing costs.
- The new ARIBA module for standardized orders, including catalog and blanket purchase orders, was rolled out this year.
- The procurement process has been mapped, and includes times for each step, enabling more effective training and process improvement.

The *Materials Billing Program*:

- Improved process, documentation, and integrity of the Price List and billings process, which reduced cycle time for billings consistent with goals.
- Consistency process management improved billing accuracy, reducing the corrections necessary.

The *Shipping and Receiving* project:

- Through the use of scheduling systems and improved coordination, more convenient transportation of people and materials was provided at no increased costs
- Electronic notifications of due dates for new orders was implemented this year, resulting in better order tracking and more timely deliveries.

Personnel & Payroll Services – In the area of Personnel and Payroll Services, the Division has been successful this year in its goals of providing effective use of assets, technology, and business processes to improve customer support. The University of Washington is adopting a new Personnel and Payroll Services software package from the Workday Corporation, and the Division has supported this effort with planning and communication. Our interviewing processes are more robust and well communicated. Staffing level adjustments and duty assignments have allowed payroll to be administered at lower costs. Additionally, in support of the identified projects, the following outcomes were achieved:

The *Personnel Database* project:

- Designed a new and more efficient database with automated upload characteristics.
- Enhanced Functionality to Personnel Database to increase accuracy of pay and benefit cost projections;
- Added Functionality to Personnel Database to provide metrics related to Hiring Process.

The *Recruitment/Hiring Process* project:

- Reduced the time it takes to post job announcements by 15%;
- Increased the number of staff trained to do Hiring Requisition Entry by 25%.

The *Performance Evaluation* project:

- Provided consultation and training to Primate Center Managers and Supervisors related to counseling staff and processing unfavorable personnel related actions.

The *Paperless Payroll System* project:

- Reduced the number of overpayment by at least 50%;
- Reduced the number of manual payroll checks;
- Processed overtime in a timelier manner to meet Union requirements.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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. | | TDB | | TBD | | Associate Director | Institutional Base Salary | 3.0 | | | 34,928.00 | 9,745.00 | 44,673.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **44,673.00**

## 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 | | | | | | |
| 5 | Secretarial/Clerical | 15.0 | | | 64,689.00 | 22,900.00 | 87,589.00 |
| 5 | Program Managers | 15.0 | | | 103,037.00 | 28,747.00 | 131,784.00 |
| **10** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **219,373.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **264,046.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 7,000.00 |
| 2. Foreign Travel Costs | 4,000.00 |
| **Total Travel Cost** | **11,000.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. Consumable office supplies to support P51 daily operations by the Center, plus non-equipment computer supplies not supported by IT. | 33,816.00 |
| 9. Campus Service (Printing; temp. service; contractual services... etc.) | 25,000.00 |
| 10. Staff Training courses through UW professional development and registration / conference fee | 7,880.00 |
| **Total Other Direct Costs** | **66,696.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **341,742.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 341,742.00 | 143,532.00 |
| | | **Total Indirect Costs** | **143,532.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **485,274.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Finance and Administration - Admin Core 5881

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

## PERSONNEL:

**SENIOR/KEY PERSONNEL:** A To Be Named individual is listed as Senior/Key on the budget because a new Associate Director will be hired prior to the start date. While this person is being hired [redacted] is fulfilling the role as lead person for this division, and will pass on the role to the new Associate Director when they are hired.

Excluded by Requester

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 5 | Program Managers | 15.0 | 103,037 | 28,747 | 131,784 |
| **5** | **TOTAL OTHER:** | **15.0** | **103,037** | **28,747** | **131,784** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Center Programs

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

Assistant Director

Specific Aim 1. The Assistant Director will work closely with the Associate Director of Primate Resources to integrate existing Training and Orientation, Occupational Health and Biosafety components with the Division of Primate Resources' emerging Quality Management Program and new Animal Records Management System. These roll-out processes will be ongoing in the start of the new grant period with respective roles and expectations clearly delineated and specific support assigned. The CPro Organizational Development Specialist will provide consultation for designated process improvements and CPro Program Coordinator will provide project management support. Emphasis will be on leveraging web-based video training, continuing education sessions, supervisor involvement, rigorous documentation, relevant testing, linkages to performance management and frequent program evaluation. Two new training modules identified in the process will be developed and implemented by the end of Year 1. Years 2 – 5 timeline will be developed incorporating feedback from initial year, stakeholder surveys and Senior Management Team strategic direction.

Specific Aim 2. The Assistant Director will continue coordination of center-wide NPRC Consortium efforts and active participation in the PIO-Education Outreach, Occupational Health/Training Working Groups. Best practices and model curricula from the work groups will be incorporated into WaNPRC web-presence and outreach and community engagement efforts with priority projects and partnership with NWABR available by October 2012. She will also continue participation in the new UW Health Sciences Emergency Preparedness Committee and Health Sciences shared resources initiative. Information developed in this effort will leveraged for promotion of WaNPRC services.

Occupational Health and Biosafety

Specific Aim 1: As part of the overall emphasis on process improvement, the Occupational Health & Biosafety Specialist will lead a center-wide effort in Safety Accountability for Supervisors. Working with front-line supervisors in DPR and research labs, and using data developed in ongoing trend reporting, [redacted] will develop a framework for an improved local process that promotes incident prevention while standardizing and streamlining incident processing. All processes will integrate with external partners' processes and be compliant with state and university requirements. Improved documentation and mapped communication flow will be the first deliverable and is targeted for completion by December 2012. Supervisory training specific to the improved processes will be developed and implemented for both existing and new hires. Outcomes will be made available to UW and NPRC consortium partners as an educational resource.

Excluded by Request

Specific Aim 2: The highly collaborative partnership between our Occupational Health & Biosafety program and Training & Orientation program will continue with additional support from the Organizational Development Specialist. The shared and overlapping processes will be reviewed and mapped to leverage additional efficiencies and depth. This work will be ongoing with Year 1 deliverables in integrated Emergency Preparedness, Chemical Hazards, and specific SOP development. Information and processes will continue to be rigorously documented, disseminated electronically and accessible to all employees and affiliates.

Training and Orientation

Specific Aim 1: The outcome of efforts identified above will result in refinement of existing training elements and strategic additions of new modules. Improved curriculum materials and production of comprehensive SOPs related to training processes and documentation will be a focus in Year 1. Future video training modules produced in-house are scheduled for June 2011 delivery and will serve as a prototype for a series of work unit-specific training for animal care and facilities staff. Ongoing process improvement and incorporation of DPR Quality Management Program will inform training subject selection. Information and data produced will be available to relevant UW and NPRC Consortium Working Groups.

Specific Aim 2: Development of a mandatory Orientation course with a working title of "Primate Center 101" will be a priority module in Year 1. This comprehensive approach will offer an overview to all personnel who access the Center and incorporate video, training clips, live speakers and identified orientation 'mentors'. Expected to be available to all new orientees by early 2013, it will also be accessible to all existing employees.

Information Operations

Specific Aim 1. This program will continue ongoing review and refinement of all web-based information and expand efforts to highlight translational research stories and investigator profiles. Continued web analytics approach and the ability to refresh information in real-time will continue to be a priority for both the internal and public websites. Queries from the public and investigators will continue to be responded to within 3 days and fielded to partner NPRCs as appropriate. Electronic fact sheets and FAQs will be developed in Year 1 for outreach, public interest and research facilitation. These items will be shared and cross-posted in support of NPRC Consortium efforts. Ongoing efforts will continue in developing mobile versions and smart phone access to designated operational information (Emergency Call Tree information, Vet on-call calendars and Center SOPs).

Specific Aim 2. While the DPR SOP Directory continues to expand, the Information Operations Specialist will promote SOP review, creation and distribution of the divisions of Finance & Administration and Facilities & Planning SOPs with a target date of early 2013 for these new sections. He will also facilitate the Program Assistant's advanced technology support training and Document Update Team and publicize this increased capacity to all users.

Program Coordination

Excluded by Request

Specific Aim 1. Early in the next grant cycle [redacted] will provide the Director and Senior Management Team with a comparative analysis of 18 months of Basecamp application and experience. Based on the outcome, she will lead the effort to expand its use, capitalize on enhanced metrics reporting or lead the transition to an improved system. The goal is to have Center users at all levels competent to use this application. She will work with Division Heads and Supervisors to standardize projects, incorporate metrics and provide expanded and continuing training.

Specific Aim 2. The Program Coordinator will incorporate strategies learned during this P51 submission to develop more efficient project plans, and timelines for monitoring progress and reporting outcomes in the Annual Progress Report. This information will also support pending transitions at the UW, our reporting structure at NIH, and provide data and information to promote the WaNPRC as a local, national and international resource. She will continue coordination of the Visiting Scientist and Affiliate programs as well as the two Primate Neural Systems Courses projected in the next grant period. Significant effort will also be directed to support of Office of the Director initiatives, including support for NPRC Consortium work groups and the current and projected Core Staff searches

**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: WaNPRC_Center_Programs_B2.pdf

**B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS**

Not Applicable

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

File uploaded: WaNPRC_Center_Programs_B4.pdf

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

Results of training and professional development are shared within the group and with other members of the Center as appropriate. Training and professional development is voluntarily recorded in the Center's training database.

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

ASSISTANT DIRECTOR:
Process improvement: Continued collaboration with members of senior management team to integrate Center Programs into other Center divisions (Finance, Facilities, DPR) in support of the Center's scientific core;
NPRC consortium efforts: Assistant Director recently named to a special committee to refine the direction of the Outreach Working Group. Directors have asked the committee to explore options, placing emphasis on public relations at a national level. Efforts will be on-going;
OCCUPATIONAL HEALTH AND BIOSAFETY:

Process improvement: Continued work with individuals and groups to train and enforce occupational health and biosafety compliance;
Collaboration: Occupational Health & Biosafety Specialist (OHBS) continues to work closely with Training & Orientation to develop trainings, processes and initiatives to respond to emerging situations and issues. Examples include the injury prevention project and ergonomics initiative. OHBS working together with DPR and principal investigator flex labs to improve safety and compliance in a challenging work space.
TRAINING AND ORIENTATION:

Refinement of training modules and additions of new modules: Training and Orientation Coordinator will continue refresher courses and explore video training on human-focused tasks. "Personnel Resource & Reference" guide will continue refinement in response to emerging situations and changes. Continued refinement of Center's Training Database allows access to Primate Center training records in one, easy-to-use location available to anyone with Center electronic access. Integration with entities across the University (EH&S, OAW, etc.) will be a goal for the next phase of the database.
Development of mandatory orientation course: Continued refinement of "Personnel Resource & Reference" guide plus continuing annual refresher trainings will be focus.

INFORMATION OPERATIONS:

Websites: Improvement of internal website will continue to allow users agility and ease when using the website. Proposed roll-out of new external website, with a focus on sharing positive news and scientific achievements;

SOPs: Information Operations Specialist (IOS) continues to assist with distribution of new SOPs. IOS has assisted in formatting and distributing new Center policies.

PROGRAM COORDINATION:

Standardization of project management using Basecamp: Program Coordinator will continue to explore other project management programs (such as Mindjet) to continue to find ways to manage large projects with many contributors;

Pending Support

Program Coordinator will continue to drive the project using strategies learned during previous submissions.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

Assistant Director (AD):

Collaboration with Associate Director of DPR: With the hire of a new Associate Director of Primate Resources, Excluded by Requester in the current reporting period, the opportunity for Center Programs to work with the Division of Primate Resources (DPR) on process improvement has increased significantly. Some specific examples of major initiatives are the assistance with restructuring the department through several new hires (including training and support surrounding the Primate Center's "Hiring Best Practices"); assistance with the development of a robust SOP training program for Center flex lab personnel and development of flex lab-specific SOPs regarding hazard mitigation; annual refresher training for all Center staff and affiliates (see "Training & Orientation" below); and program assistant support on a number of projects and initiatives.

NPRC Consortium Efforts: Assistant Director, along with representatives from Tulane and Yerkes, has been appointed to a subcommittee of the Outreach Working Group to assess the feasibility of a Public Relations subgroup or new consortium working group. While significant progress has been made by the subcommittee, the final outcome will be determined in the next reporting cycle.

Emergency Preparedness: Assistant Director was appointed the Primate Center representative of the newly re-established Health Sciences Administration (HSA) "Unit Response Committee (URC)." In the case of an emergency, AD would await direction from HSA, then report to central URC location. During a campus-wide drill in March 2014, the Primate Center proved to be very agile and responsive, utilizing several new initiatives, including an "alert" text message to all Primate Center essential personnel, activation of the Center's "Emergency Call Plan" (including a later extension to our extended Principal Investigator list), a Primate Center command center, including runners who could relay information to other floors/locations, and an up-to-the-minute blog to keep anyone with access to the internal website to be informed. While very successful, this drill also pointed out a few situations where we weren't as well prepared (ex. communication when the power is out and easily accessed instructions to staff who might be first on the scene but not necessarily office personnel.)

With the assistance of the Senior Management Team and other members of Center Programs, a new series of policies were created. (Formerly, the only Center policies were the visitor policy and photo policy.) The visitor policy was broken into three distinct instances: visitors, vendors and research colleagues. Volunteers were separated into a stand-alone policy. Other new policies include nonhuman primate safety and security and entrance and exit policy, with a number of others in the works.

Occupational Health & Biosafety Specialist (OHBS):

In an effort to provide a consistent, high level of compliance at all our locations, our Occupational Health & Biosafety Specialist (OHBS) travels between our Seattle facilities and speaks regularly with our Arizona Breeding Colony head vet and facility manager. She plans annual trips to provide relevant training to new staff and refresher training to current staff in order to ensure OHBS compliance at all locations.

Injury Prevention Project - Our OHBS has also initiated a monthly meeting where injuries are discussed with the objective of determining patterns and preventing similar injuries.

Ergonomics initiative: In conjunction with the EH&S ergonomist, Excluded by Requester is coordinating a new team to assess and train the Animal Technician staff to prevent repetitive motion and ergonomics issues. Video training modules will be explored in order to provide consistent training to new staff and refresher training to existing staff.

Emergency Evacuation & Operations Plan (EEOP) were updated for four unique locations.

Training & Orientation:

In coordination with Information Technology Services (ITS), completion of Phase II of training database resulting in a robust system that tracks employee training and sends alerts when employee is nearing or out of compliance.

Creation and distribution of new "Personnel Resource & Reference" guide, including distinctly different versions for our Seattle and Arizona facilities.

New "Refresher Training" initiative that will provide annual updates to staff training. All staff with access to animal areas are required to attend this training. Others are encouraged. Refresher Training includes updates from Training & Orientation, Occupational Health & Biosafety, and Communications, as well as any other unique site-specific needs.

Information Operations:

In this reporting period, the Information Operations Specialist (IOS) continued improvements to the internal website including a transition to converting from pdfs to web forms allowing easier completion and recording.

Design and production of a new external website format (currently in progress) will include fresh new graphics and much updated information.

IOS has served as a consultant to the new NPRCResearch.org website manager, providing assistance with analytics as well as increasing presence on Google searches.

New semi-annual "BioBulletin" – after a number of years without an external newsletter, the Center rolled out the new "BioBulletin" to an external audience consisting of other Primate Centers, NIH partners and other institutions. The response was very positive. New features, news and articles are being collected currently for the second issue slated for completion in March.

Program Coordination:

In anticipation of the [redacted] as well as increased work load, [redacted] was returned to [redacted] With the Annual Progress Report and [redacted] primary focus, she has also responded quickly to Director requests such as NIH reports and information for the semi-annual Directors' Meetings.

Continued significant support and guidance for the Visiting Scientist and Affiliate Scientist programs.

A search for WaNPRC-related publications is conducted monthly and shared to the NPRCResearch.org website

Weekly search for relevant funding opportunities to be shared with the research staff at the WaNPRC

Continued oversight and management of the Records Retention program, including the sharing of "Retention Tips" that are shared with staff and affiliates via the Internal Website and the Weekly Update

Event coordination and support

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

Training and professional development are key components of the Center Programs' Professional Development Plans (PDPs.) Center Programs staff are encouraged to take advantage of University of Washington training opportunities, offered by the Professional & Organizational Development (POD) office, as well as other UW and outside seminars, conferences and classes. Some examples of training and professional development, all attended by one or more members of Center Programs this reporting period:

- POD classes
  - "Thinking on Your Feet,"
  - "Directing and Delegating"
  - "Communication Style: Creating Positive Relationships and Results"

- POD Support Professionals Spring Retreat
- Institutional Animal Care & Use Committee (IACUC) Regional Education Conference
- Northwest Association for Biomedical Research "Security & Crisis Communication Forum."

## 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

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Excluded by Requester | | | | Assistant Director | Institutional Base Salary | EFFORT | | | 15,232.00 | 4,250.00 | 19,482.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **19,482.00**

## 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 | Program Coordinator | 19.59 | | | 126,333.00 | 36,275.00 | 162,608.00 |
| **5** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **162,608.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **182,090.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 30,259.00 |
| 2. Publication Costs | 0.00 |
| 3. Consultant Services | 0.00 |
| 4. ADP/Computer Services | 0.00 |
| 5. Subawards/Consortium/Contractual Costs | 0.00 |
| 6. Equipment or Facility Rental/User Fees | 0.00 |
| 7. Alterations and Renovations | 0.00 |
| **Total Other Direct Costs** | **30,259.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **212,349.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 212,349.00 | 89,187.00 |
| | | **Total Indirect Costs** | **89,187.00** |

**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)** | **301,536.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

| K. Budget Justification* | File Name: CenterPrograms.pdf |
|---|---|
| | (Only attach one file.) |

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

## BUDGET JUSTIFICATION: Center Programs - 5882

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

## PERSONNEL:

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 2 | Program Coordinator | 10.95 | 82,671 | 23,065 | 105,736 |
| 1 | Information Specialist | 2.64 | 13,034 | 3,636 | 16,670 |
| 1 | Training Specialist | 3.00 | 16,904 | 4,716 | 21,620 |
| 1 | Administrative Supervisor | 3.00 | 13,724 | 4,858 | 18,582 |
| **5** | **TOTAL OTHER:** | **19.59** | **126,333** | **36,275** | **162,608** |

This category does not represent a significant deviation from the prior year.

## 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?

1.Strategic Planning and Design: Provide the support for future space development to meet WaNPRC goals pertaining to facilities and resource utilization.
2.Project Management for Renovations and Construction Projects: Prepare for program needs prior, during, and post project timeline to support ongoing programs during renovations and efficient functioning program implementation upon completion.
3.Space Allocation and Other Reporting: Provide and assist with review of space metrics reports for comparisons and optimal decision making regarding use of space and resource allocation.
4.Resource and Asset Management: Initiate improvements in efficiency of usage and identify changes with cost savings potential.
5.Program Operations: Initiate improvements in efficiency of operations based on customer satisfaction surveys using metrics generated from this current 5 year period relating to the number of maintenance, repair and alteration requests, quality of work and timeliness of response and environmental security components as completed for each division. Continue ongoing efforts for Facilities and Planning staff to provide resource improvements using the tracking system and survey results.
6.Security and Facilities Access: Partner with security networks to retain mutually beneficial education, communication and training opportunities for WaNPRC staff and emergency responders.
7.BioSecurity: Continue developing and implementing required plans to accommodate select agent usage at the newly constructed laboratory suite.

### 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: WaNPRC_Facilities_B2.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?

Space resources continue to be a large factor in providing appropriate animal care and research support on campus. Most vacated space is in need of renovation and repair prior to further utilization or new occupancy and existing usable research and animal housing space is at capacity. Future planning will include continued prioritization for space utilization and funding needs to bring space up to standard for type of usage. Space usage updates are continually in progress to keep floor plans updated and new reporting will be implemented to review current usage from the GeoSims data base for decision making on space requests and usage of limited space resources. The Western cage wash and expansion project, scheduled to complete in March, 2015, will greatly improve research and animal holding capacity at the Western facility in the upcoming year. The focus will now become expansion and/or renewal funding on campus. Cost estimates will be submitted for building renewal funding to upgrade the -1, 3rd, 4th and 5th floors of I-Wing all in need of upgraded lab spaces. Space will be requested to be newly assigned to WaNPRC as it becomes available (office and lab) thru Health Sciences Administration and School of Medicine. Space requests will also be formally submitted to the University Real Estate office to secure additional local animal housing space, either leased or contracted.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

**Major activities:**
Provided space resources and change of space utilization as required to meet research resource needs. Provided recommendations on how best to address resource needs in support of research and animal care programs. Provided management oversight of construction, alterations, and logistical planning, maintenance and renewal projects.

**Specific objectives:**
Participated as committee members on various working groups directly affecting University and WaNPRC decision making. Created advocacy and opportunities for WaNPRC resource needs. Managed division for prioritization and timeliness of facilities work requests.

**Significant results:**
Merged construction grant funding awarded for expansion space with prior approved compliance funding for cage wash facility re-design to leverage and optimize existing and expansion space as funding allowed. Re-located WaNPRC business office staff from Western 4th floor to Campus facilities as part of logistical planning required for the Western construction project. Project estimated completion date is March, 2015 and described in the Improvement and Modernization division section. As participant on the AAALAC oversight committee requested and received justified funding for ongoing AAALAC guideline compliance funding. I-Wing renovations to accommodate Reproductive Biology lab and create additional animal holding by redesigning vacated lab space completed in 2014.

**Key outcomes or other achievements:**
The new facilities and planning work request system was launched in 2014. The system is integrated on the ARMS portal, user friendly and provides reporting and other tracking functions. The design and beta testing period was completed in July 2014 and metrics are currently being generated. Training sessions are ongoing and minor adjustments are being made as the system becomes more utilized for each facility.

## 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

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 27,478.00 | 7,666.00 | 35,144.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **35,144.00**

## 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)** | **35,144.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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)** | **35,144.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 35,144.00 | 14,760.00 |
| | | **Total Indirect Costs** | **14,760.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **49,904.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Facilities - 5886

This budget does not have significant deviations from the prior year's budget.

## A. COMPONENT COVER PAGE

**Project Title:** Information Technology

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1.Will provide continued ARMS system development, design, maintenance and operation, and integration with Finance & Administration department functions and other WaNPRC Divisions (Primate Resources, Facilities, Center Programs, etc.) as required or requested. Distribute ARMS and its updates to all participating NPRCs and other research centers to enhance their research goals and capacities through research resource sharing. Continue enhancing the ARMS Project by adding Grants & Contacts, Pathology, Asset Management, Facility Data Integration, Mobile Device Optimization, Hazardous Materials & Infectious Agents Alert, Document Storage & Management, Small Animals and Personal Training/Occupational Health.
2.Provide centralized management and monitoring of the Center's IT hardware infrastructure: including but not limited to; Windows Servers, Windows Desktops and Laptops, Apple Desktops and Laptops, File Storage Devices, Firewalls, Disaster Recovery appliances, etc.
3.Provide robust support for the Center's IT software environment. Windows Desktop and Server Operating systems, Microsoft Office, Adobe Creative Suite, Microsoft Exchange, Microsoft IIS, etc.
4.Provide computer hardware life cycle management for WaNPRC and other research desktops, laptops and servers.
5.Refine the Center's Backup Systems and strategies using current technology to allow for minimal disruption of service or data compromise. Develop state-of-the-art Disaster Recovery Plans to protect the WaNPRC's 50 years of valuable data into the next 50 years.
6.Enhance and contribute to collaboration and consortium activities across all NPRC's and associated facilities by work with WCC, NPRC and ARMS Multi-Center Advisory Committee.
7.Virtualize WaNPRC's desktop clients using VMware's Desktop Solutions, where appropriate, saving WaNPRC both money and resources over the next grant cycle.
8.WaNPRC will offer a data storage cloud environment as a better way to organize and manage research resources and services to enhance its offerings to researchers.

### 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: WaNPRC IT Section B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC IT Section B4.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 AIMS
The goal of the proposed project is developing an Integrated Information Technology Solution to increase the overall translational research capacity of the Animal Research Management System (ARMS) Consortium (ARMSC) through the adoption and use of data storage clouds, standards based data repositories, and improvements to the ARMS Consortium's Informatics capacities. The use of such systems are ultimately intended to support the discovery, integration, analysis, storage, and dissemination of biomedical data across a multitude of centers involved in research and support of translational hypothesis discovery and testing.

Aim 1: Create a Biomedical Data Sharing System
Significance: Substantial need for a disseminated biomedical storage environment across the center and nation, specifically amongst animal research centers, is currently unmet.
Innovation: This will allow a network of centers in the United States, funded by the National Institutes of Health, to access collective data. Standards for the Biomedical Data Sharing will provide secure biomedical data sharing, and established disaster recovery planning.
Approach: We will develop a system that is ideal to enter, store, and access valuable research data using EMC Isilon X400 powerful yet simple scale-out storage architecture to speed access to massive amounts of critical data, while dramatically reducing cost and complexity. We will contract directly with EMC to design, install, implement and support world-class biomedical data sharing and share that model with the ARMS Consortium members and other NIH funded research facilities.

Aim 2: Continued Improvements to Research Center Informatics Capabilities
Significance: Through NIH grants thus far, we've been funded to provide base system development, design, maintenance and operation. In order to meet the growing needs of researchers a consistent source of funding is needed to establish both short-term and long-term goals for informatics capabilities.
Innovation: To provide the appropriate environment to support outstanding biomedical research directed towards significant human health issues and nonhuman primate health and biology. We will extend to ARMS to include other species in order to enhance the existing Big Data Initiative. This Driving Biomedical Project (ARMS) is collaborative in nature, allowing the ARMS Consortium personnel to work jointly with investigators, both inside and outside the research community, supplying expertise in particular biomedical disciplines.
Approach: We propose to continue enhancing the ARMS Project by adding Grants & Contacts, Pathology, Asset Management, Facility Data Integration, Mobile Device Optimization, Hazardous Materials & Infectious Agents Alert, Document Storage & Management, Small Animals and Personal Training/Occupational Health.

Aim 3: Dissemination of Biomedical Data Systems
Significance: Establishing and disseminating the ARMS Informatics model as the foundation for collaboration across centers with researchers and existing research centers.
Innovation: Establishing standards across the NIH-funded research centers will allow researchers to focus on the advancement and the development of integrated approaches to conduct research that touches virtually every field of nonhuman primate biology and medicine with particular focus on the neurobiological sciences, AIDS-related research, reproductive and developmental sciences, genomics, immunogenetics, nonhuman primate models for human diseases, international outreach and conservation, and the psychological well-being needs of its colonies.
Approach: We will offer consortium membership to any NIH-funded research center that wishes to join as a Participating Institution. This entitles any member to a copy of ARMS. We will invite research centers across around the world to contribute to the ARMS Consortium as colleagues and Subject Matter Experts (SMEs). This Driving Biomedical Project (ARMS) is collaborative in nature, therefore will garner requirements from members to enhance future distribution of ARMS

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

1) Major activities
   i. Installation of ARMS 2.4 Billing
   ii. Acceptance of ARMS 2.5 Mobile – Phase 1
   iii. Creation and acceptance of the 5 year server Life-cycle Replacement Policy
   iv. Completion of the Center's Backup/Disaster Recovery Plan
   v. Portal development
   vi. Construction of new server room at Western
   vii. Completion of 16 month Lean process for Center billings
2) Specific objectives
   i. Creation of a long-term plan for the Portal
   ii. Creation of a long-term plan for ARMS development
   iii. Acquire funding to accomplish goals for ARMS and Information Technology
   iv. Creation of direct connection between SAP Business Objects and UW's EDW(Electronic Data Warehouse)
   v. Implementation of a long-term plan for server life-cycle replacement
   vi. Completion of transition from WaNPRC Exchange server to UW Exchange server
   vii. Completion of construction of a new secondary server room at the Western Facility
3) Significant results (major findings, developments, or conclusions (both positive and negative)
   i. Lack of funding for ARMS development has slowed or stopped the forward progress of ARMS
   ii. Lack of new membership to the ARMS Consortium
   iii. Enhanced Portal development by means of involvement of the WaNPRC staff in the requirement gathering
   iv. New SAP Business Object's reports which extremely enhance all aspects of the day-to-day operations of the Center
   v. Current ARMS Developer acquired by ProKarma
   vi. Information Technology Services now reporting to Director of Center
4) Key outcomes or other achievements
   i. Establishment of the requirements to create workflow for ARMS using the Portal interface
   ii. Completion of Phase 2 of the CPro Training Portal
   iii. Completion of Facilities Portal
   iv. Completion of Phase 2 of the Billing Portal
   v. Creation of Grant Applications for NIH and Private Source
   vi. University of Washington has established a twice yearly technology sharing event

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

1. Excluded by Requester attended a LabKey Conference in Seattle
2. attended advanced SAP Business Objects classes
3. attended Windows Server administration classes
4. Excluded by Requester attended VMware 5.0 seminars
5. attended Dell AppAsure seminars
6. attended Windows Server 2012 administration web seminars
7. Excluded by Requester attended a Backup Strategy seminar
8. attended a Project Management seminar

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b Resource sharing

File uploaded: WaNPRC IT Section C5b.pdf

1. Completion of the **NPRC Animal Research Management System (ARMS) Consortium Charter**
   a. **Overview**
   The ARMS Consortium is a voluntary grouping of National Primate Research Centers (NPRCs) who have joined together to promote the utilization and ongoing development of a comprehensive Animal Research Management System (ARMS). Membership in the ARMS Consortium is open to any NIH-funded NPRC that wishes to join as a Participating Institution. The current consortium includes, University of Washington, Emory University, Yerkes Primate Research Center, University of California, Davis, and Harvard Medical School, New England Primate Research Center. Harvard Medical School is considered an ex-officio member due to its closure announcement in April 2013. New England will continue to be a participating member until its wind down target date of May 2015.

2. Establishment of **ARMS Weekly Standup Meetings**
   a. **Overview**
   ARMS Common Information Technology Groups meet to discuss tools to improve communication and coordination on the ARMS project, receive updates on progress on identified problems, and identify and prioritize new ARMS-related issues and challenges.

3. Establishment of **ARMS Steering Committee Meetings**
   a. **Overview**
   Associate Directors and IT Managers from CNPRC, NEPRC, WaNPRC, and YNPRC met to communicate and coordinate on the ARMS project, receive updates on progress of identified problems, and identify and prioritize new ARMS-related issues and challenges.

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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. | | TBD | | TBD | | Associate Director | Institutional Base Salary | 0.0 | | | 0.00 | 0.00 | 0.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **0.00**

## B. Other Personnel

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 5 | Other | 15.0 | | | 124,776.00 | 34,812.00 | 159,588.00 |
| **5** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **159,588.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **159,588.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. PC Lifecycle replacements Desktops/Laptops,Software,APC Battery replacements | 35,000.00 |
| 9. Oracle db edition maintenance, Dell Sever maintenance, TOAD Pro Maintenance, Partners Data Maintenance | 12,949.00 |
| **Total Other Direct Costs** | **47,949.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **207,537.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 207,537.00 | 87,166.00 |
| | | **Total Indirect Costs** | **87,166.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **294,703.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Information Technology – Admin Core 5887**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**SENIOR/KEY PERSONNEL:** A To Be Named individual is listed as Senior/Key on the budget because a new Associate Director will be hired prior to the start date. While this person is being hired Excluded by Requester is fulfilling the role as lead person for this division, and will pass on the role to the new Associate Director when they are hired.

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 1 | IT Manager | 3 | 32,271 | 9,004 | 41,275 |
| 4 | IT Developers | 12 | 92,505 | 25,808 | 118,313 |
| **5** | **TOTAL OTHER:** | **15** | **124,776** | **34,812** | **159,588** |

This category does not represent a significant deviation from the prior year.

**SUPPLIES:** The PC Lifecycle replacement are for desktop PCs that are categorized as supplies. These replacements are cyclically scheduled, and in the coming year, we anticipate a larger replacement cycle than the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Improvement and Modernization

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1. Proactively Approach Offsite Maintenance and Renewal Issues:
Routine maintenance and repairs of animal holding and support areas are crucial to the modernization program and will continue to be high priority. While great strides have been made with regard to obtaining centralized support for campus facilities, the Western leased facility is dependent upon WaNPRC support. Ongoing repairs and upgrades are prioritized based on a 3 year rotational plan and estimated cost per sq. foot for implementation of a sustainable long-range facilities maintenance plan.

2. Provide Fabrication Supplies and Materials for High Quality Production:
Machine Shop services provides, procurement, design, fabrication, repair and maintenance of animal housing systems, assorted caging types, assemblies, compound and trapping structures, transfer boxes, husbandry support vehicles, cage lifts, and miscellaneous supplies such as animal watering system parts, grooming-contact bar panels, activity caging, mountings for mirrors and required rack and cage modifications and other miscellaneous enrichment devices.

3. Provide Ongoing Renewal of NHP Social Housing:
The WaNPRC has an insufficient number of modern cages capable of providing tactile social enrichment for study animals and therefore seeks support to purchase new innovative caging with this capability. Such caging will replace an excess of old-style cages and supplement underrepresented cage sizes.

4. Provide IM Plans to Install and Support Equipment and Alteration Requests:
The IM program in conjunction with support from operational components provide the support to initiate and install research and animal care program equipment and facilities upgrades.

### 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?

Excluded by Requester

File uploaded: WaNPRC B2.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?

Plans to proactively identify maintenance and repair issues continue with general facilities rounds done monthly. Interdivisional tours are taken to identify facility and program items that can be repaired prior to inspections. Plans to incorporate the newly renovated and constructed areas will be implemented upon occupancy. Due to the lack of available housing space during the Western construction project, painting in holding rooms was delayed and will be a primary focus in 2015, along with bumper rail, lighting and timer reviews. Plans to fabricate and modify lab products caging to accommodate a new rinse down drainage system that will be phased in over time as drain modifications are made will be ongoing for the next couple of years. Drain modifications will be made as each room is reviewed individually as to how to best accommodate the new trough drainage system. Newly renovated rooms at Western will be altered first prior to occupancy. Caging purchases are planned for 2015 as phase out of older caging continues. Modernization funds will be utilized to complement equipment as identified and prioritized based on determination of need and allocation of requested central funding for various projects and upgrades.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

### 1) Major activities:

Planning and Design for the **Animal Research Care Facility** providing expansion space for WaNPRC and the Department of Comparative Medicine has continued this year by staff normally involved working on Improvement and Modernization. This is a time commitment required for best outcome for WaNPRC. The Animal Research and Care Facility (ARCF) project will construct a new [redacted] $123.5 million centrally funded, below grade animal research facility, under the Portage Bay Vista on the University of Washington (UW) Seattle campus. The facility is intended to centralize and expand the University's animal care and research program capacity for the next 10 years. The facility will be designed to address the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) accreditation issues, a shortage of animal housing space, the need to reduce operational costs and provide flexibility to accommodate ongoing requirements for animal housing for research. This project will be the first on campus to combine NHP's with large and small animals within one vivarium and will be built between I-Wing and Foege buildings which currently provide space for both animal care programs. A Project Committee was appointed by the Provost to provide oversight of the project. The scope of the project has remained at the original estimate of providing housing space for approximately 300 additional NHP's. Construction related activities have begun such as fencing, rerouting pedestrian traffic and staging the construction site at February 2015. The project is scheduled for completion in May 2017.

Specific Animal Location

Design plans were finalized for the **Western 2nd floor Cage Wash Facility** with an original budget of $5.4 million to address deficiencies in space layout and cage wash and demolition of existing facilities began in April 2014. The occupants were moved to the former business office located on the 4th floor and that division was re-located on campus into existing office spaces which were reconfigured to support additional staff. These changes have been determined to increasingly support the Western facility as an animal care and research program. The expanded 2nd floor vivarium currently under renovation has an appropriate sized cage wash and surgical suite which are adjacent to the research labs. The construction project was complex due to the demolition of an existing loading dock requiring logistical changes such as rerouting of shipping and deliveries, temporary relocation of support staff remaining onsite such as shipping & receiving, facilities, husbandry and computer staff. The sani-pak waste disposal equipment located on the loading dock was temporarily removed requiring daily waste pick up. As reported last year, cost estimates grew due to unforeseen conditions and support structure required not previously to code. Additional funding was secured from the University Associate Vice Provost for Planning and Budgeting and departmental funding to ensure project success. Prior construction grant funding of $992,082 was used to add 4 animal holding rooms adjacent to the new cage wash and surgical suite. Space for this expansion project was planned by utilizing 2nd floor office support space allowing for an overall increase of [redacted] for animal care program space. Total project costs are estimated at $7.6 million and the completion date is on schedule as of March 11, 2015, with occupancy following in April, 2015. Surgery Lights and mobile surgery table supplied by 2014 Modernization funding.

Specific Animal Location

Planning and design continues for **I-Wing 3rd floor Facility** renovations needed to utilize vacated space in need of multiple upgrades. The first phase to renovate lab space for reproductive biology has been completed with Modernization funding and the lab is currently in use. Preliminary design plans have been completed for both a partial and a full renovation of additional vacated space. Additional I-Wing renovations on a larger scale to renovate and re-design original space in need of repair are also under review and supplemental funding is being actively pursued.

Maintenance completion in I-Wing included flooring repairs, caging repairs and modifications, and renovation of vacated lab space into new animal holding space. Offsite maintenance has greatly improved with additional centralized support for Western and 2nd floor construction funding.

### 2) Specific Objectives:

Planning is ongoing to facilitate coordination and funding mechanisms to provide the research resources requiring expansion or upgrades to space for breeding, animal holding, support and laboratory facilities.

3) **Significant results:**
Implementation of planning can be seen in the progress of continued major projects being planned and completed as discussed above. Multiple research and clinical divisions receive assistance with high quality animal research and care facilities and equipment to provide the environment for optimal scientific achievement.

4) **Key outcomes:**
I&M division continue to liaison many facets within and outside of the University to support and seek continued commitment for research resource needs. I&M division with central administration committee's has and continues to prioritize and coordinate complementary project goals and also meet ongoing maintenance and repair needs as required for animal care.

## 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

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Excluded by Requester | | | | | Assistant Director | 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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. Maintenance, fabrication, supplies, and materials | 157,203.00 |
| 9. Improvements to the cage washing systems | 161,240.00 |
| 10. Maintenance, repairs, and services | 180,725.00 |
| **Total Other Direct Costs** | **499,168.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **499,168.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 337,928.00 | 141,930.00 |
| | | **Total Indirect Costs** | **141,930.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **641,098.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Improvement and Modernization - 5888**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**SUPPLIES:** This budget has been increased by $100k to accommodate the significant costs associated with cyclical cage alterations and repairs projected for the coming year.

**ALTERATIONS AND RENOVATIONS:** As originally budgeted on the competitive application, we have been planning to perform renovations associated with new cage washing systems in Y54. This amount is consistent with the application.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Colony Services

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1) Improve Research Support
2) Improve Teamwork
3) Continue to develop productivity and accountability
4) Improve Communication

### 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: WaNPRC_Colony_Services_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_Colony_Services_B4.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?

With the implementation of the flush system, time spent by the husbandry staff dumping pans and processing the waste will be greatly decreased. This will allow for staff to provide more support for both research projects as well as clinical support which will in turn free up time for the clinical staff to provide more support to the research projects. By having husbandry staff assisting other units, they can become more involved with the projects in their work area, which will improve communication and foster a team oriented approach to raise the quality of our research projects.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

In the past year the Western Avenue facility has had a major renovation. In respect to Colony Services this has increased animal holding capacity as well as a redesigned cage wash facility with more space and updated equipment to allow for more efficient cleaning. The I-Wing facility has also had minor renovations adding an additional animal housing room.

At all three facilities the current method of using dry pans and bedding to handle daily animal waste has been reviewed and found to be outdated, specifically by having the animal care staff handle the waste multiple times in order to take it from the animal housing room through the autoclaving process and finally disposal as well as the dry pan system being less sanitary for the animals. A proposal was made and subsequently approved to change to a modern mobile manual flush rack system that will allow the waste to be disposed of in the housing room via the sanitary sewer. Currently cage conversions have been ordered so that this conversion can be started in the next year.

Husbandry staff are being trained to perform additional research and clinical support duties such as sedation/ recovery, oral medication preparation/ administration, detailed observations and sample collections. These duties are based on the current job descriptions of the Animal Technician series (AT 1 to 3) and also gives the husbandry staff the ability to pursue more technical positions within the WaNPRC by providing them with background and hands-on training while taking an active role in the research projects and clinical needs in their assigned work areas. The success of this ongoing training was seen in the past year with 25% of the Animal Technicians accepting higher level positions within the WaNPRC.

The Infant Primate Research Laboratory was divided in keeping with the standard divisions of responsibilities in the center. The care of the animals (husbandry, nursery rearing, veterinary, and behavioral aspects) were maintained within the Division of Primate Resources and are now referred to as the “RR-wing”, while the scientific/experimental components were placed in the Division of Developmental and Reproductive Services. Reporting and budgetary divisions were set along these lines. While the husbandry staff at the RR-wing have been supporting the timed mating program, in the past year a portion of these animals have been moved to the Western facility and set up into harem groups to increase production. The husbandry staff have now been trained to perform sex-skin readings to assist in tracking conception dates for these animals. We had 41 infants born and cared for in the RR-Wing 03/01/15 thru 02/17/15.

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

Colony Services staff are still supported in AALAS certification by the WaNPRC paying for the study materials, membership and exam fees. We are also able to provide some monetary reward in the form of additional pay increments for staff passing the exams. Training is also provided to the husbandry staff to perform sedation/ recovery of animals, sample collection and medication prep/administration.

## 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

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 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 | | | | | | |
| 32 | Other | 329.4 | | | 1,053,218.00 | 354,787.00 | 1,408,005.00 |
| **32** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **1,408,005.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **1,408,005.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 6,000.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **6,000.00** |

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

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

# RESEARCH & RELATED BUDGET - SECTIONS F-K

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 723,305.00 |
| 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. Laundry, equipment maintenance contracts, solid waste disposal, bedding | 296,598.00 |
| **Total Other Direct Costs** | **1,019,903.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **2,433,908.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 2,433,908.00 | 1,022,241.00 |
| | | **Total Indirect Costs** | **1,022,241.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **3,456,149.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Pathology

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1)Diagnostic Pathology Services: Diagnosis and containment of diseases affecting colony animals and provision of research and diagnostic pathology support and expertise to all projects performed at the WaNPRC
2)Tissue Distribution Program: Continue operation of the TDP as an efficient resource to provide investigators within and outside the WaNPRC valuable NHP tissues.
3)Teaching and Education: Provision of professional mentoring and instruction in gross pathology, histopathology and cytopathology of all domestic/non-human animals to residents of the WaNPRC and the UW DCM, and to present scientific findings at local, national and international meetings
4)Research: Performance of collaborative and independent research related to comparative medicine and WaNPRC studies

### 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: WaNPRC_Pathology_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_Pathology_B4.pdf

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

Besides publications (see above), CPS pathologists routinely participate and present findings in the annual Primate Pathology Workshop; the workshop now is now a component of the annual meeting of the American College of Veterinary Pathologists and is well-attended by national and international pathologists and clinicians interested in non-human primate pathology. Also, the pathologists actively participate in the NPRC Pathology Working Group Consortium; the pathologists presented an International Virtual Slide Conferences attended by PWG pathologists, NPRC clinicians, and pathologists and veterinarians from other national and international institutions working with NHP's. The Virtual Slide Conferences occur on a monthly basis, with presentations rotating between the various Centers, and CPS pathologists routinely participate in the conferences. In 2014, the CPS Virtual Slide Conference presented the following cases: Clinical malaria in an immunosuppressed pigtail macaque, polioencephalomalacia in a pigtail macaque likely secondary to water deprivation and hypernatremia, Simian-AIDS-Associated disseminated cytomegalovirus infection in a pigtail macaque, SHIV-Associated proliferative-occlusive arteriopathy without lung involvement in a rhesus macaque, and Simian-AIDS-Associated septic nephritis (due to E. coli) in a pigtail macaque.

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

The CPS plans to continue its mission to provide diagnostic and pathology research expertise for spontaneous and experimental diseases, to manage the Tissue Distribution Program, to provide professional mentoring and instruction to staff and post-DVM graduate students and residents from the Center and from the University of Washington's Department of Comparative Medicine, to perform and publish collaborative and independent research, and to assist in research project planning and development in collaboration with core and outside researchers. Two peer-reviewed manuscripts have been submitted with CPS personnel as coauthors:

Submitted

Submitted

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

The **Comparative Pathology Service** (CPS) missions are to provide diagnostic and pathology research expertise for spontaneous and experimental diseases, to manage the Tissue Distribution Program (TDP), to provide professional mentoring and instruction to staff and post-DVM graduate students and residents from the Center and from the University of Washington's Department of Comparative Medicine (DCM), to perform collaborative and independent research, and to assist in research project development in collaboration with core and outside researchers. The unit is staffed by 2.0 FTE ACVP board certified veterinary pathologists, 1.0 FTE histotechnologist who manages the Histology Laboratory, and 1.0 FTE Research Technician who assists in necropsy and manages the TDP. Both pathologists are boarded in Anatomic Pathology and one is dual-boarded in Clinical Pathology as well. This has allowed provision of cytopathology and hematology review services for the Center and the DCM.

Directed by one of the pathologists, the TDP continues to be a vital resource that conserves research animal resources while serving the needs of investigators at the UW and throughout the nation. During the last year, 412 tissues were distributed from 38 different animals to 28 clients in academia and commercial laboratories. Tissues from some of these animals were also referred for histological evaluation and screening of colony health status. TDP services are designed to keep pace with the needs of local, regional, and national investigators. The TDP service incorporates, among other methods, optimization of whole body and brain perfusions, antemortem tissue acquisition, and preparations of virtually any tissue/organ samples utilizing a variety of preservation modalities. The TDP coordinates with various WaNPRC groups to perform terminal surgeries prior to necropsy with the goal of technique development and refinement. The TDP also offers opportunities to review anatomy, practice sedation, phlebotomy, and intubation techniques.

In the last year, there were 290 accessions logged into the Center's Histology Laboratory, and in addition there were 77 special procedure requests from researchers. There were 233 full necropsies that often are research cases, and the vast majority of necropsies include gross and histopathological examination of all tissues/organs. Last year the CPS processed and analyzed 5,914 paraffin-embedded blocks, and additionally there were 57 frozen brain sections processed. Last year there were 22 cytopathology cases, 14 hematology reviews, 34 biopsies, and 97 special procedures performed such as immunohistochemistry and special stains. The CPS is now performing histopathology of breeding animals at both Arizona and Texas breeding facilities as well. Finally, numerous research necropsies on non-accessioned cases, such as perfusions, were performed with the CPS staff assisting researchers.

In 2014 CPS personnel were coauthors on 4 peer-reviewed manuscripts; and 2 other additional peer-reviewed manuscripts have been submitted. During 2014, 17 presentations were given that included seminars given to DCM residents, staff and faculty, International Virtual Slide conferences given to veterinary pathologists and pathology residents, Pathology Rounds presentations given to Center clinicians, technicians and staff, and presentations at national/international scientific meetings. CPS pathologists routinely participate in the annual Primate Pathology Workshop as well; the workshop now is a well-attended component of the annual meeting of the American College of Veterinary Pathologists. Also, the pathologists actively participate in the NPRC Pathology Working Group Consortium; the pathologists presented an International Virtual Slide Conferences attended by PWG pathologists, NPRC clinicians, and pathologists and veterinarians from other national and international institutions working with NHP's. The CPS pathologists provide regular seminar-style training of Post-DVM graduate students in the DCM, and routinely provide informal and formal pathology instruction to clinical veterinarians, and Center researchers and technicians, including didactic lectures in DCM courses. The teaching aspects prepare Post-DVM graduate students and Center clinical veterinarians to sit for the ACVP Board Examination or for the American College of Laboratory Animal Medicine Certification Examinations. The CPS has continued its teaching/training opportunities for animal technicians and comparative medicine residents as well.

**2014 Publications by the CPS:**

1. Excluded by Requester
Excluded by Requester Blood transfusion of Chagas disease in two immunosuppressed pigtailed macaques (*Macaca nemestrina*). Comp Med, 64:63-65, 2014.
2. Excluded by Requester
Excluded by Requester Oral squamous cell carcinoma in a pigtailed macaque (*Macaca nemestrina*). Comp Med, 64:234-239, 2014.

3. Excluded by Requester Excluded by Requester Deep transcriptional sequencing of mucosal challenge compartment from rhesus macaques acutely infected with simian immunodeficiency virus implicates loss of cell adhesion preceding mucosal activation. J Virol, 88:7962-7967, 2014.

4. Excluded by Requester Excluded by Requester Human embryonic-stem-cell-derived cardiomyocytes regenerate non-human primate hearts. Nature 510:273-277, 2014.

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

The TDP coordinates with various WaNPRC groups to perform terminal surgeries prior to necropsy with the goal of technique training, development and refinement. The TDP also offers opportunities to review anatomy, practice sedation, phlebotomy, and intubation techniques to investigators and Center personnel. The CPS pathologists provide weekly seminar-style training of Post-DVM graduate students in the DCM, and routinely provide informal and formal pathology instruction to clinical veterinarians, and Center researchers and technicians, including didactic lectures in DCM courses. The teaching aspects prepare Post-DVM graduate students and Center clinical veterinarians to sit for the ACVP Board Examination or for the American College of Laboratory Animal Medicine Certification Examinations. The CPS has continued its teaching/training opportunities for animal technicians and comparative medicine residents as well.

## C. COMPONENT PRODUCTS

### C.1 PUBLICATIONS

Not Applicable

### C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

### C.3 TECHNOLOGIES OR TECHNIQUES

The TDP offers opportunities for investigators and Center personnel to refine or develop techniques in a living animal. Examples during the last year include development of an indwelling catheter for lumbar cerebrospinal fluid sampling, neurosurgery refinement/improvement for placing head chambers, head posts and craniotomies, and neurosurgery refinement for spinal column implants.

### C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

### C.5 OTHER PRODUCTS AND RESOURCE SHARING

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b Resource sharing

File uploaded: WaNPRC_Pathology_C5b.pdf

The TDP is a vital resource sharing program that conserves research animal resources while serving the needs of investigators at the UW and throughout the nation. During the last year, 412 tissues were distributed from 38 different animals to 28 clients in academia and commercial laboratories. Tissues from some of these animals were also referred for histological evaluation and screening of colony health status. TDP services are designed to keep pace with the needs of local, regional, and national investigators. The TDP service incorporates, among other methods, optimization of whole body and brain perfusions, antemortem tissue acquisition, and preparations of virtually any tissue/organ samples utilizing a variety of preservation modalities.

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Excluded by Requester | | | | | Associate Director | 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 | | | | | | |
| 4 | Other | 27.17 | | | 238,027.00 | 69,126.00 | 307,153.00 |
| **4** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **307,153.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **307,153.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 3,000.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **3,000.00** |

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

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

# RESEARCH & RELATED BUDGET - SECTIONS F-K

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. Materials and supplies | 21,913.00 |
| 9. Consultant services | 9,326.00 |
| **Total Other Direct Costs** | **31,239.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **341,392.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 341,392.00 | 143,385.00 |
| | | **Total Indirect Costs** | **143,385.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **484,777.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Division of Primate Resources – Pathology - 5893

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

### PERSONNEL:

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 1 | Senior Research Scientist | 7.20 | 89,682 | 25,021 | 114,703 |
| 2 | Research Scientist | 13.20 | 112,119 | 31,281 | 143,400 |
| 1 | Husbandry/Veterinary Staff | 6.77 | 36,226 | 12,824 | 49,050 |
| **4** | **TOTAL OTHER:** | **27.17** | **238,027** | **69,126** | **307,153** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Breeding Colony Services

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1) Continue to maintain breeding programs at the Seattle Colony facilities to meet the WaNPRC's research requirements for NHP fetuses of known gestational age, infant primates, and their pregnant dams.
2) Significantly expand production of pigtail macaques available through the breeding colonies via colony expansion and importation, at SNBL USA, the NIRC, and at a newly identified animal facility in Mesa, Arizona.
3) As part of the significant import plans, to establish a Breeding Colony-wide screening and treatment program for tuberculosis (in addition to the existing screening for specific viruses).
4) In conjunction with the WaNPRC Genetics and Demographics Program, continue to apply improved population demographic monitoring and forecasting software tools to productive and economic management of the macaque breeding colonies.

### 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: WaNPRC_Breeding_B2.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?

In the coming year, we will focus on ensuring the SPF status of our breeding colony. We will segregate the colony into smaller breeding groups and test SPF animals repeatedly to ensure that they are virus free. Weanlings will also be maintained in smaller groups, and mixing of groups will be minimized. We will continue to breed questionable animals, but offspring will need to be tested repeatedly, because SRV can be transmitted vertically.
We have recently started breeding animals in the compounds in the Western building in Seattle. In addition to the timed-mating in RR-wing, this may provide an additional source of pigtailed macaques for research. We will continue to develop our relationships with our Indonesian colleagues to ensure that animals will be available when we are ready to import. Similarly, we are working with our colleagues at other facilities to develop transportation strategies for importation of nonhuman primates.
With the increased genetic characterization of the colony, we are building the tools to examine the relationship of genetics to specific phenotypes. By aligning the microsatellite MHC data with the more detailed MHC RNA analysis, we will infer specific haplotypes for all animals, and investigate possible associations with phenotypes using statistical techniques such as cluster analysis and case-control comparisons.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

Major activities: As of 2013, primate breeding operations supporting the WaNPRC are now located at four separate facilities. The on-campus breeding program (Seattle Colony) maintained within the UW Seattle facilities is a small (N=50) breeding colony of pigtail macaques (*Macaca nemestrina*) used principally for the production of time-mated pregnancies and newborn infants specifically required for some research programs. The three primary domestic-based breeding programs are housed in indoor-outdoor group harem housing facilities at the Shin Nippon Biological Laboratory's Scientific Resource Center at Alice, TX (SNBL-SRC) for pigtail macaques, at the New Iberia Research Center (NIRC, New Iberia, LA) for pigtail and rhesus macaques (*Macaca mulatta*), and at the new Arizona Breeding Colony (ABC, near Mesa AZ).

Specific objective, results, and outcomes:
1) Continue to maintain breeding programs at the Seattle Colony facilities to meet the WaNPRC's research requirements for nonhuman primate fetuses of known gestational age, infant primates, and their pregnant dams. Staff expertise, equipment, and facilities are available to provide timed-mated breeding, and 24-hour care of neonatal and infant nonhuman primates. During the past year there were a total of 40 timed-mating pregnancies, providing fetuses for research and 25 live infants which were maintained at the Infant Primate Research Laboratory.

2) Significantly expand production of pigtail macaques available through the breeding colonies via colony expansion and importation, at SNBL USA, the NIRC, and at a newly identified animal facility in Mesa, Arizona. All three off-site breeding colonies are successfully producing infants, with an increase in live births from 197 in 2013 to 255 in 2014. We have a well-developed plan to expand the breeding colony from approximately 900 pigtails macaques to at least 1400 animals to meet the current demands. The Arizona Breeding Colony (ABC) provides housing for animals in indoor-outdoor runs and a breeding program directly managed by the DPR staff. We now house 344 pigtail macaques at ABC, 276 pigtail macaques at NIRC, and 327 animals at SNBL-SRC. The WaNPRC also maintains a breeding colony of 102 rhesus macaques at NIRC to provide animals for WaNPRC-based neurosciences and transplant research programs.

3) As part of the significant import plans, to establish a Breeding Colony-wide screening and treatment program for tuberculosis (in addition to the existing screening for specific viruses). Due to more pressing concerns regarding SRV serological test results (see section below regarding challenges), imports have been delayed, and this project has been placed on hold.

4) In conjunction with the WaNPRC Genetics and Demographics Program, continue to apply improved population demographic monitoring and forecasting software tools to productive and economic management of the macaque breeding colonies. We continued to advance our demographic monitoring and management using software tools such as R, Mathematica, and Pedscope on data extracts from the WaNPRC ARMS electronic records system, both for retrospective analysis as well as prospective computer modeling for the WaNPRC colonies. This unit also provides population dynamics data regarding the effects of individual animal harvests from the breeding groups. Information of this type has been used to modify animal harvest to provide nonhuman primate resources to WaNPRC-based and other projects while still protecting the long-term health and sustainability of the breeding operations. Our genetic monitoring system currently uses microsatellite markers for genotyping of all pigtailed macaques and rhesus macaques in our breeding colony to infer parentage. In addition, this past year we have had microsatellite analysis of the MHC region performed on the animals in the breeding colony to aid in selection of animals for transplantation projects. Also, in collaboration with the Oregon National Primate Research Center (ONPRC), RNA-based MHC characterization is performed on 100-200 animals per year in our pigtail macaque colony.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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 goal of maintaining an SPF breeding colony has been challenged by concerns about SRV serological test results. Several animals have shown seropositivity to SRV on Western blot containing antigens from SRV-1, 2, and 5. Extensive efforts to detect viral antigens through PCR, viral culture, and RNA sequencing have not identified a virus, but the serologic results are of concern. Further investigation of this challenge and separation of animals into smaller groups to prevent possible viral spread will delay expansion of the colony. Also, until this situation is resolved, importation efforts are on hold.

### 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 18,330.00 | 5,114.00 | 23,444.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **23,444.00**

## 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 | Other | 15.6 | | | 131,660.00 | 36,734.00 | 168,394.00 |
| **5** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **168,394.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **191,838.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 2,357.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **2,357.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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)** | **194,195.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 194,195.00 | 81,562.00 |
| | | **Total Indirect Costs** | **81,562.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **275,757.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

**K. Budget Justification*** File Name: DPR-BreedingColonyServices.pdf
(Only attach one file.)

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

**BUDGET JUSTIFICATION: Division of Primate Resources - Breeding Colony Services_Core-5894**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 1 | Veterinarian | 3.6 | 37,892 | 10,572 | 48,464 |
| 2 | Veterinarian Supervisor | 4.8 | 43,548 | 12,150 | 55,698 |
| 2 | Program Manager | 7.2 | 50,220 | 14,012 | 64,232 |
| **5** | **TOTAL OTHER:** | **15.6** | **131,660** | **36,734** | **168,394** |

This budget is changed significantly from the prior year. The change is associated with reducing the number of personnel, especially husbandry staff, on the P51. This is consistent with the financial model of the external breeding colonies described in our *WaNPRC Macaca Nemestrina Specific Pathogen Free Breeding Colony* project (U42OD011123). Our intent is that the personnel resources associated with the operations of the breeding colony be largely funded by program income. However, at this time, not all personnel can be supported by program income activities due to the ongoing work and changes described in the narrative section of this progress report. Therefore, some support for veterinary and supervisory staff is requested for the coming year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Behavior Management Services

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1)To maintain and oversee the implementation of the IACUC approved WaNRPC Environmental Enhancement Plan (EEP).
a.Assure that nonhuman primates are housed socially unless exempted for experimental or veterinary reasons.
b.Assure that all nonhuman primates receive environmental enrichment as outlined in the EEP and attendant SOPs
2) Objectively assess behavior of nonhuman primates at the WaNPRC and provide evaluation, treatment, and assessment of treatment outcomes for those animals exhibiting moderate to severe abnormal behaviors.
3) Establish and administer a comprehensive positive reinforcement training program at the WaNPRC.
4) Actively contribute to currently accepted professional standards of animal welfare through participation in professional membership activities and publication.
5) Train WaNPRC employees, veterinary residents and students in behavioral observations, behavioral ecology of NHP species housed at the WaNRPC, and behavioral management techniques.
6) Continue active participation in consortium activities through the Behavioral Management Consortium.

### 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: WaNPRC_Behav_Mgmt_Svc_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_Behav_Mgmt_Svc_B4.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 our socialization, enrichment and behavioral monitoring/treatment functions in the upcoming year.
We will continue to train staff, students and veterinary residents regarding identification of abnormal behaviors and behavioral management techniques.
Excluded by Req will continue to serve on the Behavioral Management Consortium.
In addition we will:
•Implement the behavioral module in ARMs and assure that relevant data are available to WaNRPC staff and regulatory agencies.
•Complete research projects regarding the effects of leafy greens on alopecia and increased cage size on locomotor and prepare those data for publication.
•Continue to collaborate with veterinary staff and quantify therapeutic effects of various pharmaceutic therapies. By the end of 2015 we expect to have sufficient data to compare effects of several different drugs on behavioral outcomes.
•Continue to collect hair on NHPs during the semi-annual clinical exams in our Seattle and Arizona facilities for comparison of cortisol levels between laboratory- and indoor/outdoor group-housed macaques. We will also utilize these samples to further characterize extreme behavioral phenotypes.
•Expand the Animal Training Program to encompass additional behaviors and provide training to animal care staff regarding the principals of Positive Reinforcement Training.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

Behavioral Management Services (BMS) has made considerable strides this year in advancing both the service and research components of our Specific Aims.

Socialization of is recognized as the most best way to maintain the welfare of laboratory housed NHPs, as well as preventing and ameliorating behavioral problems. Our goal is to maintain every non-exempted animal in social contact. To that end, in the past year we have conducted 270 social introductions for pairs and trios and 12 small group introductions in our Seattle colony.

Every NHP housed at the WaNPRC receives daily enrichment in the form of food treats, destructible enrichment or foraging. Daily enrichment is distributed by animal care staff and BMS monitors documentation to assure that a wide variety of enrichment items, including complex and frozen treats are provided. In addition to daily treats, animals that are housed singly or that have behavioral problems receive additional enrichment items from Behavioral Management technicians.

In order to provide the best diagnosis and treatment for animals evincing behavioral abnormalities BMS has continued to objectively assess nonhuman primates housed at the WaNPRC to detect abnormal and atypical behaviors as well as apply standard and experimental therapies for these problems. During the last year every animal at the center was assessed through quarterly Zones monitoring (a total of 1958 observations). Additionally, our group completed 5-minute real-time quantitative homecage observations on all animals housed in the Seattle colony of the WaNPRC. These data will be used to create normative behavioral profiles for the species housed at our center and also to compare the efficacy of this monitoring method with our Zones monitoring system

In the past year we have worked closely with veterinary staff to quantitatively assess ameliorative effects of various pharmaceutic interventions on self-injurious behavior. To date we have provided quantitative data for 6 animals that have been treated with various drug interventions.

We have also published several papers on the subject of alopecia, including a methodology paper for quantitatively assessing alopecia in a large colony setting. We are currently conducting a study evaluating the efficacy of leafy green enrichment for the amelioration of alopecia.

Last year we identified a behavioral therapy for locomotor stereotypy. In a pilot study we found that locomotor stereotypy was significantly reduced when animals were given access to both a lower and an upper cage. We will be presenting these data at the 2015 annual meeting of the American Society of Primatologists. In 2014 we also screened an additional 50 animals for inclusion in a larger study.

We are continuing to collect hair samples on nonhuman primates to assay for cortisol. In 2014, collection of hair cortisol in pregnant dams and their infants housed at the Infant Primate Research Laboratory revealed a significant relationship between the increase in maternal cortisol during pregnancy and infant cortisol at birth. These data were presented at the 2014 annual meeting of the American Society of Primatologists and are currently being prepared for publication. We are also continuing to collect hair on NHPs of all ages during the semi-annual clinical exams in our Seattle and Arizona facilities for comparison of cortisol levels between laboratory- and indoor/outdoor group-housed macaques. In collaboration with Excluded by Requester Excluded by Requester at the University of Massachusetts we have also utilized hair cortisol to characterize HPA axis activity in two extreme behavioral phenotypes (hyperactivity and self-injurious behavior).

In the past year our group developed and utilized a long-term behavioral taxonomy for NHPs that is capable of assessing behavior across all ages and housing conditions (single cage to large group housing). We have utilized this taxonomy to assess the effects of early continuous socialization on 19 infants reared in the Infant Primate Research. We have also utilized this taxonomy to compare behavior in nursery-reared and mother-reared females housed in our Arizona Breeding facility. We will be presenting a portion of these data at the 2015 annual meeting of the American society of Primatologists and preparing the data for publication in the near future.

The Animal Training Program (ATP) was established to promote the well-being and safety of the nonhuman primates, reduce the need for chemical restraint, and enhance the safety of staff. Use of positive

reinforcement training (PRT) techniques based on the principles of operant conditioning brings the WaNPRC into compliance with the revised Guide for the Care and Use of Laboratory Animals (2011) which emphasizes the necessity of PRT as a means of enhancing the wellbeing of nonhuman primates in a laboratory setting. In 2014, the Animal Trainer received 16 training requests from research and the Department of Primate Resources (DPR) staff. Of the 16 training requests, 44% were from research groups while the rest were from Veterinary Services, Research Support Services, and the Behavioral unit within DPR. The Animal Trainer worked with 72 subjects; 40 *M. nemestrina*, 24 *M. fasicularis*, and 8 *M. mulatta*. Behaviors trained included: pole/collar and chair training, non-sedated blood collection, presentation for menses checks, running into trapping runs and transfer boxes, as well as desensitization to multiple research methods including head-chamber cleaning. In addition to training, the Animal Trainer consulted with research groups within the WaNPRC regarding ways the ATP could help or improve research objectives.

Our group has worked with the WaNPRC Information Technology department to create a behavioral module within ARMS. This project is near completion and will be implemented in the next fiscal year.

As listed in C.5.a (Other Products). in the previous year BMS has published 4 papers in peer reviewed journals, one of which was an invited paper by [redacted] a special issue on nonhuman primate models of human psychiatric disease for the ILAR Journal. BMS staff has also given one invited address and been presenters or co-authors on 8 other talks/presentations. In addition [redacted] served as the chair of the Scientific Program for the annual meeting of the American Society of Primatologists in 2014.

Excluded by Requester

Excluded by Requester

[redacted] continues to serve on the Behavioral Management Consortium (BMC) and participated in a BMC sponsored symposium last year. [redacted] will be submitting invited manuscripts for a special issue of the American Journal of Primatology arising from this symposium.

Excluded by Requester

Excluded by Requester

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

As outlined in Specific Aim 6, one of the aims of Behavioral Management Services is to train employees, students and veterinary residents regarding specific aspects of behavioral management. Every WaNPRC employee who will be working with the animals receives two one-hour training classes from BMS staff. One class focuses on behavioral ecology, the Environmental Enhancement Plan and behavioral management techniques and the other focuses on identifying and reporting abnormal and atypical behaviors. During the last year we have trained 68 individual in these classes. In addition, we also provided specialized one-on-one-training regarding nonhuman primate behavior and behavioral management techniques for 13 senior veterinary residents [redacted] also teaches a two-quarter for-credit laboratory for undergraduate students focusing on nonhuman primate behavior and behavioral management research techniques. During the past year 6 undergraduate students have been trained in the lab.

Excluded by Requester

## 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

#### C.5.a Other products

File uploaded: WaNPRC_Behav_Mgmt_Svc_C5a.pdf

#### C.5.b Resource sharing

NOTHING TO REPORT

Excluded by Requester (2014) Alopecia in three macaque species housed in a laboratory environment. American Journal of Primatology, doi:101002/ajp.22236.

Excluded by Requester (2014) A simple alopecia scoring system for use in colony management of laboratory-housed primates. Journal of Medical Primatology, doi 10.1111/jmp.12107.

Excluded by Requester (2014) Hair loss and hypothalamic-pituitary-adrenocortical (HPA) axis activity in captive rhesus macaques. Journal of the American Association for Laboratory animal Science, 53(3), 261-266.

Excluded by Requester (2014) Nonhuman primate models of depression: effects of early experience and stress. ILAR Journal, 55(2), 259-273.

**During the past year BMS has presented or been co-authors on eight presentations at national meetings.**

In Press

In Press

In Press

In Press

In Press

In Press

In Press

Excluded by Requester 2014, Monkeying around: Enrichment for laboratory-housed primates. *Invited Address: WBAALAS Trade Fair March 2014*

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Excluded by Requester | | | | | Associate Director | 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 | | | | | | |
| 7 | Other | 81.96 | | | 374,669.00 | 114,577.00 | 489,246.00 |
| **7** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **489,246.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **489,246.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 6,000.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **6,000.00** |

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

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

# RESEARCH & RELATED BUDGET - SECTIONS F-K

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 0.00 |
| 2. Publication Costs | 797.00 |
| 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. Materials and supplies | 14,150.00 |
| 9. Conference registration fees | 1,500.00 |
| **Total Other Direct Costs** | **16,447.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **511,693.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 511,693.00 | 214,911.00 |
| | | **Total Indirect Costs** | **214,911.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **726,604.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Division of Primate Resources - Behavior Management Services - 5895**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 4 | Research Scientist | 45.96 | 240,759 | 67,172 | 307,931 |
| 3 | Husbandry/Veterinary Staff | 36 | 133,910 | 47,405 | 181,315 |
| **7** | **TOTAL OTHER:** | **81.96** | **374,669** | **114,577** | **489,246** |

In the coming year, Behavior Management Services will add several personnel. These additional staff resources are transferred from other groups within the Division of Primate Resources to consolidate related services in one group to increase efficiencies and coordination.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Research Support Services

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1) Continue to offer outstanding research services.
2) Increase support of technical services.
3) Continue to support noninvasive imaging techniques.
4) Refine teamwork and communications

### 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: WaNPRC_Rsch_Support_Svc_B2.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 RSS group has been and will continue to provide training to the Primary Investigator staff, the Clinical staff and the Husbandry staff in technical procedures. This training along with staff covering at all three facilities will provide more consistent data as well as the ability to provide similar services and any of the facilities. RSS is taking a more aggressive approach with pre study meetings with the PI staff to ensure that thorough preparations are in place prior to the study initiation.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

During the past year the RSS group has added several new technical services. In support of AIDS research they have added fecal transplants, electroporation, rectal cytobrush and long term ART (antiretroviral therapy) treatments orally and injectable as well as support for timed mating procedures while continuing to support endoscopy studies. They have also been supporting the timed mating program to supply investigators with infants for studies. In this past year they have increased production by moving a portion of the timed mating colony to the group housing at the Western Facility and setting up harem breeding with visual sex-skin reading to track conception dates. These are then verified by ultrasound measurements. These groups are set up and monitored by RSS, behavioral, colony, and veterinary staff. We have also expanded the support for tether transplant studies to the Western and RR-Wing Facilities and expanded the AIDS studies to the RR-Wing with a pediatric SHIV study in neonatal macaques. The RSS group has taken over the research support for the cardiac infarction studies from the investigator's staff as well as increasing the capacity of animals they can maintain on tether systems. They have begun performing unsedated procedures using the Table Top Restraint Device (TTRD) for projects approved with this form of restraint. Members of this group have been mentioned in 4 publications this past year in acknowledgement of the support they have provided for these researchers.

During the past year RSS staff from all three facilities have been routinely assisting at the other facilities as needs arise. This has allowed them to standardize methods and procedures across the three facilities as well as giving the WaNPRC more flexibility in the types of procedures that can be performed in each as well as the ability to adjust for unforeseen events while maintaining scheduled procedures. RSS staff continue to provide anesthesia support for imaging and surgical procedures when needed. Recently they have rolled out an on-line fasting request which automates the majority of the previous steps required to create these types of requests. Since this takes information directly from the ARMS, the information such as project assignment and animal location are always up to date.

**RSS Procedures for 03/01/15 - 02/28/15**

| Description | Totals |
|---|---|
| Amniotic Fluid Draw | 44 |
| Biopsy, lymph node | 249 |
| Sample collection | 719 |
| Blood Draw | 3178 |
| Bone marrow aspiration | 32 |
| CSF collection | 40 |
| Infusion procedure | 21 |
| Injection | 221 |
| Inoculation | 236 |
| Tether procedure | 115 |
| MRI (Magnetic Resonance Imaging) | 24 |
| Swab | 356 |
| Transfusion | 6 |
| Ultrasound procedure | 75 |
| Biopsy, skin | 14 |
| Cytobrush | 301 |
| Fecal collection | 22 |
| Hair collection | 46 |
| Oral administration | 37 |
| Embryo Transfer | 4 |
| Biopsy, rectal | 69 |
| Bronchoalveolar lavage | 58 |
| Endoscopy | 386 |
| Lavage, rectal | 566 |

**Total RSS Procedures 6819**

Publications RSS has been involved with:

Excluded by Requester

Excluded by Requester et al. (2014). Human embryonic-stem-cell-derived cardiomyocytes regenerate non-human primate hearts. *Nature*. 2014 Jun 12;510(7504):273-7. doi: 10.1038/nature13233. Epub 2014 Apr 30.

Excluded by Requester (2014). Long-acting three-drug combination anti-HIV nanoparticles enhance drug exposure in primate plasma and cells within lymph nodes and blood. *AIDS*. 2014 Nov 13;28(17):2625-7. doi: 10.1097/QAD.0000000000000421.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Excluded by Requester | | | | | Associate Director | 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 | | | | | | |
| 7 | Other | 26.31 | | | 117,474.00 | 34,936.00 | 152,410.00 |
| **7** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **152,410.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **152,410.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 2,115.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **2,115.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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)** | **154,525.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Costs (MTDC) | 42.0 | 154,525.00 | 64,901.00 |
| | | **Total Indirect Costs** | **64,901.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center(PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **219,426.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Division of Primate Resources - Research Support Services - 5896**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 4 | Research Scientist | 10.2 | 49,593 | 13,836 | 63,429 |
| 2 | Program Manager | 6.51 | 39,059 | 10,897 | 49,956 |
| 1 | Husbandry/Veterinary | 9.6 | 28,822 | 10,203 | 39,025 |
| **7** | **TOTAL OTHER:** | **26.31** | **117,474** | **34,936** | **152,410** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Veterinary Medicine and Surgery

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1) To maintain the health of the nonhuman primate colony and improve animal welfare by implementation of the preventive medicine program and refinements in experimental techniques.
2) To investigate and treat episodes of animal illness and injury to promote animal health, and to identify and characterize new potential primate models of human diseases.
3) To provide and expand anesthetic and surgical services in support of research projects.
4) To provide training to investigators, staff, students, and residents in the care and use of laboratory animals.
5) To contribute to the knowledge base of primate veterinary medicine through presentations and publications.

### 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: WaNPRC_Vet_Svcs_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_Vet_Svcs_B4.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?

Construction of a new surgical suite at the Western facility will be completed in March 2015, and laparoscopic equipment has been purchased. We plan to increase our surgical support of AIDS-related research projects at the Western facility with this equipment in the new surgical suite. In addition, the number of AIDS-related research projects involving bone marrow transplantation supported with tethered vascular catheters is increasing, and this new facility will allow us to support these projects without having to transport animals frequently.

Excluded by Request [redacted] has been hired to augment the veterinary staff and increase research support capabilities. This will allow more opportunities for all WaNPRC veterinarians to develop and refine new experimental techniques and contribute to the knowledge base. For example, work will continue on development of bone grafting techniques for stabilization of cranial implants, and development of laparoscopic surgical techniques. Data regarding the characterization of SIV-induced coagulopathy by echocardiography and coagulation assays has been collected, animals with this condition have been successfully treated with clopidogrel, and these data will be published. We will continue to train veterinary students and veterinary residents in collaboration with the Department of Comparative Medicine. Within the WaNPRC, training of veterinary staff and research personnel in anesthesia and surgical technique will continue, and the certification process will be refined. Certification will include both written and practical examinations, which will be standardized to ensure consistent assessment of competency.
We will continue to treat clinical conditions in nonhuman primates as they arise. Recent challenges have positioned us to develop innovative strategies for prevention, containment, and elimination of infectious disease.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

Major activities: The Veterinary Services Unit (VS) is responsible for veterinary care of all nonhuman primates managed in the various locations within the WaNPRC. These responsibilities include investigation of spontaneous disease and provision of professional veterinary advice and services necessary to support research projects. Primary objectives of this unit are to provide veterinary care for humane use of laboratory nonhuman primates, provide surgery support and services necessary to maintain nonhuman primate welfare and support research programs, provide veterinary and technical expertise supporting primate-related research, provide training concerning veterinary aspects of nonhuman primate care and use, and assure compliance with various institutional, local, state and national policies, regulations, statutes, and recommendations regarding veterinary care of animals used in research and teaching. All the veterinarians in the VS unit have extensive experience regarding care and use of nonhuman primates in a research setting, are licensed to practice veterinary medicine, and are accredited by the USDA to evaluate animals and render health certificates needed for interstate or internationals shipment of animals.

Specific objectives, results, and outcomes:
1) To maintain the health of the nonhuman primate colony and improve animal welfare by implementation of the preventive medicine program and refinements in experimental techniques. VS staff performed 1,748 routine preventive medicine assessments and opened 937 cases in support of research procedures. New techniques developed during the past year include use of vascular grafts to restore arterial patency after coronary artery catheterization and placement of indwelling intrathecal catheters with access ports for administration of substances and withdrawal of CSF.

2) To investigate and treat episodes of animal illness and injury to promote animal health, and to identify and characterize new potential primate models of human diseases. During the past year, VS opened and managed 1,666 cases for spontaneous diseases or procedures related to research utilization. An additional veterinarian, Excluded by Requester was hired at the Arizona Breeding Facility to ensure optimal veterinary care for the breeding colony.

3) To provide and expand anesthetic and surgical services in support of research projects. VS supported 286 surgical procedures, 442 endoscopic procedures, and 58 imaging procedures that required general anesthetic administration. VS surgeons are investigating the use of bone grafting techniques to improve the long-term stability of cranial implants for neuroscience research. The procedure has been performed in one pilot animal, with encouraging results.

4) To provide training to investigators, staff, students, and residents in the care and use of laboratory animals. In conjunction with the Department of Comparative Medicine at the University of Washington, Veterinary Services of the WaNPRC provides training opportunities for veterinary students and veterinary residents. As part of their laboratory animal externship in Comparative Medicine, 10 fourth-year veterinary students spent a week out of their laboratory animal medicine externship at the WaNPRC, working with veterinary services personnel and gaining training and experience in primate medicine, surgery, and preventive care. Twenty-two third-year veterinary students toured the WaNPRC and were given a brief exposure to primate medicine and surgery. Two undergraduate students volunteered in order to get exposure to non-human primates, and were trained on basic procedures in sedated primates.

5) To contribute to the knowledge base of primate veterinary medicine through presentations and publications. Members of the VS unit collaborated with preparation of publications in peer-reviewed journals and presented web conferences for the NPRC Training Consortium Grand Rounds, the Clinical and Surgical Techniques Working Group, and the Integrity Compliance Working Group.

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

In conjunction with the Department of Comparative Medicine at the University of Washington, Veterinary Services of the WaNPRC provides training opportunities for veterinary students and veterinary residents. As part of their laboratory animal externship in Comparative Medicine, 10 fourth-year veterinary students spent a week out of their laboratory animal medicine externship at the WaNPRC, working with veterinary services personnel and gaining training and experience in primate medicine, surgery, and preventive care. Twenty-two third-year veterinary students toured the WaNPRC and were given a brief exposure to primate medicine and surgery. Two undergraduate students volunteered in order to get exposure to non-human primates, and were trained on basic procedures in sedated primates.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Excluded by Requester | | | | | Associate Director-Project Lead | 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 | | | | | | |
| 12 | Other | 117.9 | | | 743,940.00 | 224,697.00 | 968,637.00 |
| **12** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **968,637.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **968,637.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 6,000.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **6,000.00** |

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

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

# RESEARCH & RELATED BUDGET - SECTIONS F-K

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 0.00 |
| 2. Publication Costs | 1,000.00 |
| 3. Consultant Services | 0.00 |
| 4. ADP/Computer Services | 0.00 |
| 5. Subawards/Consortium/Contractual Costs | 0.00 |
| 6. Equipment or Facility Rental/User Fees | 0.00 |
| 7. Alterations and Renovations | 0.00 |
| 8. Clinical laboratory supplies | 8,000.00 |
| 9. Service contracts | 7,538.00 |
| 10. Training | 1,000.00 |
| **Total Other Direct Costs** | **17,538.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **992,175.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 992,175.00 | 416,714.00 |
| | | **Total Indirect Costs** | **416,714.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **1,408,889.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Division of Primate Resources – Veterinary Medicine and Surgery - 5898**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 3 | Research Scientist | 22.08 | 129,648 | 36,172 | 165,820 |
| 4 | Senior/Supervising Veterinarian | 35.82 | 385,781 | 107,633 | 493,414 |
| 5 | Husbandry/Veterinary Staff | 60 | 228,511 | 80,892 | 309,403 |
| **12** | **TOTAL OTHER:** | **117.9** | **743,940** | **354,345** | **968,637** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-Primate Diagnostic Services Laboratory

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The PDSL will continue actively assist the WaNPRC to fulfill its mission by providing laboratory support to improve the overall health and research readiness of the WaNPRC NHP colony and to provide research support to investigators upon request. To that end the PDSL aims to:

1)Continue current virus-infection-status monitoring programs and other diagnostic assays as requested by the Veterinary Staff
2)Provide services to research investigators and other institutions on a cost recovery basis as well as participate in collaborative research projects utilizing expertise and instruments
3)Maintain serum and DNA archival banks for use in retrospective surveys and genetic studies and support the NHPRC Consortium DNA Bank as keepers and distributors of select NHP genomic DNA sets

Specific Aim 1 This aim will be met by continuing existing operations as briefly described here. We anticipate a steady increase demand on the PDSL testing resources in the near term as we build our SPF M. nemestrina colony over the next several years. Moreover, through weekly laboratory meetings and frequent discussions, the PDSL routinely seeks ways to improve current assays and to shorten time to results. Due to the specialized skill set enjoyed by each PDSL member, we are able to quickly evaluate commercial diagnostic products (often designed for human diagnoses) in NHPs and to advise the veterinary staff the products use in NHP.

Specific Aim 2 The PDSL has established a price list allowing us to provide testing services to other Primate Centers commercial providers on a simple reagent and labor cost recovery basis. We also produce purified, concentrated viral antigen and have made this material available to other NPRCs and to a commercial NHP organization. The PDSL also oversees and operates on demand a FACSAria II flow cytometer and cell sorter uniquely located in a BSL-3. This instrument provides the means to safely sort live and infected cells. We have used the FACSAria to support an acute infections study where select sorted cell populations will be further analyzed with genomic and proteomic techniques and anticipate its use in support of the proposed Resource-related research project focused on pulmonary arteriopathy, [redacted] PI). The PDSL also maintains and makes available a BioRad bead-based multiplex analyzer that to support investigators serological interests. Our multiplex instrument is collaboratively used to support numerous projects including Simian Vaccine Evaluation Unit (SVEU) contract projects.

Excluded: Requested

Specific Aim 3 The archival plasma and DNA collections are a valuable and fairly unique resource recognized and queried by several over the years. Briefly, we retain plasma and DNA from every whole blood test sample submitted for routine testing. Our archives extent back for approximately 10 years and provide not only unique DNA samples but in many cases, serial plasma samples ideal for retrospective investigations. The NHP Genomic DNA Consortium is a separate project. The value of these genomic banks has increased with the availability whole full genome sequences for many NHP species. The WaNPRC through the PDSL collected, purified and maintains the Consortium's M. nemestrina, M. fascicularis, and Chlorocebus aethiops genomic DNA bank sets. Since the banks establishment, the PDSL has fulfilled 5 requests shipping a total 125 DNA samples to four investigators.

### 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: WaNPRC_PDSL_B2.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?

aims In an effort to meet the national demand for M. nemestrina, the WaNPRC will began exploring ways to produce research suitable SPF animals form non SPF animals. This has become a necessity due to low numbers of domestically available animals, import restrictions, and an accumulation of breeding capable non SPF (commonly, SRV positive) animals. The goal is to produce SPF F1 and F2 generations. Among the approaches are close monitoring and hand reaing infants from positive SRV-positive dams (short term) and

the developing candidate therapeutic SRV vaccines (long term). The PDSL will support these efforts as part of Aim 1 by providing virus diagnostic monitoring as well as characterization of responses during immunization and challenge trials.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

Although the PDSL focus is viral diagnostics, the level and type technical expertise enjoyed by the laboratory personnel is also appropriate for diagnosing other pathogens. Serological and PCR assays for other etiological agents have been performed by the PDSL as deemed appropriate by veterinary staff (see progress report for examples). In addition to this expandable capability and rapid test result turnaround the PDSL provides standard virus diagnostics (Table 1) for approximately half the cost charged by commercial laboratories such as BioReliance. As structured, the PDSL continues to fulfill the clinical laboratory requirement described in the 7th edition of the NPRC Guidelines.

As NHP models become increasingly important in biomedical research, the need for in depth understanding of the influences that innate virus pathogens may play during research applications has also risen. Removing specific pathogens from the investigator's list of concerns is a primary goal. This has become particularly important for out-bred NHPs where the size of the experimental groups is often limited for practical purposes. Small group sizes are more easily influenced by individual animal differences including the adverse effects associated with various relatively common infections. The adverse effects of many of these viral agents may not be apparent until experimental conditions favor emergence of subclinical infections. Additionally, the pathogenesis of many of the screened viruses includes features which clinically mask their presence yet these infections can influence experimental outcomes.

| Virus | Screening serological test/antigen | Confirmatory serological test/antigen | DNA PCR | Other |
|---|---|---|---|---|
| SRV | Multiplex/ SRV 1 & 2 | Immunoblot/SRV 1 & 2 | SRV 1, 2, & 5 | Virus culture |
| STLV | Multiplex/HTLV | Immunoblot/HTLV | STLV/HTLV | |
| McHV1 | Multiplex/HSV | Immuno-dip strip/McHV1 | n/a | Confirmation at national B-virus Resource Lab |
| SIV | Multiplex/SIV | Immunoblot /SIV | SIV | |
| SFV | Multiplex/SFV | Immunoblot/SFV | Nested | |
| Measles virus | Multiplex/MeV | IFA/MeV | n/a | |

Table 1 Antigens & confirmatory test summary of our current 7-plex virus (two SRV genotypes) screening assay

During this reporting period the PDSL processed and analyzed 3,465 blood samples. The samples were derived from NHP at three off site breeding colonies and the Washington Center in Seattle. The bulk of the samples supported monitoring general SPF virus status screening but also included (often with the same sample) other serological diagnostic tests. The PDSL also produced and sold (production cost recovery) 21 mg of concentrated, purified SRV as an antigen source for SRV serology to other NPRC's and commercial NHP service providers.

## C. COMPONENT PRODUCTS

### C.1 PUBLICATIONS

Not Applicable

### C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

### C.3 TECHNOLOGIES OR TECHNIQUES

The PDSL is dependent on two high throughput instruments; BioRad CFX supporting real time diagnostic PCR, and a BioRad/Luminex multiplex to support serological virus diagnostics. Both instruments are maintained by the PDSL and have been used to support non-PDSL research activities.

### C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

### C.5 OTHER PRODUCTS AND RESOURCE SHARING

#### C.5.a Other products

File uploaded: WaNPRC_PDSL_C5a.pdf

#### C.5.b Resource sharing

File uploaded: WaNPRC_PDSL_C5b.pdf

The PDSL has provided concentrate, purified SRV as an antigen source used by several NPRCs and commercial NHP vendors. Applied to SRV, this process is fairly unique resulting is some of the highest quality antigen preparations that retain a complete compliment of SRV structural antigens including gp 70 and as such, the demand has steadily increased over the reporting period. The PDSL is also in charge of the NHP genome DNA bank, maintaining a selection of DNA samples representing unrelated and trio (dam/sire/ offspring sets). The banks are part of the NHPRC Consortium and the samples are available to all NIH-funded investigators upon request at a minimal charge and after acceptance of an inter-institutional transfer agreement.

The PDSL is the Center's diagnostic laboratory. We provide, for the most part, PCR and serological data that defines the general health of all colony animals. PDSL services include SPF viral diagnostics as well as diagnostics pertaining to coccidioidomycosis and *Trypanosoma cruzi*, two infectious agents of current interest to the colony managers. Both of these are ELISA kits used in veterinary and human diagnoses. We have also provide detailed antibody response characterization by antigen, source material (mucosa or blood), and Ig subtype on serial samples form study animals included in vaccine trials both during the immunization and after viral challenge study phases.

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Excluded by Requester | | | | Associate Director | 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 | | | | | | |
| 1 | Secretarial/Clerical | 0.6 | | | 2,593.00 | 918.00 | 3,511.00 |
| 5 | Other | 31.07 | | | 160,224.00 | 48,120.00 | 208,344.00 |
| **6** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **211,855.00** |
| | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | | **211,855.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. Chemicals Products | 8,500.00 |
| 9. Biological Assays | 5,600.00 |
| 10. General lab supplies for diagnostics lab | 10,639.00 |
| **Total Other Direct Costs** | **24,739.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **236,594.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Costs (MTDC) | 42.0 | 236,594.00 | 99,369.00 |
| | | **Total Indirect Costs** | **99,369.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center(PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **335,963.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Division of Primate Resources - Primate Diagnostic Laboratory Services - 5899**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 3 | Research Scientist | 19.07 | 114,652 | 31,988 | 146,640 |
| 2 | Husbandry/Veterinary Staff | 12.00 | 45,572 | 16,132 | 61,704 |
| **5** | **TOTAL OTHER:** | **31.07** | **160,224** | **48,120** | **208,344** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources-OHSU sub

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1)To continue and expand current population demographic modeling efforts.
2)To continue maintaining a full pedigree for breeding or potential breeding animals.
3)To continue and expand current monitoring of inbreeding and founder representation.
4)To improve genetic characterization through new genotyping techniques.

### 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: WaNPRC_OHSU_Subcontract_B2.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 support the genetics management and research needs during the next year by performing MHC expressed allele analysis of newborns and research subjects, as selected by the WaNPRC staff. We will also continue to evaluate possible genetic determinants of Coccidioidomycosis risk, to provide support for genetic management questions and breeding group formation, and to address arising questions relative to genetic research or management.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

The expressed MHC allele analysis of the *M.nemestrina* colony has been fully implemented during this granting period. We are making use of the next generation sequencing methods pioneered by Excluded by Requester Excluded by Requester at the University of Wisconsin to detect MHC Class I expressed alleles, and to report t' e major an ' minor alleles identified in each individual Excluded by Requester 2009; [redacted] 2009). We identify alleles Excluded by Requester present in offspring and parent to deduce the haplotypes present. Our use of the same sequence analysis pipeline and the updated *M. nemestrina* allele sequence database, enables direct comparison of results across laboratories.

In Sept. 2014 we reported the MHC allele composition for 175 pigtail macaques selected by the WaNPRC breeding management staff. An additional 160 pigtails are currently being analyzed and those final reports will be delivered by April 15, 2015. In total, the analysis has identified over 80 MHC alleles and haplotypes in the WaNPRC colony, including both novel and previously documented alleles. All of the results are provided in a customized reporting form, and are delivered to Excluded by Requester for upload and sharing within the ARMS database.

As the significant role of MHC allele contributions to S/HIV disease susceptibility and progression continue to be discovered, the deep sequence allele characterization becomes ever more valuable. In addition, we are analyzing individuals that have shown to be susceptible to Coccidioidomycosis (valley fever) to identify any potential contributions to disease risk. Further discussion about the MHC data will continue to occur through face-to- face meetings at the WaNPRC.

In addition to the planned activities above, the ONPRC Primate Genetics group has provided support to the WaNPRC genetics management group during this past year [redacted] attended an on-site workshop Excluded by Requester held at the ONPRC in November 2014 to learn different approaches for genetic diversity analysis and breeding group design, and follow-up analysis support was provided after that meeting.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | 0.00 | 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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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 | 130,042.00 |
| 6. Equipment or Facility Rental/User Fees | 0.00 |
| 7. Alterations and Renovations | 0.00 |
| **Total Other Direct Costs** | **130,042.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **130,042.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 130,042.00 | 0.00 |
| | | **Total Indirect Costs** | **0.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **130,042.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

| K. Budget Justification* | File Name: OHSUSubk.pdf |
|---|---|
| | (Only attach one file.) |

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

**BUDGET JUSTIFICATION: Division of Primate Resources-OHSU sub - 5900**

This budget does not have significant deviations from the prior year's budget.

OREGON HEALTH & SCIENCE UNIVERSITY

Research Development & Administration

**Research Grants & Contracts**

Mail code L106RGC
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098
tel 503 494-7784
fax 503 494-7787
www.ohsu.edu/research

# STATEMENT OF INTENT TO ENTER A CONSORTIUM AGREEMENT

Date: 02/26/15

Title of Application: Washington National Primate Research Center – OR/WA genetic Collaboration

Applicant Organization: University of Washington

Applicant Organization Principal Investigator: David M. Anderson

Research Institution: Oregon Health & Science University

OHSU PI: Excluded by Requester

Research Institution Project Costs:
$130,042 Total Costs.

Proposed Project Period: 05/01/15 – 04/30/16

The appropriate programmatic and administrative personnel of each institution involved in this grant application are aware of the National Institutes of Health consortium grant policy and are prepared to establish the necessary inter-institutional agreement consistent with that policy.

Excluded by Requester

Manager, Office of Proposal & Award Management
Oregon Health & Science University
3181 SW Sam Jackson Park Road, L106OPAM
Portland, Oregon 97239-3098
Phone: (503) 494-7784
Fax: (503) 494-7787
Email: orserv@ohsu.edu

# RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 0969975150000

**Budget Type*:** ○ Project ● Subaward/Consortium

**Enter name of Organization:** Oregon Health and Science University

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 32,230.00 | 9,669.00 | 41,899.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **41,899.00**

## 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 | Research Associates | 5.4 | | | 15,248.00 | 6,447.00 | 21,695.00 |
| **3** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **21,695.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **63,594.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 0969975150000
**Budget Type*:** ❍ Project ● Subaward/Consortium
**Enter name of Organization:** Oregon Health and Science University

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 1,400.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **1,400.00** |

| **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*:** 0969975150000
**Budget Type*:** ❍ Project ● Subaward/Consortium
**Enter name of Organization:** Oregon Health and Science University

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 9,316.00 |
| 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** | **9,316.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **74,310.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Costs (MTDC) | 75.0 | 74,310.00 | 55,732.00 |
| | | **Total Indirect Costs** | **55,732.00** |

**Cognizant Federal Agency** DHHS, Patrick Smith, 415-437-7820
(Agency Name, POC Name, and POC Phone Number)

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **130,042.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Division of Primate Resources-OHSU sub - 5900

**Personnel ($63,594)**

Excluded by Requester **Ph.D.** (PI): We request EFFORT months of salary support for year 4. Dr. Excluded by Requester will oversee the MHC expressed analysis for an additional 180 members of the *M. nemestrina* colony. She will also meet regularly with WaNPRC investigators to discuss ongoing collaborative projects (Genetic characterization of *M. nemestrina* colony, S/HIV viral restriction in *M. nemestrina;* International Programs). She will be responsible for submitting an annual progress report, and will attend the scientific advisory board meeting and other relevant administrative meetings each year.

Excluded by Requester (Staff Scientist): We request EFFORT months of salary support for Excluded by Requester year 4. will be responsible for the allele calling portion of the expressed allele MHC assay for *M. nemestrina*. She will continue to work in collaboration with Excluded by Requester to update MHC assay for *M. nemestrina,* to identify novel alleles and to coordinate the validation and assignment of MHC nomenclature in a consistent manor.

Excluded by Requester (Research Assistant II): We request EFFORT months of salary support to provide sample processing, including cDNA synthesis, PCR and multiplex library construction and sequencing for MHC allele analysis.

Excluded by Requester (Research Assistant): We request EFFORT months of salary support for work on the MHC analysis pipeline, including sample receipt, cataloging, RNA extraction, database management and custom reporting for the WaNPRC.

**Travel ($1,400)**

PI to travel to the WaNPRC to meet with Investigators to discuss ongoing projects, and to identify new genetic support needs

**Other Direct Costs:**

**Materials and Supplies ($9,316)**

| | |
|---|---|
| RNA extraction, cDNA synthesis and PCR amplification of target MHC regions for deep sequencing | $6,916 |
| Service cost – MHC RNAsequencing on an Illumina miSeq | $2,400 |

OREGON HEALTH & SCIENCE UNIVERSITY

Research Development & Administration

**Research Grants & Contracts**

Mail code L106RGC
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098
tel 503 494-7784
fax 503 494-7787
www.ohsu.edu/research

# STATEMENT OF INTENT TO ENTER A CONSORTIUM AGREEMENT

Date: 02/26/15

Title of Application: Washington National Primate Research Center – OR/WA genetic Collaboration

Applicant Organization: University of Washington

Applicant Organization Principal Investigator: David M. Anderson

Research Institution: Oregon Health & Science University

OHSU PI: Excluded by Requester

Research Institution Project Costs:
$130,042 Total Costs.

Proposed Project Period: 05/01/15 – 04/30/16

The appropriate programmatic and administrative personnel of each institution involved in this grant application are aware of the National Institutes of Health consortium grant policy and are prepared to establish the necessary inter-institutional agreement consistent with that policy.

Excluded by Requester

Manager, Office of Proposal & Award Management
Oregon Health & Science University
3181 SW Sam Jackson Park Road, L106OPAM
Portland, Oregon 97239-3098
Phone: (503) 494-7784
Fax: (503) 494-7787
Email: orserv@ohsu.edu

## A. COMPONENT COVER PAGE

**Project Title:** AIDS/Virology

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1. To generate resources and knowledge by maintaining active research programs in key areas of AIDS related research;
2. To provide scientific leadership to the Virology/Immunology Service Core
3. To provide focal points for collaborative research programs with investigators outside of WaNPRC;
4. To provide training and expertise to students, fellows and other research personnel.

### 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: WaNPRC AIDS-virology B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_AIDS-virology_B4.pdf

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

Research findings have been disseminated to the scientific communities primarily through publications in professional journals. Please see the lists of publications from each Core Staff in their individual reports. In addition, research findings have been reported in seminars and professional meetings such as the Keystone meeting, International AIDS Society (IAS) annual meeting, Conference on Retrovirus and Opportunistic Infections (CROI), and Vaccines against antigenically variable viruses (VAAVV).

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

The specific aims of this Division will remain the same for the next reporting period.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

Excluded by Requester **Lab:**

The overall goal of the Excluded by Req lab is to develop and use non-human primates as a model to study host-pathogen interactions and design strategies for the prevention and treatment of primate lentivirus infection and disease. In addition, Excluded by Requester lab provides scientific leadership to the Virology/Immunology Service Core that provides standardized technical and analytical support for other investigators, inside and outside of WaNPRC, to conduct AIDS-related research at WaNPRC. Major activities in the past year consist of the following:

Oral Immunization against HIV/AIDS with prime boost strategies. Mucosal transmission is the predominant mode of HIV acquisition. Oral transmission may occur in newborns at delivery, in infants through breast milk from HIV-infected mothers, and in adults through occupational exposure or oral-genital sex. The overall goal of this project is to test if oral delivery of poxvirus and protein vaccines in a prime-boost immunization regimen will generate protective immunity against mucosal challenge. We previously demonstrated the safety and immunogenicity of an orally delivered replication-competent poxviruses in macaques. To further examine the optimal dose and route for oral immunization, we inoculated two animals sublingually with twice the dose used in the 1st pilot study and two animals were inoculated with the same dose but at the tonsil. Oral lesions were found in all animals. However, all lesions healed within 7-10 days and no other adverse effect was observed. These observations, together with previously reported findings, indicate that sublingual inoculation with $5x10^8$ PFU is likely to be the optimal dose and route for oral administration of a replication competent recombinant vaccinia virus in non-human primates. These animals generated HIV-specific antibodies which increased significantly after a single subunit gp120 boost. Neutralizing antibodies were detected in 3 of 4 immunized animals. We challenged the immunized animals with SHIVSF162P4 to determine if immunity elicited would protect against a homologous high dose intrarectal challenge. Two animals were completely protected, one animal was infected and one showed delayed acquisition. The one vaccinated animal that was infected (i.e., did not show any sign of protection or delay of acquisition) did not develop any virus neutralizing antibodies at the time of challenge, indicating the important role of neutralizing antibodies in vaccine protection. Together these results indicate that sublingual immunization recombinant vaccinia viruses was safe and effective in priming protective against a mucosal challenge with SHIVSF162. This work is supported by a grant from NIH Excluded by Requester NIDCR (R01 DE021223; PI).

Unmasking Conserved Epitopes on HIV Envelope Protein for Vaccine Design. Although broadly neutralizing antibodies (bNAbs) can be found in some HIV-infected individuals, they are often directed against conserved epitopes on the envelope glycoprotein such as the Env CD4 binding site (CD4bs), which is masked by glycans. To date, efforts to generate bNAbs by immunization have largely been unsuccessful. The goal of this project is to explore approaches to optimize the design of Env immunogens that will elicit enhanced protective responses to HIV, including bNAbs. Because the N197 glycan occludes the CD4bs and is conserved among diverse HIV-1 isolates, we sought to determine if immunization with heterologous Env bearing the N197 mutation may increase the breadth of antibody response. Macaques were immunized in a poxvirus prime, protein boost regimen with homologous Env, or heterologous Env (either sequentially or as a mixture). As expected, animals immunized with N197 Env from a single isolate generated stronger antibody responses against the homologous Env than those immunized with heterologous N197 mutant Env (either sequentially or as a mixture). Interestingly, animals immunized with a mixture of N197 mutant Env from different isolates showed stronger and broader neutralizing antibody responses against heterologous Tier 1B than animals in all other groups. Furthermore, animals immunized with a mixture of N197 Env generated broadly reactive IgG responses against multiple epitopes in gp120, including CD4i epitopes, linear V3, V2, and C5 epitopes, V1V2 (clade B–gp70_B.CaseA_V1_V2) and conformation-dependent epitopes in the coreceptor binding region. These results support our hypothesis that specific glycan modification modulates the epitope specificity of immune responses against the Env protein and that the use of multivalent Env vaccines may focus antibody responses on epitopes shared by these immunogens. This work is supported by an award from Private Source Private Source (OPP1033102; PI). Excluded by Requester

Nonhuman primate model to evaluate combination antiretroviral therapy hematopoietic stem cell therapy against HIV infection. Hematopoietic stem cell (HSC) transplantation remains the only clinically observed path to functional cure of HIV infection. To better understand the mechanism of HSC-driven HIV control, and apply this therapy to a greater number of patients, we have developed a model of combination antiretroviral therapy (cART)-suppressed HIV infection in the pigtailed macaque, applicable to both gene therapy and

allogeneic transplant-based cure strategies. Following transplantation of HIV-resistant, autologous cells into conditioned animals, we evaluated the extent to which protected cell progeny impede infection by SIV/HIV (SHIV) chimeric virus in vivo. Animals were challenged with SHIV virus containing an HIV envelope, after which a 3-drug cART regimen was initiated. Autologous HSCs were engineered to resist infection through targeted disruption of the CCR5 genetic locus using Zinc Finger Nucleases (ZFNs). Engraftment, persistence, and SHIV response of these autologous stem cells, and stem cell-derived lymphoid and myeloid cells, were measured in vivo. SHIV infection in the pigtailed macaque model resulted in sustained viremia with consequent reduction in $CD4^+$ T cells. Moreover, administration of three-drug cART led to rapid and durable suppression of plasma viremia to <30 copies/mL plasma - suggesting that this model recapitulates key features of HIV infection and treatment in humans. CCR5 targeting experiments yielded up to 60% gene disruption in $CD34^+$ cells ex vivo, translating to approximately 5% disruption in vivo following transplant. Importantly, up to 10% of transplanted cells carried two disrupted alleles of CCR5; these cells should preferentially reconstitute $CD4^+$ T-cell pools and other susceptible subsets following SHIV challenge. Consistent with this prediction, our preliminary data suggest that CCR5-deleted cells undergo positive selection following SHIV challenge in vivo. CCR5 deletion does not impair HSC engraftment or differentiation, and that CCR5-deleted cells can undergo SHIV-dependent positive selection even when present at low levels. Our model enables the evaluation of novel therapeutic approaches in targeting viral reservoir in cART controlled HIV infection. This work is supported by a grant from NIAID, NIH (U19 AI096111 Excluded by Requester).

**Virology/Immunology Service Core**

The overall mission of the Virology/Immunology Core is to provide virologic and immunologic resources and expertise to enable efficient and productive use of nonhuman primates for AIDS-related research. Currently, the Core provides the following services:

1. Sample processing, including isolation of plasma, serum, and PBMC, and processing of various tissues
2. Lymphocyte subset analysis and hematology
3. Virus isolation by co-culture
4. Viral load determination by various quantitative PCR methods
5. Serology, including ELISA immunoblots and virus neutralization assays in multiple formats
6. Virus stocks and viral antigens

To achieve its mission, the Core also maintains, equips, and provides oversight for operations in the BSL-2 (e.g. vaccinia virus lab) and the Retrovirus Laboratory (BSL-2 with 3 practices) laboratories at the Western Facilities. In addition, the Core also establishes standard operating procedures and provides training to personnel for the safe operation in these laboratories. The Core is funded by income generated through an established fee-for-service basis.

**Fuller Lab:**

Conserved Elements DNA Vaccine for HIV. We previously showed that therapeutic DNA vaccine induction of mucosal responses correlated with reduction of virus in the gut of SIV-infected macaques despite the use of a suboptimal ART regimen. This vaccine stimulated T cell responses that suppressed virus to low/undetectable levels and afforded a durable viral remission in ~50% of the animals after stopping ART. We are now investigating strategies to make therapeutic vaccination even more effective by 1) using a more potent combination of drugs (cART) 2) using a mucosal adjuvant (LT) to target immune responses to residual virus in the gut, and 3) use of a novel conserved elements (CE) DNA vaccine to focus T cell responses against highly conserved viral sequences that if mutated will impose greater fitness cost. We hypothesize that vaccine-induced viral remission is mediated by strong mucosal CD8 responses and focusing these responses to the gut in maximally suppressed infections and against more conserved epitopes will suppress a wider range of possible viral variants, select for fitness-cost escape mutations, and maximally disable the ability of residual viruses to emerge from the latent reservoir after stopping cART. Using optimized cART and mucosal targeting we are comparing traditional whole antigen and CE DNA vaccines for the ability to increase mucosal and systemic CD8 responses against conserved viral sequences, their impact on viral evolution and fitness, and their role in controlling virus. We are also investigating the role of inflammation on therapeutic efficacy. Our aims: 1) Determine efficacy of an LT-adjuvanted whole-antigen traditional SIV DNA vaccine when used with

more potent cART. 2) Determine if an SIV CE immunogen will improve therapeutic efficacy. 3) Define immune and virological mechanisms underlying viral remission. These studies will define the virological and immune profile of a vaccine-induced functional cure and the feasibility of a novel therapeutic CE DNA vaccine. A pilot study showed that immunizing infected macaques with a CE DNA vaccine can shift the CD8 repertoire from targeting predominantly variable sequences to increased recognition of the highly conserved elements, an outcome that supports the feasibility of this concept. We have initated a therapeutic efficacy study. Rhesus macaques were infected with SIV and are currently undergoing treatment with cART and immunizations. Drugs will be withdrawn in the first cohort of animals within the next few months to determine the effects of the vaccine in protection from viral rebound and immune correlates of viral control. This work is supported by a grant from NIAID, NIH (R01 AI104679; [redacted] PI). In collaboration with our private sector partne Profectus Biosciences, we are planning to start a second cohort of animals that will receive therapeutic vaccinations with a traditional whole antigen DNA vaccine in combination with adjuvant. Experiments are currently underway in mice to determine which adjuvant to advance to therapeutic efficacy studies in SIV infected macaques. This project is an separate experiment that will be run concurrently with the CE therapeutic DNA vaccine study to provide a comparison between 2 adjuvants, between CE and whole antigen DNA vaccine designs and between two different routes of DNA delivery (gene gun vs. electroporation). The collaboration with Profectus is supported by a fast track SBIR grant from NIAID awarded to Profectus (R44 AI110315-01; Excluded by Requester).

Excluded by Requester

Macaque model for gene therapy against giant axonal neuropathy: Giant axonal neuropathy (GAN) is a rare neurodegenerative disease resulting in death in the second or third decade of life. The disease is due to homozygous loss-of-function mutations in the gene encoding gigaxonin, a Cul3 ubiquitin ligase adaptor protein. The absence of gigaxonin leads to disruption in the regulation of intermediate filaments (IF), accumulation of disordered microtubules and IF in axons, enlargement of axons, and degeneration of peripheral nerves. Pre-clinical data show that delivery of the GAN gene by an AAV9 vector in GAN-null mice results in resolution of IF aggregates and provide a rationale for a gene therapy approach in GAN patients. A concern is that GAN patients may not be tolerized to normal gigaxonin. If true, then introduction of gigaxonin will elicit an immune response against the normal protein thereby exacerbating the neurodegenerative disease. The present study is designed to model a GAN gene therapy protocol in monkeys. Since a monkey model lacking gigaxonin is not available, we have chosen GFP as the transgene because GFP is immunogenic in monkeys and models a 'worst case' scenario for GAN gene therapy. We will test the hypothesis that IL-10 coupled with transient rapamycin treatment will tolerize monkeys to GFP, delivered into the CNS using an AAV9 vector. The study will assess three treatments; AAV9/GFP alone; AAV9/GFP with transient rapamycin; and AAV9/GFP plus IL-10 nanoparticles with transient rapamycin. The aims: (1) Evaluate inflammatory / immune responses to trauma alone, the AAV9 capsid protein, and the GFP transgene, (2) Analyze GFP expression in CNS, and (3) Assess pathology in the CNS after gene delivery. This will determine if IL-10 with transient rapamycin treatment results in tolerization to GFP expressed in the CNS. The data will be used to inform the design of the GAN gene therapy protocol for use in the clinic. Results to date show that Rapamycin alone suppresses AAV9 specific responses but not GFP responses. A second cohort of animals investigating Rapamycin in combination with IL-10 therapy is scheduled to be initiated within the next month. This work is funded by the Private Source (Private Source, Excluded by Request PI).

**Lab:** Excluded by Requester

The overall goals of Excluded by Requester lab include better understanding mucosal immunity during HIV infection in order to develop novel therapeutic interventions and prevention strategies for HIV infection. Excluded by Requester lab has performed 3 main studies over the last year to accomplish these goals:

Kinetics and mechanisms of mucosal dysfunction after SIV infection. In this study we infected rhesus macaques with SIVmac239 and obtained longitudinal biopsies to assess the kinetics of mucosal immunity, epithelial barrier integrity, inflammation and virus replication after SIV infection. This study was performed and we found provocative data that SIV infection results in rapid loss of Th17 cells in mucosal sites prior to local virus replication, which was associated with increased inflammatory cytokines, and preceded damage to the barrier or microbial translocation. These data indicate that initial, rapid inflammation prohibits essential cytokines such as IL-17, allowing SIV to establish infection and inflammation, demonstrating the need to induce therapies aimed at protecting Th17 cells in mucosal tissues in HIV infection.

*Status:* a manuscript was written on these data; however submission was postponed due to complications with this study. We found out after completion of the study and data analysis that antibiotics were given to the animals between baseline and SIV time points, thus rendering the data non-interpretable, and the study is being repeated in 2015. Pending Support

Pending Support

Manipulation of microbiota to enhance mucosal HIV vaccine responses. We performed a pilot study to determine how manipulating the gastrointestinal microbiome with probiotic treatment may alter immunity and vaccine responses. We found that probiotic treatment in both rhesus and pigtail macaques significantly enhances immune function, including induction of essential T cells and increased IgA in the mucosa. These data support that manipulation of microbiome may result in increased efficacy of HIV vaccination.
*Status:* Studies are complete, and these data were used for Pending Support and are currently being analyzed to write up for a publication in spring 2015.

Dynamic vaginal microbiome in pigtail macaques is associated with menstrual cycle phases and inflammation. We performed a study to determine whether microbiome and inflammation kinetics are dynamic throughout the menstrual cycle. We obtained blood and vaginal swabs from female pigtail macaques in the WaNPRC breeding colony in Seattle at time of their bi-annual TB testing. We found that pigtail macaques have a dynamic microbiota in the vagina, which is highly associated with levels of inflammation, and altered throughout the menstrual cycle. These data provide a foundation for understanding how vaginal microbial communities may impact risk of HIV/SIV transmission using non-human primate models.
*Status:* Studies are complete, and these data were used for Pending Support and final analysis is being conducted in order to publish as a manuscript in summer 2015.

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

All Core Staff Scientists of the AIDS-Related Research Division provide training to students, postdoctoral fellows, research scientists and technologists, and other professionals engaged in AIDS-related research at the WaNPRC. All Core Staff Scientists also conduct didactic training through lectures and seminars at the University of Washington and affiliated institutions the greater Seattle area. In addition, all Core Staff Scientists host national and international visiting scholars, conduct seminars and organize meetings to promote and utilize the intellectual and scientific resources at WaNPRC. The following is a list of students, postdoctoral fellows and visiting scientist in the laboratories of Excluded by Requester in the past year.

| Mentor | Trainee | Name | Department/Affiliation |
|---|---|---|---|
| Excluded by Requester | Undergraduate Students | Excluded by Requester | Anthropology |
| | | | UW Post-baccalaureate Research Enhancement Program |
| | | | Microbiology |
| | Graduate Students | | Microbiology |
| | | | Pharmaceutics |
| | Postdoctoral Fellows | | Pharmaceutics |
| | | | Pharmaceutics |
| | Visiting Scientist | | Children's Hospital New Orleans |
| | Undergraduate Students | | Microbiology |
| | | | Microbiology |
| | Graduate Students | | Microbiology |
| | | | Microbiology |
| | | | Microbiology |
| | Postdoctoral Fellows | | Microbiology |
| | | | Microbiology |
| | Undergraduate Student | | Volunteer |
| | Graduate Students | | Molecular and Cellular Biology |
| | | | Molecular and Cellular Biology |
| | Postdoctoral Fellows | | Pharmaceutics |

## 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

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 73,870.00 | 16,621.00 | 90,491.00 |
| 2. | | | | | | Core Staff Scientist | | | | | 49,263.00 | 11,084.00 | 60,347.00 |
| 3. | | | | | | Core Staff Scientist | | | | | 11,999.00 | 2,700.00 | 14,699.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **165,537.00**

## 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 | Other | 12.28 | | | 62,174.00 | 18,139.00 | 80,313.00 |
| **6** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **80,313.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **245,850.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 121,634.00 |
| 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. DNA sequencing, donor macaque blood, equipment maintenance, flow cytometry usage fee | 45,472.00 |
| **Total Other Direct Costs** | **167,106.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **412,956.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 412,956.00 | 173,442.00 |
| | | **Total Indirect Costs** | **173,442.00** |

| | |
|---|---|
| **Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number) | U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820 |

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **586,398.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

| | |
|---|---|
| **K. Budget Justification*** | File Name: AIDSVirology.pdf (Only attach one file.) |

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

## BUDGET JUSTIFICATION: AIDS/Virology - 5917

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**SENIOR KEY PERSONNEL** Excluded by Requester K23 award has ended, and we are requesting salary support in the coming year.

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 2 | Research Scientist | 6.52 | 37,849 | 10,559 | 48,408 |
| 1 | Program Manager | 0.36 | 2,012 | 561 | 2,573 |
| 1 | Research Associate | 3.00 | 11,737 | 3,275 | 15,012 |
| **4** | **TOTAL OTHER:** | **9.88** | **51,598** | **14,395** | **65,993** |

This category does not represent a significant deviation from the prior year.

**SUPPLIES:** The modest increase (of $10k) in supplies cost from the prior year is due to projected price increases.

**OTHER:** The increase to this category ($9,722) is due to projected price and volume increases.

## A. COMPONENT COVER PAGE

**Project Title:** NHP Systems Biology

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The Division of Nonhuman Primate Systems Biology is organized into a Research Component (composed of Virology and Integrative Analysis, Mucosal Immunology, and Animal Models) and two Cores (the High-throughput Molecular Profiling Core and the Statistical Analysis and Modeling Core). The Research Component and both Cores are involved in each Divisional project. General information related to the Research Component (including study background and results) is provided here. Detailed descriptions of the roles of each Core in these projects can be found in the Progress Reports for the Cores.

Specific Aim:

To apply the techniques of systems biology to examine the host response to virus infection or to vaccination, particularly to support the development of new resources to characterize mucosal immunity.

We are using rhesus and pig-tail macaque models for the integrative analysis of global molecular profiles, examining specific subsets of mucosal T cells as well as correlations to detailed, functional assays of such cells. The development of these tools requires comparing treatments resulting in distinct outcomes for the host, variations that are achieved in studies that compare viruses of differing pathogenicity or vaccination protocols differing in protective efficacy.

### 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: WaNPRC_NHP_Sys_Bio_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_NHP_Sys_Bio_Core_B4.pdf

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

Sharing of division-generated resources and information to the scientific community is an essential component of the Division of Nonhuman Primate Systems Biology. All resources are made publicly accessible within four weeks of publication. In addition, all aspects of our data dissemination plan comply with NIH research grants and contracts on obtaining and disseminating biomedical research resources. Complete details of data dissemination can be found in the progress report for the Statistical Analysis and Modeling Core.

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

There have been no changes in our specific aims; we will continue 1) to provide resources and expertise in high-throughput molecular profiling as applied to nonhuman primate models of human disease, 2) to act as a resource for obtaining datasets by microarray, proteomics, and RNA-Seq, 3) to provide well-proven protocols for sample collection/storage, and for primary isolation of suitable RNA or protein extracts to the NHP research community, 4) to expand our protocols and pipelines to accommodate cutting edge technologies, 5) to provide the hardware infrastructure and the expertise for the computational analysis of highthroughput datasets, including the integrative techniques of systems biology and 6) to apply the techniques of systems biology to examine the host response to virus infection or to vaccination, particularly to support the development of new resources to characterize mucosal immunity.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

The overarching goal of the Division of Nonhuman Primate Systems Biology is to facilitate the NHP research community in embracing the newly emergent paradigms of systems biology and next-generation transcriptomics. Resource development and research occurs through internal and external projects managed through one of the Research Components and supported by the Cores. This support includes: 1) using rapid and cost-effective methods for high-throughput molecular profiling, 2) providing computational infrastructure and cutting edge techniques to mine the resulting data sets and 3) disseminating the generated resources to the project PIs and the research community at large.

During the last year, the seamless Divisional workflow which integrates the activities of the Research Component and the Cores has resulted in the generation of substantial community resources and many significant biological findings in several areas of research. These accomplishments are detailed below and fall into seven general areas:

1) *In vivo* and *in vitro* SIV/HIV-related studies
2) NHP models of respiratory diseases
3) NHP models of viral hemorrhagic fever
4) Improvements of NHP reference transcriptomes
5) Community outreach
6) Dissemination of Division-generated resources to the public (See Section B5 below.)
7) Development of new genomics tools for NHP systems biology applications (See Section C3 below.)

### *In vivo* and *in vitro* SIV/HIV-related studies

Host transcriptional response to RhCMV/SIV vaccination

We have completed or are nearing completion of a number of AIDS-related *in vivo* studies which have resulted in several significant findings. The DAIDS NHP Functional Genomics Core (NHP-FGC) – housed in the Katze laboratory – has the prime mission of providing RNA profiling and functional analysis to the Simian Vaccine Evaluation Unit (SVEU). The Division supports NHP-FGC projects by providing crucial computational infrastructure in addition to microarray and nextgen sequencing equipment, protocols, and expertise. One such study in collaboration with Excluded by Requester Private Source, compared the host response to vaccination with gp96-Ig secreting cells carrying SIVmac251 peptides, plus and minus a boost with gp120 protein Excluded by Requester *et al., 2014**). The RNA profiling and associated functional analysis indicated: 1) vaccination can alter the (non-)immunizing effect of low-dose challenges in a time-dependent manner, 2) immunized animals show evolving host response in the course of multiple challenges, and 3) persistently protected animals have a particularly strong innate and humoral immune response only after the first challenge, and show both prevailing innate and adaptive cellular responses after further challenge.

RNA-seq of mucosal challenge compartment during acute SIV infection

Using samples collected from the Division's large SIV/rhesus macaque acute infection model, we carried out the first deep mRNA sequencing analysis of mucosal host responses in the primary infection compartment Excluded by Requester *et al., 2014**) and found that during acute infection, a significant host response was mounted in the mucosa before inflammation was triggered. Our analysis indicates that this response has a detrimental effect on tissue integrity and emphasizes the importance of mucosal host responses preceding immune activation in preventing systemic SIV infection. In collaboration with Excluded by Requester (University of Pittsburgh), Division resources are being utilized to expand on this initial study by performing a comparative total RNA-seq analysis between the rhesus acute infection model and a similar acute infection model using African Green Monkeys, a natural host of SIV. Total RNA-seq data from the rectal challenge compartment and draining lymph nodes, spanning the necropsy collections at 1, 2, 3, 6, 12, and 84 days post infection from both model systems have been generated and the functional analysis comparison between the two species is near completion.

Microbial translocation during SIV infection

During chronic HIV/SIV infection, CD4+IL-17-producing T cells (TH17) are significantly depleted from mucosal tissues, and their absence is highly associated with gastrointestinal (GI) dysfunction. However, the kinetics of immune dysfunction, in sequence with microbial translocation and how this dysfunction may affect the establishment of viral reservoir remains unknown. Excluded by Requester a Primate Center staff scientist, is the PI on a rhesus macaque study performed at the Primate Center with the goal of elucidating the kinetics of acute host/pathogen interactions and identifying early events after SIV infection that could reveal potential targets of therapeutic strategies. Longitudinal GI tract biopsies and blood at early acute time points from six rhesus

macaques following intrarectal SIV challenge with SIVmac239x were collected and immunophenotype, functionality, inflammation, virus kinetics, and microbial translocation were measured. Strikingly, TH17 cells were significantly depleted from all GI tract sites by day 3 post-SIV infection but this localized depletion was not associated with generalized CD4 depletion, viral load, nor to generalized loss of cytokine production. These data suggest that the loss of TH17 cells from the GI tract at the earliest stages of infection uniquely precedes microbial translocation and a systemic proinflammatory state, and occurs as the reservoir is being established. In 2014, the Division performed microarray assay on GI tract biopsies and blood samples throughout the acute infection and the associated host RNA profiling and functional analysis is underway.

*In vitro* CD4+ T cell line projects

AIDS-related research projects continue to be a priority for the Division. One research platform for these investigations is an *in vitro* model based on a synchronous, high-efficient infection with HIV1 strain LAI, with the $CD4^+$ T cell line SupT1. Using this system, we previously published several studies that characterized the early host response to HIV infection utilizing mRNA-seq, microRNA-seq or global proteomics data sets. The integration of two additional data sets with the mRNA-seq data resulted in two publications. [redacted] *et al. 2014 (J. Virol.)* reports on the integration of total RNA-seq data set - which provides quantitation of non-coding and non-polyadenylated RNAs – with mRNA data and demonstrated large numbers of differentially regulated transcripts early after infection, many of which corresponded to nascent transcripts that had not been processed to mature, polyadenylated forms. We computationally derived and validated the underlying regulatory programs. A constructed network of these early-regulated genes was used to predicted compounds that would antagonize the transcriptional changes and we show that one of the predicted drugs, lycorine, potently inhibited HIV-1 infection. To further investigate several of the genes predicted to be part of the regulatory programs, we are employing the CRISPR/Cas9 technology, a simple and efficient method for gene disruption and have produced several clonal SupT1 KO lines that we are currently characterizing to determine their roles in HIV infection with and without lycorine treatment.

Excluded by Requester

Excluded by Requester

In collaboration with [redacted] (University of Pennsylvania) using the Sup T1 model system, we analyzed the alterations to histone post translational modifications (PTM) profiles using nano-LC-MS/MS, as well as the expression of chromatin-associated enzymes using microarray analysis [redacted] *et al., 2014**). We observed major changes in histone PTM abundances which we linked to massive fluctuations in mRNA expression of associated chromatin enzymes. We are now utilizing the CRISPR/cas technology to create knockouts of several of the chromatin enzymes to further characterize the epigenetic changes associated with HIV infection.

Excluded by Requester

**NHP models of respiratory diseases**

In 2014, the Division continued work on models of respiratory disease focusing on two important viruses, MERS coronavirus and influenza virus.

MERS coronavirus

In 2013, the Division was involved in the establishment of a rhesus macaque model of MERS-CoV, however, this model lacks uniform and severe disease which complicates the analysis of countermeasure studies. Our colleagues at Rocky Mountain Laboratories (RML, an NIAID intramural research facility) discovered that unlike the rhesus macaque model, the common marmoset provides a severe, partially lethal, disease model of MERS-CoV. The Division collaborated in generating total RNA-seq data from marmoset lung specimens to characterize expression changes consistent with the development of pulmonary fibrosis, as well as alterations in serum cytokine transcripts Excluded by Requester *et al. 2014**).

Influenza virus

Excluded by Requester is leading the Division's investigation into DNA vaccines as an approach for a universal influenza vaccine to protect against a wide range of diverse circulating and emerging seasonal and pandemic strains of influenza. In a vaccine efficacy trial in nonhuman primates, cynomolgus macaques were immunized with an adjuvanted DNA vaccine that was designed to induce broadly neutralizing antibody and cross reactive T cell responses in the lung mucosa. Following three doses, the adjuvanted DNA vaccine alone induce robust antibody titers and mucosal T cell responses that were comparable to levels previously achievable only through DNA prime-viral vector or recombinant protein boost regimens. The macaques were challenged mucosally with a high dose of highly virulent H1N1 pandemic strain that is heterologous to the strain from which the vaccine was derived. Analysis of viral load by PCR and immunohistochemical staining of the lung showed that the vaccinated animals all become infected but viral loads were significantly lower than in the

controls. However, the antibody responses induced by the vaccine did not neutralize the challenge strain suggesting that protection from the hetersubtypic challenge may be mediated by the mucosal T cell responses induced by the vaccine. Influenza infections result in strong inflammatory responses in the lung that can lead to secondary infections such as pneumonia. To determine if the vaccine was able to reduce inflammatory responses, we performed an extensive microarray analysis on lung tissues collected from a subset of 3 monkeys from each group that were sacrificed 3 days after challenge during peak viral replication. RNA expression patterns showed that vaccination significantly suppressed inflammatory responses in the lung when compared to controls suggesting this vaccine could be effective in reducing post-influenza susceptibility to secondary infections. Interestingly, the RNA expression also showed that vaccinated animals had higher recruitment of T cell responses into the lung, an outcome that further supports a role of the mucosal T cell response induced by the vaccine in mediating protection.

Influenza A virus H7N9 emerged early in 2013, and human cases have continued to emerge since then. To better understand the pathogenicity of this virus, our colleagues at RML inoculated cynomolgus macaques with influenza A virus H7N9. Cynomolgus macaques were used as a model because the receptor distribution for H7N9 virus in macaques was shown to be more similar to that in humans than that of other frequently used animal models. As reported [redacted] *et al. 2014** , when compared to previous studies, the emerging H7N9 influenza virus was more pathogenic in cynomolgus macaques than seasonal influenza A viruses and most isolates of the pandemic H1N1 virus but less pathogenic than the 1918 Spanish influenza virus or highly pathogenic avian influenza (HPAI) H5N1 virus. Gene expression profiling of lung lesions was performed by the Division; we constructed a network of critical molecules based on direct interactions in the IPA knowledge base. These results suggested that molecules that recruit infiltrating effector leukocytes are increased at the site of lesions which correlates with the observed influx of neutrophils and macrophages observed microscopically in the lungs. Through additional computational analysis, we identified drugs reported to act as upstream regulators of some of these genes. We showed that one of the predicted drugs, rosiglitazone, modestly reduced replication of influenza virus A/Anhui/1/2013 *in vitro*.

Excluded by Requester

**NHP models of viral hemorrhagic fever**

Vesicular stomatitis virus expressing Zaire Ebola virus (EBOV) glycoprotein (VSVΔG/EBOVgp) could be used as a vaccine to meet the 2014 Ebola virus outbreak. To characterize host response to this vaccine, we used mRNA sequencing to analyze PBMC from cynomolgus macaques after VSVΔG/EBOVgp immunization and subsequent EBOV challenge. We found a controlled transcriptional response that transitioned to immune regulation as the EBOV was cleared. This observation supported the safety of the vaccine [redacted] *et al. 2015**).

Excluded by Requester

To identify host factors associated with arenavirus virulence, in collaboration with colleagues at RML, we used a cynomolgus macaque model to evaluate the pathogenesis of Lujo virus (LUJV), a recently emerged arenavirus that caused an outbreak of severe viral hemorrhagic fever in southern Africa [redacted] *et al. 2014**). In contrast to human cases, LUJV caused mild, non-lethal illness in macaques. These results were compared to macaques infected with three highly pathogenic lines of Lassa virus (LASV), the causative agent of Lassa fever (LF). The Division performed RNA profiling analysis on PBMC samples and detected a 72-hour delay in induction of host responses to infection during the less pathogenic LUJV infection compared to the animals infected with the more pathogenic LASV and an early differential expression of a subset of genes specific to LUJV infection that accounts for the delayed inflammatory response. Cell-type enrichment analysis suggested that host response induction delay and LUJV-specific profile may be due to a different proportion of natural killer cells responding in LUJV infection compared to the LASV-infected animals. Together, these data indicate that delayed pro-inflammatory and pro-apoptotic host responses to arenavirus infection could ameliorate disease severity.

Excluded by

There are three ongoing NHP studies at RML for which the Division will perform transcriptional analysis to define the specific host responses: 1) determination of host responses in whole blood during interferon and ribavirin treatment in rhesus macaques infected with Ebola virus, 2) comparative analysis of early transcriptional responses in PBMC from cynomolgus macaques infected with Lassa virus or Marburg virus, and 3) direct comparison of the host response to West and Central African Ebola isolates in rhesus macaques.

**Improvements of NHP transcriptomes**

Complex immune loci

There are certain rhesus complex immune genes/genomic regions that are known to be critical in the host response to SIV infection such as the MHC, KIR and Ig loci. The structure and sequences of these complex genomic regions as well as the corresponding transcripts and splice variants are important topics in the field of SIV infection and vaccine efficacy. To reap the full benefits from RNA-seq technologies and data sets, accurate and complete reference transcriptomes are required in these regions. In collaboration with the NHP-FGC and Excluded by Requester Private Source we are developing a strategy for accurately quantifying rhesus MHC allele expression, taking into full account the complexities of the MHC class I gene family in macaques. Our strategy leverages a large collection of full-length rhesus MHC genomic sequences and a custom-developed computational pipeline, and only requires regular macaque RNA-seq data from users. With this approach we find that the expression of both MHC class I and class II genes are highly tissue specific and there is an overall increase in the expression of class I alleles in acutely infected rhesus macaque PBMC samples.

Multiple NHP reference transcriptomes

The Nonhuman Primate Reference Transcriptome Resource (NHPRTR) is an R24-funded resource that is a collaboration involving the Division, Illumina Inc. and Cornell Medical College. There were two publications during this reporting period describing additional resources generated through this collaboration. Prior to the results described in Excluded by Requester *et al. 2014*(J. Med Primatol.)* the genome annotations of rhesus (Macaca mulatta) and cynomolgus (Macaca fascicularis) macaques, two of the most common non-human primate animal models, were limited. Through this work, we uncovered thousands of novel isoforms and un-annotated intergenic transcripts including coding and non-coding RNAs, polyadenylated and non-polyadenylated transcripts. This resource will greatly improve future macaque studies, as demonstrated by their applications in infectious disease studies. Excluded by Requester *et al. 2015** describes Phase II of the NHPRTR project in which 10.1 billion fragments of tissue-specific RNA-seq data was generated and released to the public. These data come from ~15 individual tissues from 11 NHP species and subspecies. The sequence quality was such that 88% of the reads align to human reference sequences, allowing for the full listing of expression abundance across all tissues for each species, using the reads mapped to human genes. These comprehensive reference transcriptomes from multiple primates serve as a valuable community resource for genome annotation, gene dynamics and comparative functional analysis.

NHP cell-specific transcriptomes

In collaboration with Excluded by Requester Private Source, we are using RNA-seq to build transcriptome databases of immune cells relevant to primate models of lentivirus infection. Division infrastructure aids this project at several levels including sample processing, data processing/analysis and data disseminating to the community.

**Citations refer to the P51 supported publications that are listed elsewhere in the progress report*

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

Please see the progress report for the Statistical Analysis and Modeling Core (Bioinformatics Workshop at the conference on Systems Biology of Infectious Diseases, Seattle, Washington; August 17, 2014).

## C. COMPONENT PRODUCTS

### C.1 PUBLICATIONS

Not Applicable

### C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

### C.3 TECHNOLOGIES OR TECHNIQUES

Technology developments associated with the Division of Nonhuman Primate Systems Biology are described in the Progress Report for the High-Throughput Molecular Profiling Core.

### C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

### C.5 OTHER PRODUCTS AND RESOURCE SHARING

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b Resource sharing**

File uploaded: WaNPRC_NHP_SysBio_C5b.pdf

**Genomic Data Sharing**

We make all sequence data and microarray data generated by the High-Throughput Molecular Profiling Core available to the scientific community no later than the date of publication of the main findings from the final data set. Data are submitted to the following repositories:

- NCBI Sequence Read Archive (SRA)
  - Gastrointestinal microbiome data uploaded as raw paired-end Illumina MiSeq 16S rRNA reads
  - Gene expression data uploaded as raw RNA-seq reads (through the corresponding GEO submission).
- NCBI Gene Expression Omnibus (GEO):
  - Gene expression data uploaded as normalized gene expression matrix
- Virus Pathogen Resource (ViPR):
  - Expression data uploaded as normalized gene expression matrix
  - Relevant associated data, including experimental conditions and animal phenotypes
- PRIDE, the PRoteomics IDEntification database
  - Proteomics data is submitted here.

In some cases, in addition to submitting data to these repositories, data sets can be publically accessed through websites such as the Nonhuman Primate Reference Transcriptome Resource (http://nhprtr.org/), Excluded by Requester https://viromics.washington.edu/publications.html) and the NHP Functional Genomics Core (https://www.nhp-fgc.org/).

*If applicable:* If the initial research plan addressed, or the terms of award require, a formal plan for sharing final research data, model organisms, Genome Wide Association Studies data, or other such project-specific data, describe the progress in implementing that plan. For sharing model organisms, include information on the number of requests received and number of requests fulfilled during this reporting period. If the sharing plan is fully implemented, provide a final statement on data sharing

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | Principal Investigator - Primary | Institutional Base Salary | EFFORT | | | 4,216.00 | 949.00 | 5,165.00 |
| 2. | | | | | | Principal Investigator | | | | | 8,886.00 | 1,999.00 | 10,885.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **16,050.00**

## 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 | | | | | | |
| 3 | Secretarial/Clerical | 16.14 | | | 104,793.00 | 29,535.00 | 134,328.00 |
| 3 | Other see justification | 7.8 | | | 50,443.00 | 13,871.00 | 64,314.00 |
| **6** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **198,642.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **214,692.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 3,000.00 |
| 2. Foreign Travel Costs | 3,000.00 |
| **Total Travel Cost** | **6,000.00** |

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

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

# RESEARCH & RELATED BUDGET - SECTIONS F-K

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 10,883.00 |
| 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. Service contracts, flow cytometry services | 2,225.00 |
| **Total Other Direct Costs** | **13,108.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **233,800.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 233,800.00 | 98,196.00 |
| | | **Total Indirect Costs** | **98,196.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **331,996.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: NHP Systems Biology- 5919

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

## PERSONNEL:

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 2 | Research Scientist | 7.2 | 46,810 | 12,872 | 59,682 |
| 1 | Program Manager | .60 | 3,633 | 999 | 4632 |
| **7** | **TOTAL OTHER:** | **7.8** | **50,443** | **13,871** | **64,314** |

**TRAVEL:** International travel is being requested this year for the Division Lead to attend two international conferences.

**SUPPLIES:** The funding requested for supplies this year is higher than in prior years. Taqman assays, miscellaneous consumables, immunology reagents, custom peptides and recombinant proteins are projected to be larger expenses in the coming year because of the increased focus on in vitro studies of HIV/AIDS.

## A. COMPONENT COVER PAGE

**Project Title:** Neuroscience

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The central aims of the Division of Neuroscience are (i) to advance the nonhuman primate (NHP) model for studies of the nervous system, (ii) to advance understanding of the nervous system in ways that are uniquely supported by the NHP model, (iii) to serve as a focal point for research in systems and translational neuroscience, (iv) to disseminate technical knowledge concerning the NHP model as well as the novel discoveries derived from fundamental neuroscience research in NHPs.

### 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: WaNPRC_Neuroscience_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_Neuroscience_B4.pdf

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

The results of our work in the Neuroscience Division have been disseminated through the publication of scientific manuscripts, presentations at international and national conferences, review articles, book chapters, our laboratory websites, and the BrainInfo website.

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

During the next reporting period, we plan to continue making progress on each of our specific aims: to advance the nonhuman primate (NHP) model for studies of the nervous system, to advance understanding of the nervous system in ways that are uniquely supported by the NHP model, to serve as a focal point for research in systems and translational neuroscience, to disseminate technical knowledge concerning the NHP model as well as the novel discoveries derived from fundamental neuroscience research in NHPs.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

During the last year, the Neuroscience Division continued to provide the intellectual and physical resources to support outstanding neuroscience research on the nonhuman primate model. The seven Core Staff and ten Research Affiliates with laboratories in the Center have provided unique research opportunities, training, consulting and collaborative expertise in the areas of primate sensory, motor and cognitive neuroscience. These services are possible because each of the laboratories is equipped with state-of-the-art instrumentation purchased in large part through extramural funding.

The diverse opportunities offered by the Core Staff and Affiliate labs can be illustrated by brief descriptions of their research highlights in the last grant year. [redacted] reports that the neuroinformatics component of the Biostructure Technology Laboratory has further developed the BrainInfo website, which provides primate neuroanatomical information and brain data mapping services to neuroscience investigators and the general public world-wide. The number of users in 2014 was extremely high, averaging over 400 visitors each day and approximately 100,000 unique visitors for the year. [redacted] lab continues to characterize the synaptic mechanisms that generate the diverse functional pathways in the primate visual system. In 2014 they discovered that NMDA type glutamate receptors surprisingly mediate the major fraction of excitatory synaptic input to midget ganglion cells and that a strong glycinergic synaptic inhibition modulates this pathway. [redacted] lab has continued work on their brain-computer interface, which has clinical potential to aid patients paralyzed by ALS, spinal cord injury, or stroke. They have made significant progress toward further development of their interface in order to empower more sophisticated paradigms, including 16 channels of high-resolution recording, multiple feedback loops, and greater on-board storage. [redacted] lab performed psychophysical studies to identify differences in the spectral sensitivity of humans and rhesus monkeys. They also examined the size-distance illusion and demonstrated that V1 receptive fields shift along with the perceived object size, potentially serving as the neural basis for the perception of angular size. [redacted] lab discovered that dysconjugate eye movements associated with strabismus receive abnormal binocular signals from motor and premotor neurons. Their data suggest that early onset strabismus causes a miscalibration in brainstem centers responsible for binocular coordination of eye movements. [redacted] lab examined the roles of visual area V4 and the prefrontal cortex in our ability to successfully recognize objects even when they are partially occluded. Their data suggest that occluded stimuli produce amplified responses in the prefrontal cortex and these responses likely serve as a feedback modulation, enhancing shape selectivity in V4. [redacted] lab has implemented novel spatial memory tasks with monkeys trained to use a joystick to navigate a virtual environment. In addition, they have collaborated with colleagues in Freiburg and Frankfurt to develop a novel thin-film array electrode to enable large channel count chronic recordings from deep structures in the nonhuman primate brain.

Research Affiliates also pursued cutting-edge research in Primate Center labs [redacted] identified the role of the cerebellar oculomotor vermis in the process of saccade adaptation. In particular, they identified that the superior colliculus provides an error signal that drives saccade adaptation and are currently investigating the pathway of this error signal through microstimulation in the superior colliculus and simultaneous recording in the oculomotor vermis. In related work [redacted] demonstrated that complex spikes in Purkinje cells of the oculomotor vermis directionally modulate saccade adaption, and her work also demonstrated that optogenetic activation of the superior colliculus produces effects similar to electrical stimulation. [redacted] identified activity in cortical areas MT/MST which may provide the neuronal basis for on-line visual control in smooth pursuit eye movements. [redacted] demonstrated that paired associative stimulation can induce changes in synaptic strength in cortico-cortical connections, and he is currently further characterizing the stimulation parameters necessary for this effect and the nature of the cortical connections that can be modified. [redacted] has examined the longitudinal performance of an implantable vestibular prosthesis in rhesus macaques. *Bair* examined shape representation in visual cortical area V4, and his results suggest that a full understanding of these mechanisms requires complex models that both preserve phase information and address object segmentation. [redacted] demonstrated that the cerebellum controls the activity of neurons in the ipsilateral abducens nucleus to keep saccades accurate. [redacted] lab performed functional analyses of broad thorny ganglion cells in the macaque retina, which made possible the first direct cross-species comparison of putative homologs, including rabbit local edge detector ganglion cells. They also demonstrated that the receptor protein syntaxin-4 is enriched beneath S-cones in both the baboon and marmoset, which, together with results from humans suggests that this specialization may have evolved for the purpose of mediating unique color vision capacities that are exclusive to primates. All of these laboratories rely on the nonhuman primate and sophisticated experimental

tools to reveal the neural processing that underlies functional capabilities, which are highly relevant to understanding the human brain and to informing clinical treatment.

In addition to the research labs, the Bioengineering Division, headed by Excluded by Requester has provided critical support in creating custom instrumentation for researchers within and outside of the Center. This has included the development of novel electronic instrumentation in the electronics shop, and construction of requisite devices by the machine shop.

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

The laboratories in the Neuroscience Division are involved in training many young scientists, including postdoctoral fellows, graduate students in the UW Neuroscience program, and UW undergraduate students. Trainees receive experience in conducting research with behaving nonhuman primates, experimental design, neurophysiological techniques, data analysis techniques, surgical techniques, and scientific writing. In addition, several of our faculty are involved in teaching, both at UW and in summer programs at Cold Spring Harbor and Friday Harbor.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | Research Scientist | Institutional Base Salary | EFFORT | | | 41,792.00 | 9,403.00 | 51,195.00 |
| 2. | | | | | | Research Scientist | | | | | 18,330.00 | 5,114.00 | 23,444.00 |
| 3. | | | | | | Research Scientist | | | | | 36,114.00 | 8,126.00 | 44,240.00 |
| 4. | | | | | | Research Scientist | | | | | 33,888.00 | 7,625.00 | 41,513.00 |
| 5. | | | | | | Lead, Neuroscience Division | | | | | 22,088.00 | 4,970.00 | 27,058.00 |
| 6. | | | | | | Research Scientist | | | | | 36,660.00 | 8,249.00 | 44,909.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **232,359.00**

## 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 | Husbandry/Veterinary Staff | 24.59 | | | 94,704.00 | 26,423.00 | 121,127.00 |
| **7** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **121,127.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **353,486.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 20,000.00 |
| 2. Foreign Travel Costs | 5,000.00 |
| **Total Travel Cost** | **25,000.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 82,396.00 |
| 2. Publication Costs | 0.00 |
| 3. Consultant Services | 8,000.00 |
| 4. ADP/Computer Services | 0.00 |
| 5. Subawards/Consortium/Contractual Costs | 0.00 |
| 6. Equipment or Facility Rental/User Fees | 0.00 |
| 7. Alterations and Renovations | 0.00 |
| 8. Animal use fees, per diem, procedures | 58,404.00 |
| 9. Electrical/mechanical shop | 25,000.00 |
| **Total Other Direct Costs** | **173,800.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **552,286.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 552,286.00 | 231,960.00 |
| | | **Total Indirect Costs** | **231,960.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **784,246.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Neuroscience Core - 5924

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

## PERSONNEL:

**SENIOR/KEY PERSONNEL:** Excluded by Requester has assumed the lead role for this division; however, this change does not impact the budget.

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Developmental and Reproductive Sciences

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1. Continue to improve and expand our consultation and collaborative services regarding the most appropriate nonhuman primate animal models, research designs, methods, and data analysis techniques.
2. Continue to assist investigators with the development of new NHP animal models.
3. Continue to improve our developmental assessment battery to provide investigators with a broad range of techniques to evaluate experimental interventions and outcomes.
4. Continue to improve our educational and outreach programs to provide quality undergraduate and graduate training in a state-of-the-art research setting and provide our expertise and protocols to investigators world-wide.

### 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: WaNPRC_DDRS_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_DDRS_B4.pdf

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

Members of the Burbacher laboratory presented their research results at the annual meeting of the Neurobehavioral Teratology Society (NBTS). This international society is focused on promoting scientific research on the developmental origins of nervous system disorders at all life stages. [redacted] served as the elected President of the NBTS at the 2014 annual meeting.
Excluded by Requester
Excluded by Requester
Members of the [redacted] laboratory presented their research results in meetings open to the public and professionals from all areas of endeavor. For example, lab members participated in the annual meetings of the Society for Neuroscience, Gained in Translation, Association for Vision Research and Ophthalmology.
Excluded by Req
[redacted] attended the Society for the Study of Reproduction and International Society for Stem Cell Research annual meetings to interact with colleagues and discuss future collaborative efforts in the realm of primate reproductive biology and stem cell sciences. In addition, she presented an invited talk on M. fascicularis assisted reproductive biology and NHP chimera production to the Oregon National Primate Research Center's Reproductive and Developmental Sciences Division and provided on-going support for transfer of ART techniques from the rhesus macaque to the fascicularis macaque. Excluded by [redacted] was also invited to present research status and findings to the NICHD on her project to generate a NHP model of Fragile X- associated Primary Ovarian Insufficiency.

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

Excluded by Requester
[redacted] laboratory- Lab members are working towards defining the maternal and fetal risk of low-level exposure to domoic acid during pregnancy in a nonhuman primate model. To accomplish our goals, we will continue with our reproductive and developmental studies of domoic acid in the laboratory. Adult females will begin exposure in April with breeding closely following thereafter. The first infants will be born in late 2015. To better understand this excitatory biotoxin, plans include collaborating with Excluded by Re at Private Source to collect electrophysiological measures from the domoic acid infant cohort. In addition, blood samples from dams and infants will be shared with [redacted] at NOAA to help establish the first biomarker of domoic acid exposure in nonhuman primates.
Excluded by Requester
In addition, the collection of hair samples for cortisol analysis will continue to better define the biological and psychological significance of this corticosteroid. The first manuscript from this project will be published in 2015. Collaborations with [redacted] laboratory on the manuscript "Biomarkers of Neonatal Encephalopathy in the Nonhuman Primate Model" will also be maintained in the coming year. Excluded by Requester
Excluded by Requester
[redacted] laboratory- Lab members are working towards conducting eye movement studies in infant nonhuman primates using non-invasive eye tracking methods. The plan is to incorporate a Tobi Eye Tracker into the infant testing laboratory. This tracker is able to maintain eye position registration even in the presence of some head movements. Other trackers tried in [redacted] lab have not lived up to this challenge. If successful, studies involving visual preferential looking and gaze can be conducted with more precision. Excluded by Requester
Studies involving treatment of infant eye muscles with select growth factors will continue. Results have indicated that slow release of growth factors including IGF-1, GDNF increase eye muscle strength and innervation in infant nonhuman primates. Efforts are currently underway to identify the best approach to strengthening underacting muscles in infants to improve treatment and develop a cure for strabismus.
Excluded by Requester
[redacted] laboratory- To maximize attainment of study goals, ESC (embryonic stem cell) culture conditions have been modified to a feeder-

free monolayer system that supports culture of a homogenous undifferentiated cell population more suitable for chimera production and embryo aggregation and culture protocols refined to support better embryo development. Testing of these new methods is underway with on-going embryo production and transfer.

To fill a significant gap in knowledge about primate stem cell pluripotency, [redacted] lab will investigate the biological and functional significance of the naive and primed state of PSCs in a macaque model. To address this goal we will a) systematically characterize macaque ES and iPS cells derived and cultured under conditions that support PSCs in the naïve and primed state, and b) utilize the macaque PSCs in an embryonic chimera assay as the 'gold' standard assessment of PSC pluripotent potential. These studies are necessary for improving the predictability of stem cell based treatments and will ultimately lead to the better selection of informative model systems for regenerative medicine. Excluded by Requester

With the rapid advancement of gene editing tools such as the TALEN and CRISPR/Cas9 systems the opportunity now exists to generate, with high rates of efficiency, site-specific gene modification of nonhuman primate embryos. The RBSCC is undertaking the generation of a nonhuman primate model of Fragile X syndrome using TALEN-mediated gene mutagenesis that is designed to disrupt function of the FMR1 gene. Outside collaborators, both academic and commercial, have also expressed interest in using the RBSCC for the generation of other disease models using the TALEN and/or CRISPR/Cas9 technologies

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

The major activities in the DDRS over the last year have revolved around the successful implementation of funded research projects, the professional sharing of original research findings and attainment of new grants in the developmental sciences.

To meet the objectives of the individual laboratories in the Division, the following activities and accomplishments have taken place:

Burbacher laboratory- A new four year project on the reproductive and developmental consequences of prenatal exposure to domoic acid, an emerging marine biotoxin, was awarded to [redacted] and his [redacted] interdisciplinary team (1RO1ES023043). In addition [redacted] continued to serve as a Co-Investigator on [redacted] NIH-funded project aimed at the identification of biomarkers reflecting hypoxic-ischemic brain injury in macaque neonates

Presented 3 posters at the Neurobehavioral Teratology Society (NBTS) meeting, where [redacted] served as the elected 2014 President. Poster presentations addressed several new research findings on important pediatric themes:

a) The number of neurons in the hippocampus is increased following early postnatal thimerosal exposure.
b) Early reflexes and responsivity to the environment are normal in thimerosal-exposed neonatal macaques.
c) The relative rise in maternal cortisol over pregnancy is highly correlated with infant hair cortisol at birth. The rise in maternal cortisol is significantly predictive of offspring performance on a test of early spatial memory and reasoning.

Members of the [redacted] lab also successfully collaborated with [redacted] of Behavioral Management Services on the biological and psychological characterization of nursery-reared macaque infants through the collection of hair samples for cortisol analysis. In addition to the collection of samples from mothers and infants currently housed at the IPRL, we were also able to obtain hair samples from IPRL-reared animals now living in adult breeding groups in Arizona. This dataset, important to understanding chronic stress, will be published in 2015.

[redacted] laboratory- Published 2 new papers on motor aspects of strabismus in the Journal IOVS. Members of the lab discovered that dysconjugate eye movements associated with strabismus receive abnormal binocular signals from motor and premotor neurons. Evidence suggests that early onset strabismus causes a miscalibration in brainstem centers responsible for binocular coordination of eye movements.

In addition, a new project on motor aspects of strabismus was funded (EY024848- [redacted] P.I.)

[redacted] laboratory- Published 2 new papers, one in collaboration with colleagues at the [redacted] where M. fascicularis ESCs (embryonic stem cells) generated in the Curnow lab were used as part of a larger study of evolutionary analyses in the primate. The second paper was a review of current and new model systems for understanding the etiology of fragile X-associated primary ovarian insufficiency.

During the last year, accomplishments in [redacted] lab include the generation of ESC-chimeric embryos at rates comparable to control animals. Recent results have also demonstrated a significant contribution of the ESC derived cells to the embryo proper, which to date has not been achieved in the nonhuman primate model (NHP).

[redacted] laboratory- [redacted] continued to serve as the local PI on a project aimed at developing a primate model to assess the developmental consequences of the pediatric thimerosal vaccine regimen. During the last year, data from the infant neurobehavioral assessments were analyzed and written up for publication. The paper [redacted] in the next few weeks [redacted] is also a co-author). Results do not support adverse effects of pediatric vaccines on cognitive development. This paper is particularly important given the recent national debate on the safety of childhood vaccinations.

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

Excluded by Requester laboratory has four students training, one graduate and three undergraduates. Students are receiving training on several assessments to evaluate the reproductive and developmental consequences of maternal-fetal domoic acid exposure.

1. Excluded by Requester is a M.S. student in the Department of Environmental and Occupational Health Sciences conducting her thesis work on the maternal kinetics of domoic acid during pregnancy in a primate model. As a student in Toxicology, she is completing her standard graduate level course work and is being mentored by the division director, Excluded by Requester in Pharmaceutics.
2. Excluded by Requester are undergraduate students in the Department of Psychology. They are receiving training in the behavioral evaluation of adult and infant macaque monkeys exposed to low-level domoic acid. Their training includes learning how to 1) work in a collaborative research environment, 2) train animals to perform basic behaviors essential to the goals of the study and 3) collect experimental data in a precise and standardized manner.

Excluded by Requester laboratory has two junior scientists in training. They receive training in conducting research in the visual and oculomotor systems of behaving nonhuman primates.

1. Excluded by Requester is a Ph.D. student conducting her thesis work in visual system. She is receiving training and mentoring in systems neuroscience. As member of the UW Neurobiology and Behavior program she also completed standard graduate level course work in Neuroscience and Responsible Conduct of Research in National Research Service Awards. More details of training offered is describe in our program's website (http://depts.washington.edu/uwbri/) Excluded by Requester is also receiving mentoring in aspects of conducting collaborative research, surgical techniques, experimental design and grant writing.
2. Excluded by Requester is receiving training in oculomotor neuroscience related to our project "Visual Processing and Smooth Eye Movements". Excluded by Requester is also receiving mentoring in aspects of conducting collaborative research, surgical techniques, experimental design and grant writing.
3. We have provided training to postdoctoral scientist Excluded by Requester in conducting single unit recordings from dorsal stream visual areas (MSTI, MSTd) of strabismic nonhuman primates.

Excluded by Requester participate in our annual clinical basic science symposium "Gained in Translation" by presenting their work in poster sessions. The Gained in Translation meeting bring together clinicians and basic scientist from University of Washington, University of British Columbia and Oregon Health Sciences University.

## 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

**C.5.a Other products**

File uploaded: WaNPRC_DDRS_C5a.pdf

**C.5.b Resource sharing**

File uploaded: WaNPRC_DDRS_C5b.pdf

In Excluded by Requester lab, the RBSCC is currently evaluating a macaque embryonic stem cell line that has been genetically modified with a knock-out of the FMR1 gene. Work to generate an AAV vector to host a pre-mutation length of the FMR1 gene is on-going and nearing completion.

Excluded by Requester laboratory- Excluded by Requester laboratory is responsible for sharing the extensive neurobehavioral test battery that has been developed at the Infant Primate Research lab over the last thirty years. Standard operating procedures for evaluating physical, cognitive, motor and social development in macaque infants will continue to be made available to interested parties in academia, the federal government and the pharmaceutical industry.

Excluded by Requester laboratory- As a core service, RBSCC activities (provision of macaque ESCs) within the Division have driven interactions within the UW (IPRL, CHDD, ISCRM and UW Medicine) and other US Institutes (Whitehead, Howard Hughes Medical and Boston Children's Hospital, and UCLA).

Following isolation and characterization of macaque ESC lines with the FMR1-KO and FMR1-KI, these lines will become available to the broader research community.

## 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?**

Excluded by Requester

aboratory- Nonhuman primate studies undertaken as part of a pilot study funded through the ITHS/WaNPRC Ignition grant has aided in the formation of Ovastasis, a spin-out company from the University of Virginia focused on non-hormonal strategies for female contraception.

**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

Excluded by Requester

laboratory- Delays to RBSCC production and attainment of goals were encountered due to necessary laboratory shut-down, relocation and renovation over a period of 18 mths (Dec 2012-May 2014).

### 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | Principal Investigator | Institutional Base Salary | EFFORT | | | 22,035.00 | 4,958 00 | 26,993 00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **26,993.00**

## 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 | Research Scientist, Husbandry/ Veterinary | 19.0 | | | 89,671.00 | 19,690.00 | 109,361.00 |
| **4** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **109,361.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **136,354.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 4,545.00 |
| 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** | **4,545.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **140,899.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 140,899.00 | 59,178.00 |
| | | **Total Indirect Costs** | **59,178.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center(PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **200,077.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Division of Developmental and Reproductive Sciences

- **5932**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

## PERSONNEL:

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 2 | Research Scientist | 12.6 | 73,159 | 16,751 | 89,910 |
| 2 | Husbandry/Veterinary Staff | 6.40 | 16,512 | 2,939 | 19,451 |
| **4** | **TOTAL OTHER:** | **19** | **89,671** | **19,690** | **109,361** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Global Programs

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

Excluded by Request

The Division of Global Programs at the Washington National Primate Research Center oversees the Center's international programs and activities. The Division, directed by [redacted] initiates and maintains essential international programs that facilitate access to critical primate resources. The objectives of the Division of Global Programs include:

1) Resource Support: Assist with the development of international breeding programs and the efficient acquisition and sharing of existing captive primates to ensure the availability of primates at a local, national and international level;
2) Research: Facilitate joint research projects relating to the biology, management, and conservation of wild primate populations with collaborating institutions;
3) Training: Provide educational/training opportunities in primatology, conservation biology and global health for students, staff, and faculty from collaborating institutions;
4) Outreach: Engage and educate the general public about the importance of primate conservation, the significant achievements in biomedical research, and the translational value of the work.

The Division's research focus includes joint research in the area of Conservation Biology to contribute to the improvement of primate population health, management strategies, and long-term viability as well as providing data that is pertinent to the operation of primate breeding programs both international and domestic. The Division's research projects involve joint participation with 13 foreign collaborating institutions in 11 countries and are conducted at those institutions or related field sites. These countries are: Indonesia, Russia, Nepal, China, Bangladesh, Thailand, Dem. Rep. of Congo, Mexico, India, Brazil (program in development), and Laos (program in 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: WaNPRC_Div_Global_Programs_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_Div_Global_Programs_B4.pdf

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

We maintain active, up-to --date postings on our University-affiliated websites to provide news about research, training, and outreach programs, as well as recent publications of interest. We also regularly participate in local science festivals/expos to help inform the general public about important research finding and relationship to human health (e.g., UW's annual PAWS-on-Science Festival)

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

Global Programs will continue to build on our main objectives: resource support, research, training, and outreach. We will continue to assist with the development of international breeding programs and the efficient acquisition and sharing of existing captive primates so as to ensure the availability of nonhuman primate resources at a local, national and international level.
We will assist our international partners who have ongoing breeding programs and research facilities (i.e, PSSP-IPB, Indonesia; RIMP-RAMS, Russia) and those who have an interest in developing breeding programs (NPRC-NEBORS, Nepal; AU, China; and MU, Thailand) in support of primate resources and biomedical research. Our support will entail consultative assistance, on-site training, and visiting scientist training at the WaNPRC relating to all aspects of infrastructure development and operations such as primate facility design, colony management, SPF screening, clinical care, animal care and use oversight, research facilities, etc.
The Division also will maintain the PRRS, a service-based program that provides critical primate-resource support for the national and international primate research community by facilitating the efficient acquisition and sharing of existing captive primates and primate-related resources by investigators and institutions.
Research and training represent the backbone of international collaboration. We will continue to initiate and support collaborative research in the area of Conservation Biology, primate population health, management strategies, and long-term viability as well as issues related to global health, at the human-primate interface. This research program also complements and supports the Division's resource objective by generating data that is often pertinent to the development and operation of primate breeding programs both international and domestic. Our goal is to broaden our assessment approach and standardize our data collection protocols to facilitate the acquisition of

reliable, quantitative data that permit comparison on a global scale. We will develop a comprehensive and integrative approach to population assessment that includes of a number of important variables: abundance, habitat viability, and genetic diversity.
We will conduct/assist with population surveys of both endangered species and those important to biomedical research. Continuing projects include surveys in Indonesia (Javan gibbon, Sulawesi and long-tailed macaques), Nepal (Assamese and rhesus macaques), China (Tibetan macaque), Bangladesh (rhesus macaque), Mexico (black howler monkey), and planned in Thailand (long-tailed macaque) and Laos (long-tailed macaque). Our recent survey of the long-tailed macaque population on Java, Indonesia suggests a potentially alarming situation. We found vast areas of forest where the local people consistently reported "no monkeys." The fact that the macaque populations are often located in areas of human habitation, where sightings and conflict occur daily, may lead to the perception of over-abundance in regions where actual population size may be much smaller. We do not have adequate data on the current status of the "common species" – those primates that represent the critical resource link in support of biomedical research (longtailed, pigtailed, and rhesus macaques). It would seem prudent to expand population surveys of key research species to confirm their current population status and take appropriate action as needed to ensure the long-term viability of these critical resources.
GIS technology and remote sensing imagery will be incorporated as part of the standardized assessment protocol. This technology facilitates an integrative approach to population assessment by combining the population data with forest-cover changes, human settlement expansion, etc. to model population changes and long-term viability. GIS is not only relevant to our research on habitat viability, but is also becoming an essential tool in our work on population distribution and abundance, genetic characterization, as well as population management strategies.
Maintaining genetic diversity among regional populations is critical to the long-term viability of a species. Genetic characterization of wild primate populations is not only important for conservation and management, it is also helpful in identifying potential groups from which to acquire breeders/replacements for captive breeding so as to ensure genetic variability in the breeding colony. Specific ancestry of subjects can influence their suitability as human disease models since differential ancestry can equate to genetic differences linked to phenotypic differences that impact disease susceptibility. Chinese rhesus, for example, show differences in their resistant to infection with SIV compared with Indian rhesus, and so, are considered by many to be less suitable as subjects for HIV research than Indian rhesus. The long-tailed macaques show extensive geographic distribution and so comparative genomic analysis of regional representatives will be particularly important for identifying critical genetic differences and for informing the selection of appropriate subspecies for specific biomedical research studies. Characterizing the genomes of geographically diverse long-tailed macaques will require acquisition of DNA from the animals with verifiable geographical origins in the wild for these efforts to be meaningful. We plan to expand our evaluation of wild primate populations and we will continue our ongoing genetic assessment in Indonesia, Nepal, and China and begin work in Bangladesh, India, Thailand, and Laos. Much of our DNA analysis to date has been accomplished through the use of serum samples collected during trapping, but we also have begun using noninvasive techniques to acquire DNA for genetic testing (i.e., via fecal samples). Both sample collection techniques will be used during the upcoming grant period. DNA testing (including analyses of mtDNA, STRs and MHC and targeted gene sequencing) will be conducted by [redacted] (WaNPRC & ONPRC) or per her consultation with our partners, and via ongoing collaboration with [redacted] (CNPRC).
Our Division has always placed a high priority on providing educational and training opportunities for our intl collaborators. We will continue to conduct the annual field training programs ("Field Course in Conservation Biology & Global Health: At the Human-Environment Interface") with our partner institutions in Bangladesh, China, D.R. Congo, Indonesia, India, Mexico, Nepal, and Thailand. Working with WaNPRC, UW, and Center for Global Field Study, we also will continue to provide intl research and training opportunities in primatology for students and staff from the UW, other U.S. institutions (including NPRC's). We will continue to host intl colleagues participating in the Visiting Scientist Program at the WaNPRC.
We plan to expand our outreach efforts to local area schools (K-12) to promote an appreciation of the importance of biomedical research, conservation, the sustainable use of nonhuman primates, and to inspire students to pursue careers in the biological sciences. We present information about primate conservation together with that of biomedical research - discussing the importance of conserving the natural populations of primates along with the concept of sustainable use of primates for important biomedical research. The message acknowledges the importance of the conservation of animals in the wild and at the same time demonstrates how critical they are to biomedical research and the translational science. By discussing the importance of conservation along with primate use in biomedical research, you help "humanize" the perception of the biomedical researcher – and in turn, the views on biomedical research. When possible, we will invite our UW students to participate in the outreach presentations.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

To date, the Division has completed 90 field training programs for over 1,500 participants (including university students, park rangers, NGO staff, lab-based researchers, etc.) in the program countries. These collaborative training programs provide field courses focusing on "*Conservation Biology & Global Health: At the Human-Environment Interface.*" In addition, we also have conducted 113 outreach education programs (to date) dealing with primatology, conservation biology and global health for over 5800 students (K-12).
Other notable programs conducted jointly with the Division include:

- The *Intl Field Study Program-Indonesia* (with the UW Center for Global Field Study (CGFS) and Dept. of Psych) is an annual interdisciplinary study abroad program, in collaboration with the Primate Research Center at Bogor Agricultural U. (PSSP-IPB), Indonesia, designed to provide field-based educational, training, and research opportunities for UW/U.S. students interested in Primatology, Conservation Biology, and Global Health. Training takes place at the Tinjil Island Natural Habitat Breeding Facility.
- The *UW-inSPIRE* Program (*Students Presenting International Research Experiences*) is shared with the CGFS and Dept. of Psych. The program allows UW students to provide presentations on their international research experiences to local schools in the greater Seattle area.
- Excluded by Requester The affiliated Center for Global Field Study [redacted] Founder and Director) aims to facilitate and provide international field based educational, research, and outreach opportunities for students and professionals from the UW and partnering institutions around the world in areas relating to Global Health and the Environment – at the human-environment interface.
- The Division also continued the oversight of the NIH P40 grant program "Primate Resource Referral Service [redacted] PI). This program provides the communications/database network needed for efficient acquisition and sharing of existing captive primates and primate-related resources by investigators and institutions both nationally and internationally. The demand for nonhuman primates for use in biomedical research in the U.S. continues to surpass resource availability. Over the past few years, U.S. research facilities have experienced critical shortages of key primate models such as the Indian-origin rhesus macaque (*Macaca mulatta*) [redacted] 2008; [redacted] et al., 2009). More recently, pigtail macaque (*M. nemenstrina*) resources in the U.S. have become in short supply requiring the need for importation from source countries. The concern over the supply of primate resources was highlighted in the 2004-08 NCRR Strategic Plan (NCRR, 2004) through formulation of a specified objective: *"Increase the number of nonhuman primates available for biomedical research, and evaluate the other methods to address the shortage of nonhuman primates. The need for these animals has risen substantially and is expected to escalate even more due to their essential role in biodefense, gene transfer research, and the increased risk of transmission of infectious agents…"* (pg. 14). The supply concern remains and was addressed in the recent 2009-2013 NCRR Strategic Plan (NCRR, 2008) as a stated strategy: *"Expand and ensure the development of and access to animal models"* (pg. 16).
  Excluded by Requester
  Excluded by Requester
- *Indonesia Program:* The Division continued consultative support for the Indonesian-based breeding facility (at PSSP-IPB) and the Natural Habitat Breeding Facility on Tinjil Island. [redacted] continued his annual surveys of the *M. fascicularis* on Tinjil Island and of the endangered *M. nigra* at the Tangkoko Nature Reserve in North Sulawesi. He and his Indonesian colleagues also completed a major island-wide distribution survey of the *M. fascicularis* on Java and Bali. He also conducted his annual 3-week Field Courses in Conservation Biology & Global Health at the following locations: 1) the Tangkoko Nature Reserve for 16 participants and 2) on Tinjil island for 10 participants from IPB and other regional universities and 3 U.W./U.S. participants in the International Field Study Program-Indonesia- in collaboration with PSSP-IPB. He also conducted 3 community outreach education programs for local school children (K-12).
  Excluded by Requester
- *Nepal Program:* Collaborative training, outreach, and research efforts continue in Nepal [redacted] traveled to Nepal in Feb to conduct the 14th annual Field Training Program in Conser Biol & Global health and continued the ongoing collaborative research. He also conducted 2 outreach education programs for local school children (K-12) [redacted] also serves as co-advisor for one PhD student in the Dept. of Zoology at [redacted]
  Excluded by Requester
  Excluded by Requester
  Private Source
- *Bangladesh Program:* The annual field course was postponed due to politic issues in the country.
- *Thailand Program:* Collaborative research and training efforts continue in Thailand with Chiang Mai University, Mahasarakham Univ., and Mae Fah Luang University. [redacted] conducted the 1st annual Field Courses in Conser Biol & Global Health in July at Mae Fah Luang Univ. and the 3rd annual field course at Mahasarakham Univ. He also conducted 5 community outreach education programs for school children (K-12).
  Excluded by Requester

- *Mexico Program:* The "Field Course in Conser Biol & Global Healthin collaboration of Instituto de Ecologia, Mexico was postponed in 2014 but is scheduled for April 2015..
- *India Program:* Excluded by Requester traveled to Assam, India in Dec to conduct the 4nd annual field course as part of the collaborative program with the Gibbon Conservation Centre and Guahati University. An outreach program was also conducted.
- *China:* Excluded by Requester Private Source hosted a Visiting Scholar (senior PhD student) from our collaborating institution – during 2014. The student worked on manuscript writing and learning population assessment software.
- *USA Program:* In June, Excluded by Reques conducted a three day mini field course at Chief Leschi Tribal Schools in Puyallup, Washington (Grades 8-12, 18 students.) The course was modeled version of his university-level course and titled: "*college prep-Field Course in Conser Biol & Global Health: At the Human-Environment Interface*" Excluded by Requester also exhibited at two science fairs in Seattle, UW's PAWS-on-Science Festival in April.

**Resource Support:** One of the primary aims of our Division is to help international institutions (particularly those in habitat/range countries, i.e., "source country" or "country of origin") develop captive breeding programs that will ensure the availability of primate resources. The Summary Statement from our P51 grant review (2006) highlighted the significance of these international endeavors. *"The WaNPRC has developed strong relationships, and continues to partner with source countries to ensure a continuing supply of NHPs for emerging threats to world health. The Division of International Programs has made substantial efforts in countries rich in primate biodiversity, including countries upon which the WaNPRC (and the United States Government) depends for NHPs."* (p 64). In light of the continuing demand for primates in U.S.-based research 2008) and the Excluded by Requester diminishing primate resource options nationally and abroad, the global significance of establishing and maintaining scientific partnerships with multiple habitat/source countries cannot be overstated.
In addition to the mutual benefits derived through joint research and training, habitat-country breeding programs, supported through international collaboration, provide immediate and long-term priority resource support for biomedical research addressing human health concerns of both countries. The priority of access afforded via a formal collaborative program is an important consideration and something that cannot be assured through reliance solely on commercial suppliers. Strategically, primate breeding programs in habitat countries not only ensure a resource supply but more importantly, serve a critical role as **"primary resource facility"** contributing to the genetic viability of our domestic colonies or providing breeder stock for U.S.-based breeding facilities in the event of catastrophic loss. Past events (i.e., hurricane Katrina) have illustrated the potential risks associated with total reliance on domestic supply. Most of the U.S.-based breeding facilities are located along the southern seaboard, the potential for loss due to natural disaster is a real concern. Likewise, if a domestic colony was decimated as a result of disease, it would be very difficult to rebuild the national capacity (in a timely fashion) solely from domestic stock. Therefore, establishing international partnerships with habitat countries and assisting with the development of international breeding programs represents a strategic solution to ensuring the availability of resources needed to address global human health concerns.

**Support of Translational Research**. Maintaining collaborative partnerships with research institutions in habitat countries offers yet another opportunity of strategic importance to the future of biomedical and translational research. On many levels, the expense of conducting biomedical research with primates in the U.S. is becoming increasingly difficult. Increasing costs and a decreasing funding base are frequently forcing researchers to consider other options such as conducting their research projects and programs abroad. Such a move is not easily accomplished without a well-developed, collaborative infrastructure already in place (namely, facilities, logistical support, and trust). Having collaborative programs already established with partner institutions that can accommodate the logistical and animal-use requirements of U.S.-approved research protocols can help ensure a smooth, timely transition and the likelihood of success. In a recent issue of *Nature* (Dec. 2010) Excluded by Requester Director of the Institute of Translational Medicine and Therapeutics at the Univ. of Pennsylvania discussed the establishment of NIH's new National Center for Advancing Translational Sciences (NCATS) and the Center's focus on translational medicine and therapeutics (TMAT). He noted that the NCATS could act as a visible point of contact for extramural partners, including industry, charitable foundations and the US Food and Drug Administration who collectively might facilitate a more efficient approach to drug discovery and development. He concluded by outlining the greatest challenge for the new Center: *"...we will need common standards of data protection and privacy, and shared infrastructure that allows secure and compliant sharing of diverse types of information, including clinical data,* ***across countries*** *and sectors. This is the foundation upon which a* ***global*** *TMAT enterprise can be established" (pg. 869).*

Clearly, the presence of well-established international partnerships is critical to the efficient and timely implementation of translational research. With an increasing number of researchers and organizations moving their preclinical studies and drug development to Asia, **the WaNPRC's existing network of international partners (many of whom are already following U.S. Primate Center SOPs, have participated in our annual training programs, and have a good knowledge of U.S. standards and expectations) could provide exceptional on-site research support and aid in the harmonization of global research practices.**
**Research**: Clearly, the Division of Global Programs plays a central role in the Center's mission and in support of the NIH community by initiating and maintaining international partnerships that can facilitate access to critical primate resources. The objectives of the Division, however, go well beyond resource support. The Division also encompasses a broad range of scientific and service-oriented programs including collaborative research, training, outreach (and conservation) – many of which address issues of national and international concern. The significance of maintaining and expanding these areas of collaboration has been cited consistently by reviewers of the WaNPRC's P51 grant over the past 15 years. **In many respects, these activities represent the backbone of international collaboration and are essential to the long-term viability of the partnerships.** This point is also expressed in the following: *"It is also important to recognize that all of us who work with primates in the US benefit from these activities as Randy's program is often seen as 'giving back' to countries of origin in a way that is seldom done, that is, by providing the kind of research and management training that helps indigenous programs"* [redacted] Director, Private Source Excluded by requester Primate Center, *24 Mar. 2011*, see Section 14.a., "Letters of Support"). The Division conducts and assists with collaborative field research in the area of primate conservation biology (e.g., population status, genetic characterization, habitat viability, population management, reprod. biology, disease risk, etc.) to aid in our understanding and improvement of primate population health, management strategies, and long-term viability. The research is directed at the study of both endangered species and those of importance to biomedical research (e.g., pigtail, rhesus, and long-tailed [*M. fascicularis*] macaques). This research program also complements and supports the Division's resource objective by generating data that is often pertinent to the development and operation of primate breeding programs both international and domestic. For example, genetic characterization of wild primate populations is becoming increasingly important to the management of U.S. holdings and identification of suitable models for research. With respect to U.S. breeding colonies, there is increasing attention on the geographic ancestry of our animals. The specific ancestry of subjects can influence their suitability as human disease models since differential ancestry can equate to genetic differences that are linked to phenotypic differences that impact disease susceptibility. Therefore, field studies that can provide genetic data to help verify the geographic origins of our domestic colonies will facilitate better genetic management and ultimately definition of more suitable animal models.

*Resource Support:* Ensuring Primate Resource Options. The Division of Global Programs has a successful track record of developing international primate resource options in support of the global primate research community. The Scientific Review Administrator's note in the Division's Summary Statement from our previous P51 grant review (2006) identified the Division as a model for the other NPRCs. "Continuation of the international effort to develop infrastructure to assure a continuing supply of NHPs for critical studies is important for all primate users in this country, especially those funded by the PHS. The WaNPRC has a long history in such programs and serves as a model for other Centers." (p. 65). *Predicting Primate Demand*. The Division's "Primate Resource Referral Service" (PRRS) is a P40- supported service that has provided critical primate-resource support (acquisition and sharing of existing primates and biomaterials) for the U.S. and international research community for more than 30 years. As part of the research component of the service, data on primate availability and requests will be analyzed in an effort to predict emerging trends and future demand for specific primate models. This will enable us to take a more proactive role in identifying potential supply concerns, hopefully forestalling future shortages such as the critical rhesus macaque shortage that came to national attention in 2002. The results can be relayed to the relevant NIH divisions so that appropriate action may be taken to deal more effectively with an impending shortage.
*Research: Developing a Comprehensive Approach to Primate Population Assessment*. Primate field researchers are now in a position to utilize a number of technological advances in equipment, web-based computer modeling, GIS (geographic information system) and remote sensing imagery (via Landsat), genetic and genomic testing, and disease assessment to facilitate a multivariate assessment of a population. Building on these advances, we will continue to develop a comprehensive and integrative approach to population assessment that includes consideration of a number of important variables including abundance (population size); habitat viability (e.g., existing area, rates of decline); and genetic diversity (conservation genetics).

Additionally, identifying and quantifying anthropogenic threats - at the human-primate interface (e.g., pathogen transmission, hunting, illegal trade, etc.) - are essential to this task and help to establish a complete database needed to model population viability scenarios. Collectively, this allows for a more pro-active approach to population management and conservation which ultimately translates into benefits for human health [Excluded by Requester] et al., 2004).

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

Training: The Division of Global Programs has always placed a high priority on providing educational and training opportunities for our international collaborators. [redacted] has been instrumental in establishing collaborative field-based training programs that encompass Primatology, Conservation Biology and Global Health for our UW students, WaNPRC staff, and students and professionals from other NPRCs and U.S. institutions professionals affiliated with our international programs. Beginning with his first "Field Course in Primate Behavior and Ecology" conducted on Tinjil Island, Indonesia in 1991, the training and educational opportunities for both international and U.S. participants has grown steadily [redacted] al., 2008 [redacted] et al., 2009). These training programs are typically conducted concurrently with Division-related research projects, thus helping to maximize efficient use of funds. For his international collaborators, training ("transfer of information") is central to the success of the collaboration. This position was conveyed very clearly during the early development of our Indonesia Program and has been echoed by our all our other partners Most recently, the Directors of the eight NPRCs submitted a statement to the NIH Scientific Management Review Board on the "Critical Role of Primate Centers in Translational Research" and highlighted "...education and conservation efforts with international academic partners." (pg. 2) as elements of themes of importance identified by NIH Director [redacted] (NPRC Consortium, 2010). Our training programs involve collaborative annual field courses in "Conservation Biology & Global Health" with our partner institutions. These courses are critical in helping to establish a growing body of well-trained, regional experts who are capable of implementing the programs needed to ensure the future of their country's important resources - thereby helping to ensure the conservation of existing primate species and the availability of primates for human health research. The field courses also provide an opportunity to discuss the significance of biomedical research - supported with scientific facts - and address the claims made by animal rights groups (both in the US and abroad) who often spread misinformation about animal research and use the media to distort the facts and confuse the general public regarding biomedical research. To assist [redacted] with the field course trainings, statistical analysis, population modeling and GIS, a new Research Scientist, [redacted] was hired in November.

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Community engagement and educational outreach are vital to ensuring the future of biomedical research, translational science and the advancement of global health. Integrating some form of community outreach into every NIH-supported grant would be an extremely effective approach to broaden the support for biological and biomedical research and ensure that important research results reach the general public. Community outreach and engagement also has been identified as an action strategy in the NCRR 2009-2013 Strategic Plan (NCRR, 2008). The Division's expanding emphasis on outreach education for K-12 students at the local, national and international level is seen as a significant step in helping to promote sound conservation practices while also demonstrating the value of biomedical research and the important translational benefits to human health. Our goal is to promote an appreciation of the importance of biomedical research, the importance of conservation and sustainable use of nonhuman primates, and to inspire students to pursue careers in the biological sciences. From our past outreach experience, we have found it especially effective to present information about primate conservation together with that of biomedical research - discussing the importance of conserving the natural populations of primates along with the concept of sustainable use of primates for important biomedical research. The message acknowledges the importance of the conservation of animals in the wild and at the same time demonstrates how critical they are to biomedical research and the translational science. This holistic message is powerful since people typically don't associate a laboratory researcher with conservation. By discussing the importance of conservation along with primate use in biomedical research, you help "humanize" the perception of the biomedical researcher – and in turn, the views on biomedical research. We plan to conduct outreach programs in the local schools (targeting K-8) that will involve Powerpoint presentation and discussion, handouts, equipment demonstrations with hands-on activities (e.g., use of microscope, pipettor, etc.), activity-based handouts, and an art/essay contest. Presentations will highlight the cutting-edge biomedical research being conducted at the WaNPRC as well as at the other NPRCs and research institutions. A key element of the presentations will be to demonstrate the **translational benefits of the research**. When possible, we will invite our UW students (particularly those involved in primate research) to participate in the outreach presentations.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | | Staff Scientist | Institutional Base Sala | EFFORT | | | 96,800.00 | 21,780.00 | 118,580.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **118,580.00**

## 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 | Research Scientist | 12.6 | | | 72,655.00 | 20,271.00 | 92,926.00 |
| **2** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **92,926.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **211,506.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 1,500.00 |
| 2. Foreign Travel Costs | 25,550.00 |
| **Total Travel Cost** | **27,050.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 6,500.00 |
| 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. Software, computer hardware, and poster production/printing | 1,256.00 |
| 9. Mailing, shipping to program countries | 1,890.00 |
| **Total Other Direct Costs** | **9,646.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **248,202.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Costs (MTDC) | 42.0 | 248,202.00 | 104,245.00 |
| | | **Total Indirect Costs** | **104,245.00** |

| | |
|---|---|
| **Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number) | U.S. Department of Health and Human Services (DHHS) Program Support Center(PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820 |

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **352,447.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

| | |
|---|---|
| **K. Budget Justification*** | File Name: GlobalPrograms.pdf (Only attach one file.) |

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

**BUDGET JUSTIFICATION: Division of Global Programs - 5933**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**PERSONNEL:**

**SENIOR/KEY PERSONNEL:** ORIP has approved the % Effort effort level of the division lead, Excluded by Requester

**OTHER PERSONNEL:** Excluded by Requester has been hired as a Research Scientist and reports to the Center Director to avoid conflict with the division lead, though her work supports the Division of Global Programs. Her salary represents the overall increase on this budget.

## A. COMPONENT COVER PAGE

**Project Title:** Pilot Studies

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The purpose of the WaNPRC Pilot Program is to provide support for high risk, potentially high impact studies in nonhuman primates (NHP). The program goals include developing and expanding NHP models for biomedical research, acquiring preliminary data for subsequent grant application or successive human clinical trials. This program is particularly significant when funding for preliminary, explorative investigation is very limited. Although the studies conducted through this Pilot Program are speculative in nature (models development, "proof of concept"), these studies can potentially have significant impact, providing essential preliminary data for subsequent grant submissions. The WaNPRC has established a cooperative arrangement with the Institute for Translational Health Sciences at the University of Washington. This arrangement is to the mutual benefit of both the WaNPRC and ITHS, provides a broader base for the dissemination of the RFP announcement, and expands the diversity of the Review Committee, by including scientists from both components.

### 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: WaNPRC_Pilot_Program_B2.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 research studies described in the Accomplishment section are still underway.

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

No significant changes are anticipated. The RFP for the FY54 program has been released and applications are being received. The awardees will be identified and notified by April 1, with funding to begin May 1.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

Pilot Project Program: Accomplishments

The WaNPRC has continued its join support of the development of a model pilot study program in collaboration with the Institute for Translational Sciences (ITHS) at the University of Washington. These consortium-based activities are focused on the more efficient use of existing funding through the development and encouragement of collaborative research activities that are likely to lead to significant advances in biomedical research. The WaNPRC and Clinical Translational Science Award (UL1TR000423) (CTSA)-funded ITHS at the University of Washington co-sponsor the 'Ignition Award' program. This program provides funding for pilot studies to support development of innovative and/or translational studies utilizing nonhuman primate resources that would lead to subsequent grant applications, new nonhuman primate models, or human clinical studies. The Request for Proposals announcement was disseminated through both the ITHS and WaNPRC websites, email notifications to affiliates at other institutions, and posted notices at key locations in the Health Sciences Center. In FY53, the WaNPRC commitment was to award up to $65,000 for each of the three studies.

The Review Committee membership has representation from both the ITHS and the WaNPRC. The review process goal is to identify up to three promising studies, at least one of which must have a focus on translational science.

The members of the FY53 review committee were:

| WaNPRC | ITHS |
|---|---|
| | |

Excluded by Requester

Ten applications were received. The applications were assigned to members of the review committee for directed review, review and summary; all applications were available to all committee members. Each application was reviewed and scored by at least two committee members. All applications were then discussed at a general meeting, and top three scored application received awards.

The recipients were:

Excluded by Requester

"Testing CD180-based Hepatits B Virus vaccine in macaques"

We have developed a novel vaccine platform utilizing monoclonal antibodies (mAbs) specific for a Toll-like receptor (TLR) family member, CD180 (RP105). Appropriate viral antigens (Ags) attached to anti-CD180 when inoculated into mice induce strong and rapid IgG antibody (Ab) responses and protective immunity. Based on our preclinical studies in mice, we have filed patents through the University of Washington Center for Commercialization. Here we propose to validate the CD180 vaccine platform in macaques and to compare a CD180-based vaccine for Hepatitis B virus (HBV) to an FDA-approved HBV vaccine. We will attach recombinant Hepatitis B surface Ag (HBsAg) to our anti-human/macaque CD180 mAb, G28-8 and verify that the HBsAg-anti-CD180 contains epitopes capable of inducing neutralizing Ab responses. We will then prime and boost long-tailed macaques (M. fascicularis) with either the HBsAg-anti-CD180 vaccine formulated with the CpG-B adjuvant or a licensed HBV vaccine formulated with Alum. Blood samples taken after primary and secondary immunization will be compared for neutralizing Ab levels and for HBsAg-specific T cell responses. We predict that the CD180-based HBV vaccine will induce stronger and longer lasting Ab and T cell responses than the current HBV vaccine.

Excluded by Requester

"Surfactant Protein A to prevent preterm birth"

Intrauterine infection and inflammation are major causes of preterm labor, which is the leading cause of perinatal morbidity and mortality not due to congenital anomalies. We have refined a unique chronically catheterized nonhuman primate (NHP) model of preterm birth (Macaca nemestrina; pigtail macaque) that allows us to investigate temporal relationships between infection, inflammation and preterm birth in the amniotic fluid and maternal blood. The objective of this proposal is to perform pilot studies to demonstrate the potential for developing surfactant protein A (SP-A) as a therapeutic or preventive agent for preterm labor. We have partnered with [redacted] (co-investigator), who has demonstrated in mice that SP-A (endogenous protein made by the fetal lung) is a powerful inhibitor of inflammation induced by microbial activators of the immune response even when administered well after the microbial stimulus. As SP-A is itself a fetal protein, it presumably has a high fetal safety profile, which also makes it an excellent therapeutic candidate. Our unifying hypothesis is that SP-A prevents inflammatory-mediated preterm birth induced by Group B Streptococcus infection in our NHP model of preterm labor. These studies would enable translation to prospective human studies of women in preterm labor and women at risk for preterm birth.

Excluded by Requester

Excluded by Requester In vivo directed evolution of AAV vectors that transduce photoreceptors and the retinal pigment epithelium when injected into the vitreous"

The purpose of the proposed project is to generate adeno associated virus (AAV) vectors for ocular gene therapy in human blinding diseases. This proposal seeks to perform an in vivo evolution procedure to identify AAV vectors capable of delivering therapeutic genes to the photoreceptors and retinal pigment epithelium of the retina when injected into the vitreous of the eye. AAV vectors available now can only be used to delivery therapeutic genes to these tissues when injected subretinally, which is an invasive procedure that carries a high risk for permanent retinal damage and blindness when performed on diseased retinas.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | | Director | 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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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 project1 | 75,000.00 |
| 9. Pilot project2 | 75,000.00 |
| 10. Pilot project3 | 75,000.00 |
| **Total Other Direct Costs** | **225,000.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **225,000.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 225,000.00 | 94,500.00 |
| | | **Total Indirect Costs** | **94,500.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **319,500.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Pilot Studies - 5940

This budget does not have significant deviations from the prior year's budget.

## A. COMPONENT COVER PAGE

**Project Title:** Bioengineering

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

(1) Selection or design of equipment for new experiments
(2) Fabrication of customized instrumentation
(3) Modification of existing instrumentation for new or expanded investigations
(4) Development of devices to enhance or monitor the health of nhps
(5) Development of technology that reduces the physical restraints of experimental animals
(6) Training of researchers and students in the best use of existing equipment
(7) Rapid diagnosis and repair of equipment and systems to maximize experimental productivity
(8) Make designs available to the larger nhp 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: WaNPRC_Bioengineering_B2.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?

As a service entity – one whose existence is focused on supporting the technical/equipment needs of the primate research community – our plans are largely shaped by the needs of that community. Where new or changing trends in research directions become clear and affordable, we try to gain knowledge, skills, and tools that support new research directions; to make these known and useful to the community, and to learn from the imperfections of our previous efforts so that we may deliver our services more efficiently.
Therefore, while the majority of efforts in the coming period will support activities much like the previous period, there will be new specific efforts including:
•An expansion of our use of 3D printing. We expect this to increase on a longer term basis as better materials, multi-material products, and tighter tolerances and surface finishes become practical;
•Expand our ability to analyze and develop wireless communication devices and power transmission for use with neural recording and stimulation devices;
•Work with some engineering faculty and students to help develop a practical single-chip stimulator device; and
•Expand the existing project-control database system to help users keep better track of ongoing activities.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

Our primary activity, as always, is the development and support of medical research using non- human primates. In the past year Bioengineering made 17 repairs and was involved in 51 projects (some of which had numerous sub-projects). Representative examples of these projects follow:

*Remotely-controlled battery/line powered camera systems: Seattle Colony*. We completed design and construction on a series of systems for monitoring animal activities. With these systems the investigators can observe monkey behavior and control camera orientation securely over the Internet. [Aims 1, 2, 3, 4]

*NeuroChip-3B* and *NeuroChip-2HV*: Excluded by Requester . Completed design and delivered prototype NC-3B devices for firmware and experimental development. We anticipate modifications and construction of additional devices. We also produced a new batch of NC-2HV devices. These complex board-sets can replace numerous complex instruments, as they include electrode headstages, ADCs, signal analysis, and stimulators. Packages of NC-2 and NC-2HV schematics were downloaded 167 times from the Bioengineering web site in 2014. We have provided technical assistance towards the development of a one-chip stimulator [aims 1, 2, 5, 6, 8]

*Rotating infusion stands*: Excluded by Requester *OrNPRC* Excluded by Requester Private Source We produced a series of devices which enable delivery of medications, transfusions, and obtaining blood samples in a series of experiments involving safe gene transfer with hematopoietic stem cells involved in genetic infectious and malignant diseases while minimizing restrictions on animal movement [aims 2, 3, 5, and 8].

Other projects include supporting new experiment spaces (particularly fo Excluded by Requester ; new sensor devices (e.g. accelerometers, gyros, blink detectors); and modifications to commercial equipment for use in specialized research settings. Repairs to equipment have taken a smaller fraction of available time, but occasionally involve sophisticated diagnostics and are always important in achieving high experimental productivity [aims 3, 6, 7].

## 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

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b Resource sharing**

File uploaded: WaNPRC_Bioengineering_C5b.pdf

As time permits we assemble information packets detailing our designs and upload them to the Bioengineering web site, where they are publically available.

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 77,996.00 | 21,761.00 | 99,757.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **99,757.00**

## 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 | Other | 15.6 | | | 82,430.00 | 29,180.00 | 111,610.00 |
| **3** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **111,610.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **211,367.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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)** | **211,367.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 211,367.00 | 88,774.00 |
| | | **Total Indirect Costs** | **88,774.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **300,141.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Bioengineering - 6089

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

### PERSONNEL:

**SENIOR/KEY PERSONNEL:** A new Senior/Key Person is not being added Excluded by Requester is listed as Senior/Key Person to fulfill the report form requirements.

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 1 | Instrument Maker Lead | 6.00 | 34,858 | 12,340 | 47,198 |
| 1 | Instrument Maker | 3.60 | 16,760 | 5,933 | 22,693 |
| 1 | Engineering Technician | 6.00 | 30,812 | 10,907 | 41,719 |
| **3** | **TOTAL OTHER:** | **15.6** | **82,430** | **29,180** | **111,610** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Biostructure Technology Laboratory

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

1) Map image data from classical neuroanatomic publications into the NeuroMaps macaque brain atlas. The value of NeuroMaps as a repository of image data mapped to a common canonical atlas is a direct function of the amount of existing data there for comparison. During the coming grant period Excluded by Requester will map the architectonic cortical areas from publications by such authorities as Paxinos et al., Pandya, Preuss, Price to the NeuroMaps Canonical Atlas. They will map thalamic nuclei as defined by Excluded by Requester and they will map the amygdalar nuclei as defined by Amaral.
2) Map image data of the distribution of experimental data such as recording sites, stimulation sites, gene expression, other neurochemical and immunochemical markers and regions of fMRI and PET activation and suppression will be mapped beginning with the most recent publications.
3) Recruit investigators to submit data to NeuroMaps for creating figures for publication and for comparison with data submitted by others Excluded by will contact authors who have published illustrations most suitable for storage in the data archive and work with them to map data from those images into the NeuroMaps repository. Neuroscientists associated with the National Primate Research Centers will be among the first to be approached.
4) Program NeuroMaps to enable users to warp sections from the Atlas to corresponding sections of an MRI so that they can estimate the stereotaxic location of structures that are not visible in the MRI. Excluded by will seek outside funding to develop this 'tool', which will be particularly useful to investigators wishing to implant stimulating or recording electrodes or chemitrodes into subcortical structures of the macaque.

### 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: WaNPRC_BSTL_B2.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?

BrainInfo/NeuroMaps (http://braininfo.org) served approximately 100,000 unique visitors in 2014. The website was visited an average of 406 times per day. We are confident that most visitors find information of value, because: 1) more than 25% of identifiable visitors return to the website one or more times within 30 days; 2) the average number of pages viewed per visit is 3, the number required to navigate from the home page to the Central Directory that provides the definition and other basic information about the brain structure a visitor seeks; 3) the heaviest users from identifiable .edu and .gov sources are institutions with large neuroscientific programs, such as NIH, Harvard, Oxford, UCLA, RIKEN (Japan); and 4) About 15% of visitors are referred by other websites that provide links to BrainInfo/NeuroMaps; they include Wikipedia, Mouse Brain Library, Genes to Cognition Online, Human Cortex Involved in Language, etc.

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

1) Continue adding new information to the BrainInfo knowledge base.
2) Complete upgrade of NeuroMaps Viewer
3) Continue mapping image data from classical neuroanatomic publications to NeuroMaps
4) Recruit investigators to submit data to NeuroMaps

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

1) Added to the value of BrainInfo/NeuroMaps (http://braininfo.org) as a source of authoritative neuroanatomical information for neuroscientists, students, and the general public
2) Updated the BrainInfo knowledge base to include information from new editions of authoritative neuroanatomical textbooks and brain atlases; Upgrade the NeuroMaps Viewer for greater precision and more intuitive use by remote users of the website.
3) Incorporated several hundred neuroanatomical terms and definitions from the functional model of the mammalian nervous system (L. Swanson) into the nomenclature (NeuroNames) of BrainInfo.
4) Produced and incorporated into Braininfo drawings of cortical areas and nomenclature from latest editions of textbooks: Principles of Neural Science [Excluded by Requester] et al.) and The Human Nervous System [Excluded by Requester] [Excluded by Requester] The drawings are thoroughly labeled with hyperlinks to definitions and other information about structures in the drawings.
5) Hired NeuroMaps programmer [Excluded by Requester] PhD to upgrade the NeuroMaps Viewer and further develop the Mapper.
6) Provided authoritative neuroanatomical information to neuroscientists, instructors, students and the general public (See B.5 Dissemination below)

## 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

**C.5.a Other products**

File uploaded: WaNPRC_BSTL_C5a.pdf

**C.5.b Resource sharing**

NOTHING TO REPORT

The NeuroNames ontology of some 3200 brain structures and 15,000 synonyms in seven languages has been formatted in XML and is now available for download from the BrainInfo website.

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | 15,684.00 | 4,376.00 | 20,060.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **20,060.00**

## 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 | Other | 9.08 | | | 59,068.00 | 14,586.00 | 73,654.00 |
| **3** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **73,654.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **93,714.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 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 |
| **Total Other Direct Costs** | **900.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **94,614.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Costs (MTDC) | 42.0 | 94,614.00 | 39,738.00 |
| | | **Total Indirect Costs** | **39,738.00** |

**Cognizant Federal Agency**
(Agency Name, POC Name, and POC Phone Number)

U.S. Department of Health and Human Services (DHHS) Program Support Center(PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **134,352.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Biostructure Technology Laboratory - 6091

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

### PERSONNEL:

**SENIOR/KEY PERSONNEL:** A new Senior/Key Person is not being added. Excluded by Requester is listed as Senior/Key Person to fulfill the report form requirements.

**OTHER PERSONNEL:** The table below provides detail for the "Other" category in the budget Other Personnel list. The total line in the table below matches what is reported in the budget for the "Other" category.

| **OTHER PERSONNEL** (Detailing Budget Page) | | | | | |
|---|---|---|---|---|---|
| # | PROJECT ROLE | CAL. | REQ. SAL. | FRINGE | FUNDS REQ. |
| 1 | Research Scientist | 1.20 | 6,830 | 1,906 | 8,736 |
| 1 | Programmer | 5.24 | 33,476 | 9,340 | 42,816 |
| 1 | Husbandry/Veterinary Staff | 2.64 | 18,762 | 3,340 | 22,102 |
| **3** | **TOTAL OTHER:** | **9.08** | **59,068** | **14,586** | **73,654** |

This category does not represent a significant deviation from the prior year.

## A. COMPONENT COVER PAGE

**Project Title:** Division of Primate Resources Associate Directors Office

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

Specific Aims:
1) Improve the quality of services and programs in the DPR.
2) Provide additional animal resources for the WaNPRC.
3) Develop the DPR personnel through a comprehensive training program.
4) Continue to improve the DPR functions through the ARMS database system.
5) Improve the quality and characterization of the Colony.
6) The Associate Director and the DPR staff will continue to work closely with investigators within the WaNPRC and outside the center to improve the role of M. nemestrina (pigtail macaques) in human 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: WaNPRC_DPR_AD_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_DPR_AD_B4.pdf

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

The Associate Director has participated in both the Directors Meetings as well as the Breeding Colony Management and Genetics/Genomics consortiums calls and the face to face meetings in Oregon.
Seven publications have also been generated during this period:

1 Excluded by Requester
Excluded by Requester Antifibrotic Therapy in Simian Immunodeficiency Virus Infection Preserves CD4+ T-Cell Populations and Improves Immune Reconstitution With Antiretroviral Therapy. J Infect Dis. 2014 Sep 22. pii: jiu519. [Epub ahead of print]

2 Excluded by Requester
Excluded by Requester
T. Selection of unadapted, pathogenic SHIVs encoding newly transmitted HIV-1 envelope proteins. Cell Host Microbe. 2014 Sep 10;16(3):412-8. doi: 10.1016/j.chom.2014.08.003.

3 Excluded by Requester
Excluded by Requester
Excluded by Requester Effect of suberoylanilide hydroxamic acid (SAHA) administration on the residual virus pool in a model of combination antiretroviral therapy-mediated suppression in SIVmac239-infected indian rhesus macaques. Antimicrob Agents Chemother. 2014 Nov;58(11):6790-806. doi: 10.1128/AAC.03746-14. Epub 2014 Sep 2.

4 Excluded by Requester
Excluded by Requester HIV-1-induced AIDS in monkeys. Science. 2014 Jun 20;344(6190):1401-5. doi: 10.1126/science.1250761.

5 Excluded by Requester
Excluded by Requester Vaccine-induced myeloid cell population dampens protective immunity to SIV. J Clin Invest. 2014 Jun 2;124(6):2538-49. doi: 10.1172/JCI73518. Epub 2014 May 16.

6 Excluded by Requester
Excluded by Requester Molecularly tagged simian immunodeficiency virus SIVmac239 synthetic swarm for tracking independent infection events. J Virol. 2014 Jul;88(14):8077-90. doi: 10.1128/JVI.01026-14. Epub 2014 May 7.

7 Excluded by Requester Tracking the luminal exposure and lymphatic drainage pathways of intravaginal and intrarectal inocula used in nonhuman primate models of HIV transmission. PLoS One. 2014 Mar 25;9(3):e92830. doi: 10.1371/journal.pone.0092830. eCollection 2014.

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

The Associate Director will continue to engage in LEAN quality improvement with process improvement, SOP development, training and

certification of staff to provide a better trained and qualified workforce to support our investigators and animals. Better coordination and communication with our investigators and between our veterinary, behavioral, husbandry, and research support staff to will continue to continue to improve our support consistent with the goals of the studies. DPR will also continue to strive to better understand and develop novel techniques to meet the experimental goals of its investigators as well as to improve its processes to optimize animal care and experimental support. Evaluation of standard practices such as the effects of routine postoperative procedures on experimental results will be explored and optimized. A specific example would be the effects of antibiotics commonly employed to reduce the incidence of post-operative infections in immunocompromised animals on the microbial flora/immune system. Effects of improved biosafety and husbandry practices will be explored on rates of disease transmission along with different strategies for decolonization of animals to reduce the number of animals that are carriers of agents such as MRSA and shigella.
Funds to further expand the ABC will be sought along with completion of the current planned expansion of the space for the colony. Further characterization of the breeding colony including using nextgen sequencing and Nanostring technologies to further enhance our detection of viral pathogens will be explored. Novel disease prevention strategies with the potential to improve colony management, such as vaccination for SRV, will be explored.
Efficient data entry into ARMS for common procedures will be a priority. The process of refining entry for common research procedures should be completed and refinements for entering clinical procedures will begin. Estimates by the staff involved suggest that this will result in as much as 50% labor savings on the time needed to do data entry which will allow our techs and vets to focus on their primary missions of providing research support and veterinary care.

**B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?**

The Associate Director for the Division of Primate Resources (DPR) provides the animal and personnel resources to support research at the Washington National Primate Research Center (WaNPRC). The DPR staff provides the husbandry, diagnostic, behavioral, and veterinary care for the WaNPRC's nonhuman primates as well as the personnel to perform research procedures and manage the service components for research protocols.

During the current reporting period Excluded by Requester DVM, MS, DACLAM was hired into the role of the Associate Director Excluded by Requester has sought to address each of the specific aims noted above. There has been a real emphasis on training and education of the husbandry, veterinary, and technical staff with the objective of ensuring that all aspects of the support provided by DPR are optimized to meet both the animal's needs and the experimental objectives. This has been combined with a LEAN approach to ensure that the increases in quality are matched by increases in efficiency. Over 20 SOP's and policies were either created or updated with associated training and certification of technical staff to ensure understanding and compliance. SOP's such as PPE, veterinary observations, blood collection, etc were standardized across the three Seattle based facilities and the Arizona Breeding Colony(ABC). The consistency created has allowed staff to cross over efficiently between the Seattle facilities allowing for accomplishment of increasing experimental demands without an associated increase in staff. Our husbandry staff has been training on sedation and recovery of primates to allow them to deliver to and receive animals back from our technical and veterinary staff which will allow more efficient research support and veterinary care operations. Procedures that DPR commonly performs in support of experimental protocols are being optimized, such as lymph node biopsies, endoscopic biopsies, and BALs with improved results reported by investigators and less intra and post-procedure complications reported by the veterinary staff. Several new experimental procedures have also been developed and in some cases already performed in support of experimental protocols, including subdural catheter placement in the lumbar spine for substance administration and CSF collection, fecal transplant via endoscopy, and laparoscopic mesenteric lymph node biopsy. Timed mating practices have been modified to include the use of timed compound breeding, and early indications are that this change has improved breeding efficiency/pregnancy rates and reduced labor requirements to meet the needs of our investigators for timed mated animals.

Improvements to the ARMS data base have allowed for the inclusion of behavioral data and behavioral case management, the ability to look at previous pairing attempts, and to determine an animal's contacts to help in isolation and disease management. A workflow process improvement is currently underway to improve the user friendliness of the system and to reduce the time necessary to completely document common procedures such as blood collection, lymph node biopsy, etc.

Under the Associate Director's leadership approval from the University IBC was sought and granted for a change in husbandry practices from the current bedding system to a flush system that will allow for1) better ergonomics/safety for the staff, 2) more efficient husbandry operations, 3) cleaner environment with less risk of disease transmission for the animals, and 4) less waste going to the landfill. The DPR will be implementing these changes over the upcoming months. The Associate Director also worked with the Environmental Health and Safety group to ensure adequate biosafety practices for various laboratories/procedure spaces operated by investigators with the result being improved personnel safety and reduced risk of disease transmission.

Supplemental funding was sought and granted to further expand the ABC, and that expansion is currently in the final planning stages. This should result in an improvement in the housing capabilities for pigtail macaques and allow for better breeding/production from this facility to meet the growing demand for these animals. A renovation of the Western Facility in Seattle was also overseen and is nearing completion. It will add space for ~100 additional primates as well as expanded surgical, endoscopy, procedure, and cagewash space.

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

The Associate Director has participated in both the Directors Meetings as well as the Breeding Colony Management and Genetics/Genomics consortiums, including face to face meetings in Oregon. At these meetings there was a great exchange of information and best practices around SPF colony management including breeding practices, genetic monitoring to ensure genetic diversity in the colony, diagnostic and quarantine practices for ensure appropriate SPF status as well as protecting the colony from TB. At the directors meeting updates on the status and work of each center was presented, along with important discussions around future directions, budgets, collaborations with CFARs, etc.

The Associate Director also participated in a Tradeline conference where important information on the state of the art in vivarium design and construction were presented. This information has translated into improved plans for the ongoing renovations as well as the upcoming construction at the ABC.

## C. COMPONENT PRODUCTS

### C.1 PUBLICATIONS

Not Applicable

### C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

### C.3 TECHNOLOGIES OR TECHNIQUES

Novel techniques such as Laparoscopic Mesenteric Lymph node Biopsy techniques will be written up for technical/procedural publications. Other techniques such as fecal transplant will be incorporated into the publications of the results generated from their use. Finally, evaluations of the effects of antibiotics on common immune parameters and the microbial flora of the GI track, effects of improvements of biosafety practices on disease transmission, etc will be published in appropriate journals.

### C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

### C.5 OTHER PRODUCTS AND RESOURCE SHARING

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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 Associate Director has been working with the WaNPRC to deal with a number of challenges many of which have achieved or are nearing positive resolutions. Renovations have had a short impact on our operations with obvious long term benefits. Ongoing renovations in two of our Seattle facilities have reduced the number of primates that could be housed and caused some operational inefficiencies. The Western renovation is nearing completion with a projected April 1st occupancy date and will add space for approximately 100 macaques as well as more cagewash capacity, surgical/procedural space, and better workflow. Infectious diseases including MRSA have presented some challenges for our veterinary staff, however improved isolation/biosecurity practices and associated training are well underway and should result in an even better ability to contain these concerning agents. As previously noted we have investigations underway to improve diagnostics for conditions (such as SRV) where our results indicate that the current state of the art at US based diagnostic laboratories is less than ideal, especially for the pigtail macaque. Our veterinarians are also evaluating options for treating/eliminating these conditions which should also result in a series of publications which will provide significant benefit to the field at large. Improvements in diagnostics/treatments/prevention could also have impacts beyond the lab animal field, to include improvements in conservancy for wild populations of macaques which have consistently demonstrated high levels of SRV infection.

### 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Excluded by Requester | | | | Associate Director | Institutional Base Salary | EFFORT | | | 119,145.00 | 33,241 00 | 152,386 00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **152,386.00**

## 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)** | **152,386.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **0.00** |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | 14,162.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **14,162.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. Conference registrations | 1,856.00 |
| **Total Other Direct Costs** | **1,856.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **168,404.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 168,404.00 | 70,730.00 |
| | | **Total Indirect Costs** | **70,730.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **239,134.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

## BUDGET JUSTIFICATION: Division of Primate Resources Associate Director - 6093

This budget does not have significant deviations from the prior year's budget.

## A. COMPONENT COVER PAGE

**Project Title:** Working Groups

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The WaNPRC has a long history of participation in both formal and informal National Primate Research Center network activities. Consortium activities are an important means to accomplish two main objectives: conserving limited resources and increasing programmatic capabilities. The WaNPRC serves as both participant and leader across a variety of consortium activities and expects these to increase in both number and scope moving forward.

The Consortium/working groups report on here include:

Breeding Colony Management
Occupational Health and Safety
Pathology
Behavioral Management Services
Center Outreach

### 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: WaNPRC_Working_Groups_B2.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?

BCMC/BMC Plans for the Coming Year: In conjunction with the Genetics-Genomics Working Group (GGWG), a survey was prepared and performed regarding extreme phenotypes. Based on the results, the combined working groups plan to pursue investigation of these phenotypes based on pedigree and genetic data to determine the contribution of genetics to the phenotypes.

The BCMC plans to increase collaboration with the Behavior Management Consortium to better coordinate colony management with behavioral management. This collaboration will initially focus on best practices for nursery rearing, as well as establishment of endpoints for behavioral management.

The BCMC is working to establish a reference library of materials regarding NHP care and management to provide to regulatory agencies for training and guidance. Emphasis will be placed on areas where reviewers have expressed concern, including nursery rearing, preventive medicine, breeding colony management, and behavior.

Occupational Health and Safety: The OHS group will continue to hold discussions on best practices for Occupational Health screening and other topics of interest.

Outreach: The Assistant Director of Center Programs, along with representatives from Tulane and Yerkes, has been appointed to a subcommittee of the Outreach Working Group to assess the feasibility of a Public Relations subgroup or new consortium working group. While significant progress has been made by the subcommittee, the final outcome will be determined in the next reporting cycle.

Pathology: The plans for next year are to continue having weekly international Pathology Virtual Slide Conferences that are attended by NPRC pathologists and pathologists from various other national and international academic institutions that work with NHP's. Additionally, expansion of the Primate Pathology Image Database, which contains digital gross photographs of lesions and scanned/digitized images of histology slides, will continue via addition of new cases to the database. Further, a face-to-face meeting of the Pathology Working Group is planned sometime during the next year, with date and site to be determined.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

**Behavioral Management Consortium (BMC):** BMC members meet monthly via web conference with annual meetings scheduled in conjunction with the national meeting of the American Society of Primatologists (ASP) where members can engage in on-site presentations and discussions. Subcommittees with assignments for specific deliverables meet as needed, typically every other month. Additional web conferences consisting of consortium members and selected invitees are organized to explore topics of mutual interest, for example, nonhuman primate (NHP) socialization techniques. Information exchange is further enhanced through extensive sharing of documentation including; SOPs, Environmental Enhancement Plans, training materials and images. Other topics including staffing, prevalence and possible treatments for abnormal behavior cases, regulatory trends, and others are routinely addressed in consortium interactions. BMC members have constructed behavioral taxonomies and testing methodologies that are shared with other facilities via the NHPRC Consortium website. BMC has formally shared selected documentation (SOPs, environmental enhancement materials) with members of the European Primate Network (EUPRIM-NET). Excluded by Requester continues to serve on the Behavioral Management Consortium (BMC) and participated in a BMC sponsored symposium last year.

**Breeding Colony Management Consortium (BCMC):** The goal of the BCMC is to strengthen communications between individual NPRC breeding colony management teams in order to collectively improve and maximize the use of the resource.

Members of the BCMC Working Group meet monthly via web conference with extensive email discussions between meetings. A face-to-face meeting was held in November 2014 at the Oregon National Primate Research Center in conjunction with the Genetics-Genomics Working Group (GGWG) to increase collaborations between the two working groups among the primate centers. Members of the GGWG demonstrated software that can be used in genetic analysis of NHP breeding colonies, and techniques to be used to establish and maintain genetic goals for the colonies.

Progress has been made in the past year on several BCMC projects. The multi-center evaluation of the M-vac measles vaccine has been competed. Under Review

Under Review

Phase I of the Colony Health Benchmarks using a subset of breeding colony population data has been completed, and preparation for phase II has been initiated. The BCMC is working to establish standardized automated methods for the extraction of relevant demographic data from the animal records of the different primate centers to allow for consolidated analysis.

The BCMC has prepared and performed surveys regarding TB testing, necropsy guidelines, and disaster recovery plans among the primate centers to establish best practices, and to provide mutual support among the centers in the event of an emergency.

**Pathology:** During 2014, 17 presentations were given that included seminars given to DCM residents, staff and faculty, International Virtual Slide conferences given to veterinary pathologists and pathology residents, Pathology Rounds presentations given to Center clinicians, technicians and staff, and presentations at national/international scientific meetings. CPS pathologists routinely participate in the annual Primate Pathology Workshop as well; the workshop now is a well-attended component of the annual meeting of the American College of Veterinary Pathologists. Also, the pathologists actively participate in the NPRC Pathology Working Group Consortium; the pathologists presented an International Virtual Slide Conferences attended by PWG pathologists, NPRC clinicians, and pathologists and veterinarians from other national and international institutions working with NHP's. The CPS pathologists provide regular seminar-style training of Post-DVM graduate students in the DCM, and routinely provide informal and formal pathology instruction to clinical veterinarians, and Center researchers and technicians, including didactic lectures in DCM courses. The teaching aspects prepare Post-DVM graduate students and Center clinical veterinarians to sit for the ACVP Board Examination or for the American College of Laboratory Animal Medicine Certification Examinations. The CPS has continued its teaching/training opportunities for animal technicians and comparative medicine residents as well.

**Occupational Health and Safety:** The initial goal of the Occupational Health and Safety group was to identify opportunities for the NPRC health and safety professionals to communicate and collaborate regarding shared programs, materials, and benchmarks, and to collectively identify methods to create stronger and more efficient Occupational Health and Safety programs.

The group has been meeting in person annually as well as holding conference calls every other month. We met at Oregon NPRC in April of 2014 and will be meeting at Wisconsin NPRC in early May 2015. We are finding these face to face meetings with facility tours to be valuable in learning how something that works for one facility may or may not be feasible to use at another.

**Outreach:** The Assistant Director of Center Programs, along with representatives from Tulane and Yerkes, has been appointed to a subcommittee of the Outreach Working Group to assess the feasibility of a Public Relations subgroup or new consortium working group. While significant progress has been made by the subcommittee, the final outcome will be determined in the next reporting cycle.

## 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

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## A. Senior/Key Person

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Excluded by Requester | | | | Assistant Director | Institutional Base Salary | 0.0 | | | 0.00 | 0.00 | 0.00 |
| 2. | | | | | | Director | | 0.0 | | | 0.00 | 0.00 | 0.00 |
| 3. | | | | | | Associate Director | | 0.0 | | | 0.00 | 0.00 | 0.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **0.00**

## B. Other Personnel

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

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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) | 7,614.00 |
| 2. Foreign Travel Costs | 0.00 |
| **Total Travel Cost** | **7,614.00** |

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 1,350.00 |
| 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** | **1,350.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **8,964.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified total direct costs (MTDC) | 42.0 | 8,964.00 | 3,765.00 |
| | | **Total Indirect Costs** | **3,765.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Tel.(415) 556-5766 Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **12,729.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Working Groups - 7353**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**TRAVEL:** Domestic travel costs are requested for a total of 9 trips at $846 per trip for the working groups, as follows: Behavior Management, Pathology, Breeding Colony Management, Outreach and Occupational Health. This is the same as what was requested in the prior year; however, this year all of the working groups are combined into a single request.

**SUPPLIES:** Funds for supplies are requested, specifically for the outreach working groups for development, production, and distribution of outreach materials. This is consistent with the prior application.

## A. COMPONENT COVER PAGE

**Project Title:** High-throughput Molecular Profiling Core

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The Division of Nonhuman Primate Systems Biology is organized into a Research Component (composed of Virology and Integrative Analysis, Mucosal Immunology, and Animal Models) and two Cores (the High-throughput Molecular Profiling Core and the Statistical Analysis and Modeling Core). The Research Component and both Cores are involved in each Divisional project. Information directly related to the High-Throughput Molecular Profiling Core is provided here, and a more detailed description of all studies and results can be found in the Research Component portion of the Division's progress report.

Specific Aim:

To provide resources and expertise in high-throughput molecular profiling as applied to nonhuman primate models of human disease. The High-Throughput Molecular Profiling Core is a resource for obtaining datasets by microarray, proteomics, and next-generation RNA sequencing (RNA-Seq). This includes furnishing well-proven protocols for initial sample collection and storage and for primary isolation of suitable RNA or protein extracts. For RNA-Seq, the Core supports sequence read acquisition for comparative mRNA profiling, global transcriptome profiling, and microRNA abundance measurements.

### 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: WaNPRC_HTMP_Core_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_HTMP_Core_B4.pdf

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

Sharing of division-generated resources and information to the scientific community is an essential component of the Division of Nonhuman Primate Systems Biology. All resources are made publicly accessible within four weeks of publication. In addition, all aspects of our data dissemination plan comply with NIH research grants and contracts on obtaining and disseminating biomedical research resources. Complete details of data dissemination can be found in the progress report for the Statistical Analysis and Modeling Core.

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

There are no changes in our specific aims; we will continue to provide resources and expertise in high-throughput molecular profiling as applied to nonhuman primate models of human disease; to act as a resource for obtaining datasets by microarray, proteomics, and RNA-Seq; and to provide well-proven protocols for sample collection/storage, and for primary isolation of suitable RNA or protein extracts to the NHP research community.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

The overarching goal of the Division of Nonhuman Primate Systems Biology is to facilitate the NHP research community in embracing the newly emergent paradigms of systems biology and next-generation transcriptomics. Resource development and research occurs through internal and external projects managed through one of the Research Components and supported by the Cores. This support includes: 1) using rapid and cost-effective methods for high-throughput molecular profiling, 2) providing computational infrastructure and cutting edge techniques to mine the resulting data sets and 3) disseminating the generated resources to the project PIs and the research community at large.

During the last year, the seamless Divisional workflow which integrates the activities of the Research Component and the Cores has resulted in the generation of substantial community resources and many significant biological findings in several areas of research. These accomplishments fall into seven general areas and are detailed below:

1) *In vivo* and *in vitro* SIV/HIV-related studies
2) NHP models of respiratory diseases
3) NHP models of viral hemorrhagic fever
4) Improvements of NHP reference transcriptomes
5) Community outreach
6) Dissemination of Division-generated resources to the public (See Section B5 below.)
7) Development of new genomics tools for NHP systems biology applications (See Section C3 below.)

### *In vivo* and *in vitro* SIV/HIV-related studies

Host transcriptional response to RhCMV/SIV vaccination

In collaboration with Excluded by Requester Private Source we have compared the host response to vaccination with gp96-Ig secreting cells carrying SIVmac251 peptides, plus and minus a boost with gp120 protein Excluded by Requester *al., 2014**). The RNA profiling and associated functional analysis indicated: 1) vaccination can alter the (non-)immunizing effect of low-dose challenges in a time-dependent manner, 2) immunized animals show evolving host response in the course of multiple challenges, and 3) persistently protected animals have a particularly strong innate and humoral immune response only after the first challenge, and show both prevailing innate and adaptive cellular responses after further challenge.

- GEO Accession number: GSE59608
- Number of samples analyzed: 225
- Platform: Agilent-015421 Rhesus Macaque Gene Expression Microarray

RNA-seq of mucosal challenge compartment during acute SIV infection

Using samples collected from the Division's large SIV/rhesus macaque acute infection model, we carried out the first deep mRNA sequencing analysis of mucosal host responses in the primary infection compartment Excluded by Requester *al., 2014**). This study revealed that during acute infection, a significant host response was mounted in the mucosa before inflammation was triggered, which had a detrimental effect on tissue integrity. In collaboration with Excluded by Requester (University of Pittsburgh), Division resources are being utilized to expand on this initial study by performing a comparative total RNA-seq analysis between the rhesus acute infection model and a similar acute infection model using African Green Monkeys, a natural host of SIV. Total RNA-seq data from the rectal challenge compartment and draining lymph nodes, spanning the necropsy collections at 1, 2, 3, 6, 12, and 84 days post infection from both model systems have been generated and the functional analysis comparison between the two species is near completion.

- GEO Accession number: GSE56845
- Number of samples analyzed: 23
- Platform: Illumina Genome Analyzer IIx (RNA-seq)

Microbial translocation during SIV infection

During chronic HIV/SIV infection, CD4+IL-17-producing T cells (TH17) are significantly depleted from mucosal tissues, and their absence is highly associated with gastrointestinal (GI) dysfunction. However, the kinetics of immune dysfunction and microbial translocation, and how this dysfunction may affect the establishment of viral reservoir, remains unknown. In collaboration with Dr. Nikki Klatt (WaNPRC), we have obtained longitudinal GI tract biopsies and blood at early acute time points from six rhesus macaques following intrarectal SIV

challenge with SIVmac239x. The Division performed microarray assay on GI tract biopsies and blood samples throughout the acute infection and the associated host RNA profiling and functional analysis is underway.

*In vitro* CD4+ T cell line projects

We previously published several studies that used mRNA-seq, microRNA-seq, or global proteomics to characterize the early host response to HIV infection of SupT 1 cells. The subsequent integration of two additional data sets with the mRNA-seq data has resulted in two new publications. The first [redacted] *et al., 2014** *(J. Virol.)* reports on the integration of a total RNA-seq data set, which provides quantitation of non-coding and non-polyadenylated RNAs, with mRNA data and demonstrated large numbers of differentially regulated transcripts early after infection, many of which corresponded to nascent transcripts that had not been processed to mature, polyadenylated forms. Excluded by Requester

- GEO Accession number: GSE53993
- Number of samples: 16
- Platform: Illumina HiSeq 2000 (RNA-seq)

The second new publication reports on the results of a collaboration with Excluded by Requester (University of Pennsylvania). Using the Sup T1 model system, we analyzed the alterations to histone post translational modification (PTM) profiles using nano-LC-MS/MS, as well as the expression of chromatin-associated enzymes using microarray analysis [redacted] *et al., 2014**). We observed major changes in histone PTM abundances which we linked to massive fluctuations in mRNA expression of associated chromatin enzymes. Excluded by Requester

- GEO Accession number: Pending
- Number of samples: 8
- Platform: Agilent 4 × 44k Human WG microarrays (G4112F)

**NHP models of respiratory diseases**

MERS coronavirus

Our colleagues at Rocky Mountain Laboratories (RML, an NIAID intramural research facility) discovered that unlike the rhesus macaque model, the common marmoset provides a severe, partially lethal, disease model of MERS-CoV. We collaborated with investigators at RML to generate total RNA-seq data from marmoset lung specimens to characterize expression changes consistent with the development of pulmonary fibrosis, as well as alterations in serum cytokine transcripts Excluded by Requester *et al. 2014**).

- GEO Accession number: GSE55023
- Number of samples: 43
- Platform: Illumina MiSeq (RNA-seq)

Influenza virus

Excluded by Requester is leading the Division's investigation into DNA vaccines as an approach for a universal influenza vaccine to protect against a wide range of diverse circulating and emerging seasonal and pandemic strains of influenza. In a vaccine efficacy trial in nonhuman primates, cynomolgus macaques were immunized with an adjuvanted DNA vaccine that was designed to induce broadly neutralizing antibody and cross reactive T cell responses in the lung mucosa. To determine if the vaccine was able to reduce inflammatory responses, we performed an extensive microarray analysis on lung tissues collected from a subset of 3 monkeys from each group that were sacrificed 3 days after challenge during peak viral replication. RNA expression patterns showed that vaccination significantly suppressed inflammatory responses in the lung when compared to controls suggesting this vaccine could be effective in reducing post-influenza susceptibility to secondary infections. Interestingly, the RNA expression also showed that vaccinated animals had higher recruitment of T cell responses into the lung, an outcome that further supports a role of the mucosal T cell response induced by the vaccine in mediating protection.

We also performed gene expression profiling for a study conducted at RML in which cynomolgus macaques were infected with influenza A virus H7N9. As reported in [redacted] *al. 2014**, when compared to previous studies, the emerging H7N9 influenza virus was more pathogenic in cynomolgus macaques than seasonal influenza A viruses and most isolates of the pandemic H1N1 virus but less pathogenic than the 1918 Spanish influenza virus or highly pathogenic avian influenza (HPAI) H5N1 virus. Excluded by Requester

- GEO Accession number: GSE48976

- Number of samples: 24
- Platform: Agilent-048534 Rhesus 60k version of 44k

**NHP models of viral hemorrhagic fever**

We used mRNA sequencing to analyze PBMC from cynomolgus macaques after VSVΔG/EBOVgp immunization and subsequent EBOV challenge. We found a controlled transcriptional response that transitioned to immune regulation as the EBOV was cleared. This observation supported the safety of the vaccine [Excluded by Requester] *et al. 2015**).

- GEO Accession number: GSE64538
- Number of samples: 30
- Platform: Illumina Genome Analyzer IIx (RNA-seq)

To identify host factors associated with arenavirus virulence, in collaboration with colleagues at RML, we used a cynomolgus macaque model to evaluate the pathogenesis of Lujo virus (LUJV), a recently emerged arenavirus that caused an outbreak of severe viral hemorrhagic fever in southern Africa [Excluded by Requester] *et al. 2014**). The Division performed RNA profiling analysis on PBMC samples and detected a 72-hour delay in induction of host responses to infection during the less pathogenic LUJV infection compared to the animals infected with the more pathogenic LASV and an early differential expression of a subset of genes specific to LUJV infection that accounts for the delayed inflammatory response.

- GEO Accession number: GSE49838
- Number of samples: 61
- Platform: Agilent-015421 Rhesus Macaque Gene Expression Microarray

There are three ongoing NHP studies at RML for which the Division will perform transcriptional analysis to define the specific host responses: 1) determination of host responses in whole blood during interferon and ribavirin treatment in rhesus macaques infected with Ebola virus, 2) comparative analysis of early transcriptional responses in PBMC from cynomolgus macaques infected with Lassa virus or Marburg virus, and 3) direct comparison of the host response to West and Central African Ebola isolates in rhesus macaques.

**Improvements to NHP transcriptome resources**

Complex immune loci

In collaboration with [Excluded by Requester] [Private Source] ), we are developing a strategy for accurately quantifying rhesus MHC allele expression, taking into full account the complexities of the MHC class I gene family in macaques. Our strategy leverages a large collection of full-length rhesus MHC genomic sequences and a custom-developed computational pipeline, and only requires regular macaque RNA-seq data from users.

Multiple NHP reference transcriptomes

The Nonhuman Primate Reference Transcriptome Resource (NHPRTR) is an R24-funded resource that is a collaboration involving the Division, Illumina Inc. and Cornell Medical College. There were two publications during this reporting period describing additional resources generated through this collaboration. Prior to the results described in [Excluded by Requester] *al. 2014*(J. Med Primatol.)* the genome annotations of rhesus (*Macaca mulatta*) and cynomolgus (*Macaca fascicularis*) macaques, two of the most common non-human primate animal models, were limited. Through this work, we uncovered thousands of novel isoforms and un-annotated intergenic transcripts including coding and non-coding RNAs, polyadenylated and non-polyadenylated transcripts [Excluded by Requester] *et al. 2015** describes Phase II of the NHPRTR project in which 10.1 billion fragments of tissue-specific RNA-seq data was generated and released to the public. These data come from ~15 individual tissues from 11 NHP species and subspecies. The sequence quality was such that 88% of the reads align to human reference sequences, allowing for the full listing of expression abundance across all tissues for each species, using the reads mapped to human genes.

- DATA SUMMARY: The complete tissue-specific RNA-seq dataset consists of 157 libraries across 14 species/subspecies. The raw data sets contain over 10 billion read pairs (100 × 100bp) totaling to 2.44 terabases of Illumina sequence. A summary of the amount of tissue-specific raw RNA-seq data can be found at: http://nhprtr.org/

NHP cell-specific transcriptomes

In collaboration with Excluded by Requester (Private Source), we are using RNA-seq to build transcriptome databases of immune cells relevant to primate models of lentivirus infection. Division infrastructure aids this project at several levels including sample processing, data processing/analysis and data disseminating to the community.

**Community outreach**

In 2014 the WaNPRC created a publically available custom sequencing cost center, Sound Genomics, housed Excluded by Requester laboratory. The center specializes in RNA-Seq analysis, microarray processing, DNA/RNA library preparation/QC and bioinformatics analysis and support. The creation and maintenance of the center is a direct by-product of the Division's extensive computational and instrumental infrastructure in combination with our expertise in sample processing and big data processing/analysis.

**Citations refer to the P51 supported publications that are listed elsewhere in the progress report*

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

Please see the progress report for the Statistical Analysis and Modeling Core (Bioinformatics Workshop at the conference on Systems Biology of Infectious Diseases, Seattle, Washington; August 17, 2014).

## C. COMPONENT PRODUCTS

### C.1 PUBLICATIONS

Not Applicable

### C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

### C.3 TECHNOLOGIES OR TECHNIQUES

Defining the NHP microbiome

The Division has developed, optimized, and validated a microbiome sample processing pipeline to perform in-depth 16S metagenomic sequencing on NHP samples. We performed this type of analysis on samples from the [redacted] SIV/rhesus macaque acute infection study described above (In vivo SIV/NHP studies) and our preliminary analysis indicates that the composition of the rhesus macaque gut microbiome changed rapidly during acute SIV infection. We will compare this microbiome analysis with a similar one that we are deriving from the Division's SIV/rhesus macaque acute infection study. Excluded by Requester

Optimization of oligonucleotide capture assays for use with NHP samples

In collaboration with Illumina and the NHP-FGC, the Division has optimized and validated several Illumina protocols for NHP samples which rely on Illumina's capture technique to enrich for specific transcripts prior to sequencing.

For use with NHP RNA samples: The Illumina TruSeq RNA Access allows for doing transcriptomics on low quality human RNA samples such as RNA isolated from FFPE samples or RNA samples that have been degrades for other reasons. In 2014, we optimized, tested and validated a protocol for using this product with NHP samples and NHP RNA.
Viral RNA and NHP host RNA detection: We have designed capture assays to capture 100s of host genes known to be differentially expressed during specific viral infections and a panel of pathogenic viruses such as SIV and SRV. This assay can be used to screen animal tissues for specific viruses and at the same time perform RNA profiling of 100s of host genes.

NanoString technology

The nCounter Elements Analysis System is used for rapid screening of targets from samples such as crude cell lysates or RNA purified from FFPE tissue, blood products, fine-needle aspirates or cell lines. This technology delivers digital detection of up to 216 unique targets. We are collaborating with NanoString Technologies to design probes that uniquely detect env, gag, and pol for multiple SRV strains with the goal of developing a fast and accurate SRV screening method for use with NHP samples.

### C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

### C.5 OTHER PRODUCTS AND RESOURCE SHARING

#### C.5.a Other products

NOTHING TO REPORT

#### C.5.b Resource sharing

File uploaded: WaNPRC_HTMP_Core_C5b.pdf

Complete details of resource can be found in the progress report for the Statistical Analysis and Modeling Core.

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | PI - Primary | Institutional Base Salary | EFFORT | | | 8,065.00 | 1,815.00 | 9,880.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **9,880.00**

## 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 | Research Scientists | 28.2 | | | 146,838.00 | 40,772.00 | 187,610.00 |
| **5** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **187,610.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **197,490.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| 1. Master cycler Pro Thermocycler | 10,000.00 |
| **Total funds requested for all equipment listed in the attached file** | **0.00** |
| **Total Equipment** | **10,000.00** |

**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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | 39,801.00 |
| 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. Service contracts | 19,556.00 |
| 9. Spotfire analytical software | 2,500.00 |
| **Total Other Direct Costs** | **61,857.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **269,347.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 259,347.00 | 108,926.00 |
| | | **Total Indirect Costs** | **108,926.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **378,273.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: High-throughput Molecular Profiling Core - 7642**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**EQUIPMENT:** Funds are requested for the purchase of a Mastercycler Pro Thermal Cycler. This equipment will support the generation of multiple high-throughput genomics data types including PCR, microarrays and next-generation sequencing by the HTMP Core within the Division of Systems Biology. This thermal cycler is unique in that it is equipped with a programmable heated lid with a range of temperatures from 37-110°C. The ability to accurately control the temperature of the heated lid is crucial for both current methods for the generation of high-throughput genomics data and development of new methods for advanced molecular biology applications.

**SUPPLIES:** Less funds than last year are requested for supplies. In the coming year, less emphasis will be placed on NextGen sequencing, reducing the need for these supplies.

**OTHER**: We are requesting almost the same amount for this category as the prior year, but for slightly different line items.

*Service Contracts*: We are requesting slightly more funding for our ongoing scanner service contract, we are requesting support for 20% of this service contract. Similarly, we are now requesting funds for 47% of the annual cost for our NextGen Sequencer service contract. However, we are not requesting funding for a mass spectrometer service contract.

*Spotfire Analytical Software*: Support is requested to pay for this software, which is an industry leading software package to analyze high-throughput data.

## A. COMPONENT COVER PAGE

**Project Title:** Statistical Analysis and Modeling Core

**Component Project Lead Information:**

Excluded by Requester

## B. COMPONENT ACCOMPLISHMENTS

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

The Division of Nonhuman Primate Systems Biology is organized into a Research Component (composed of Virology and Integrative Analysis, Mucosal Immunology, and Animal Models) and two Cores (the High-throughput Molecular Profiling Core and the Statistical Analysis and Modeling Core). The Research Component and both Cores are involved in each Divisional project. Information directly related to the Statistical Analysis and Modeling Core is provided here, and a more detailed description of all studies and results can be found in the Research Component portion of the Division's progress report.

Specific Aim:
To provide the hardware infrastructure and the expertise for the computational analysis of highthroughput datasets, including the integrative techniques of Systems Biology.

The Statistical Analysis and Modeling Core provides guidance in experimental design and assists with software tools for simple quantitative statistical comparisons and visualization techniques. The computational biology group performs more advanced statistical techniques for correlations or classifications based on other experimental data, and with suitable kinetic datasets, network-modeling strategies is used to infer critical regulators or bottlenecks. For next-generation RNA sequencing (RNA-seq) data from macaque models, the Core maintains computational resources for identifying known and novel transcripts and for generating quantitative transcript abundance levels; the latter are then used for quantitative statistical comparisons.

### 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: WaNPRC_SAM_Core_B2.pdf

### B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: WaNPRC_SAM_Core_B4.pdf

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

Sharing of division-generated resources and information to the scientific community is an essential component of the Division of NHP Systems Biology. All resources are made publicly accessible within four weeks of publication. In addition, all aspects of our data dissemination plan comply with NIH research grants and contracts on obtaining and disseminating biomedical research resources.
We have several modes for disseminating Division-generated resources which include:
Presentations at national scientific meetings – The primary investigators associated with the Division are highly regarded scientists and are invited to present their research findings at numerous scientific meetings annually. These venues provide excellent opportunities to disseminate research findings and establish new collaborations.
Publications in scientific journals – All of our publications are currently listed on the [redacted] Lab website with links to the articles. As the associated data is made available through the public repositories, the accession number or associated links are added to these listings. Excluded by Requester
Public Repositories – All sequence data, microarray data and proteomic data generated by the High-Throughput Molecular Profiling Core are submitted to the following repositories:
•NCBI Sequence Read Archive (SRA)
oGastrointestinal microbiome data uploaded as raw paired-end Illumina MiSeq 16S rRNA reads
oGene expression data uploaded as raw RNA-seq reads (through the corresponding GEO submission).
•NCBI Gene Expression Omnibus (GEO):
oGene expression data uploaded as normalized gene expression matrix
•Virus Pathogen Resource (ViPR):
oExpression data uploaded as normalized gene expression matrix
oRelevant associated data, including experimental conditions and animal phenotypes
•PRIDE, the PRoteomics IDEntification
oProteomics data is submitted here.
Publically accessible websites – In some cases, in addition to submitting data to these repositories, data sets can be publically accessed through websites such as the Nonhuman Primate Reference Transcriptome Resource (http://nhprtr.org/) [redacted] Lab (https://viromics.washington.edu/publications.html) and the NHP Functional Genomics Core (https://www.nhp-fgc.org/). Excluded by Requester

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

There have been no changes in our specific aims; we will continue to: 1) expand our protocols and pipelines to accommodate cutting edge technologies, 2) provide the hardware infrastructure and the expertise for the computational analysis of high-throughput datasets, including the integrative techniques of systems biology and 3) apply the techniques of systems biology to examine the host response to virus infection or to vaccination, particularly to support the development of new resources to characterize mucosal immunity.

## B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

The overarching goal of the Division of Nonhuman Primate Systems Biology is to facilitate the NHP research community in embracing the newly emergent paradigms of systems biology and next-generation transcriptomics. Resource development and research occurs through internal and external projects managed through one of the Research Components and supported by the Cores. This support includes: 1) using rapid and cost-effective methods for high-throughput molecular profiling, 2) providing computational infrastructure and cutting edge techniques to mine the resulting data sets and 3) disseminating the generated resources to the project PIs and the research community at large.

During the last year, the seamless Divisional workflow which integrates the activities of the Research Component and the Cores has resulted in the generation of substantial community resources and many significant biological findings in several areas of research. These accomplishments fall into seven general areas and are detailed below:

1) *In vivo* and *in vitro* SIV/HIV-related studies
2) NHP models of respiratory diseases
3) NHP models of viral hemorrhagic fever
4) Improvements of NHP reference transcriptomes
5) Community outreach
6) Dissemination of Division-generated resources to the public (See Section B5 below.)
7) Development of new genomics tools for NHP systems biology applications (See Section C3 below.)

### *In vivo* and *in vitro* SIV/HIV-related studies

Host transcriptional response to RhCMV/SIV vaccination

In collaboration with Excluded by Requester Private Source, we have compared the host response to vaccination with gp96-Ig secreting cells carrying SIVmac251 peptides, plus and minus a boost with gp120 protein (Excluded by Requester *et al., 2014**). The RNA profiling and associated functional analysis indicated: 1) vaccination can alter the (non-)immunizing effect of low-dose challenges in a time-dependent manner, 2) immunized animals show evolving host response in the course of multiple challenges, and 3) persistently protected animals have a particularly strong innate and humoral immune response only after the first challenge, and show both prevailing innate and adaptive cellular responses after further challenge.

♦ Analysis support: Primary gene expression data processing; Statistical analyses (using the R package limma) and maximal log likelihood (right-tailed $\chi^2$ test); Functional enrichment analysis (using Ingenuity Pathway Analysis); Graphical representations.

RNA-seq of mucosal challenge compartment during acute SIV infection

Using samples collected from the Division's large SIV/rhesus macaque acute infection model, we carried out the first deep mRNA sequencing analysis of mucosal host responses in the primary infection compartment (Excluded by Requester *et al., 2014**). This study revealed that during acute infection, a significant host response was mounted in the mucosa before inflammation was triggered, which had a detrimental effect on tissue integrity. In collaboration with Excluded by Requester (University of Pittsburgh), Division resources are being utilized to expand on this initial study by performing a comparative total RNA-seq analysis between the rhesus acute infection model and a similar acute infection model using African Green Monkeys, a natural host of SIV. Total RNA-seq data from the rectal challenge compartment and draining lymph nodes, spanning the necropsy collections at 1, 2, 3, 6, 12, and 84 days post infection from both model systems have been generated and the functional analysis comparison between the two species is near completion.

♦ Analysis support: Primary RNA-seq gene expression data processing and read mapping; Differential expression analysis (using a generalized linear model implemented in the Bioconductor package edgeR); Functional enrichment analysis (using Ingenuity Pathway Analysis); Co-expression analysis (using the Ward method and adaptive branch pruning).

Microbial translocation during SIV infection

During chronic HIV/SIV infection, CD4+IL-17-producing T cells (TH17) are significantly depleted from mucosal tissues, and their absence is highly associated with gastrointestinal (GI) dysfunction. However, the kinetics of immune dysfunction and microbial translocation, and how this dysfunction may affect the establishment of viral reservoir, remains unknown. In collaboration with (Excluded by Requester) (WaNPRC), we have obtained longitudinal GI tract biopsies and blood at early acute time points from six rhesus macaques following intrarectal SIV

challenge with SIVmac239x. The Division performed microarray assay on GI tract biopsies and blood samples throughout the acute infection and the associated host RNA profiling and functional analysis is underway.

*In vitro* CD4+ T cell line projects

We previously published several studies that used mRNA-seq, microRNA-seq, or global proteomics to characterize the early host response to HIV infection of SupT 1 cells. The subsequent integration of two additional data sets with the mRNA-seq data has resulted in two new publications. The first [redacted] *al., 2014* Excluded by Requester *(J. Virol.)* reports on the integration of a total RNA-seq data set, which provides quantitation of non-coding and non-polyadenylated RNAs, with mRNA data and demonstrated large numbers of differentially regulated transcripts early after infection, many of which corresponded to nascent transcripts that had not been processed to mature, polyadenylated forms. We computationally derived and validated the underlying regulatory programs. A constructed network of these early-regulated genes was used to predict compounds that would antagonize the transcriptional changes and we showed that one of the predicted drugs, lycorine, potently inhibits HIV-1 infection.

♦ Analysis support: Primary RNA-seq gene expression data processing and read mapping; Differential expression analysis (using edgeR); Custom human genome annotation; Identification of genes preferably detected by Total RNA-seq relative to mRNA-seq; Transcription factor binding site enrichment analysis with ChIP-seq data; Functional enrichment analysis (using Ingenuity Pathway Analysis); Gene set enrichment analysis; Gene module construction and regulatory model learning; Co-expression network analysis (using the R package WGCNA).

The second new publication reports on the results of a collaboration with Excluded by Requester (University of Pennsylvania). Using the Sup T1 model system, we analyzed the alterations to histone post translational modification (PTM) profiles using nano-LC-MS/MS, as well as the expression of chromatin-associated enzymes using microarray analysis Excluded by Requester *et al., 2014**). We observed major changes in histone PTM abundances which we linked to massive fluctuations in mRNA expression of associated chromatin enzymes.

♦ Analysis support: Primary gene expression data processing; Combination of microarray and proteomics datasets to correlate expression trends for candidate PTM enzymes.

**NHP models of respiratory diseases**

MERS coronavirus

Our colleagues at Rocky Mountain Laboratories (RML, an NIAID intramural research facility) discovered that unlike the rhesus macaque model, the common marmoset provides a severe, partially lethal, disease model of MERS-CoV. We collaborated with investigators at RML to generate total RNA-seq data from marmoset lung specimens to characterize expression changes consistent with the development of pulmonary fibrosis, as well as alterations in serum cytokine transcripts Excluded by Requester *et al. 2014**).

♦ Analysis support: Primary RNA-seq gene expression data processing and read mapping; Differential expression analysis; Functional enrichment analysis (using Ingenuity Pathway Analysis).

Influenza virus

Excluded by Requester is leading the Division's investigation into DNA vaccines as an approach for a universal influenza vaccine to protect against a wide range of diverse circulating and emerging seasonal and pandemic strains of influenza. In a vaccine efficacy trial in nonhuman primates, cynomolgus macaques were immunized with an adjuvanted DNA vaccine that was designed to induce broadly neutralizing antibody and cross reactive T cell responses in the lung mucosa. To determine if the vaccine was able to reduce inflammatory responses, we performed an extensive microarray analysis on lung tissues collected from a subset of 3 monkeys from each group that were sacrificed 3 days after challenge during peak viral replication. RNA expression patterns showed that vaccination significantly suppressed inflammatory responses in the lung when compared to controls suggesting this vaccine could be effective in reducing post-influenza susceptibility to secondary infections. Interestingly, the RNA expression also showed that vaccinated animals had higher recruitment of T cell responses into the lung, an outcome that further supports a role of the mucosal T cell response induced by the vaccine in mediating protection.

We also performed gene expression profiling for a study conducted at RML in which cynomolgus macaques were infected with influenza A virus H7N9. As reported in [redacted] *et al. 2014**, when compared to previous Excluded by Requester studies, the emerging H7N9 influenza virus was more pathogenic in cynomolgus macaques than seasonal

influenza A viruses and most isolates of the pandemic H1N1 virus but less pathogenic than the 1918 Spanish influenza virus or highly pathogenic avian influenza (HPAI) H5N1 virus. Using gene expression data generated by the High-Throughput Molecular Profiling Core, we constructed a network of critical molecules based on direct interactions in the Ingenuity Pathway Analysis knowledge base. These results suggested that molecules that recruit infiltrating effector leukocytes are increased at the site of lesions which correlates with the observed influx of neutrophils and macrophages observed microscopically in the lungs. Through additional computational analysis, we identified drugs reported to act as upstream regulators of some of these genes. We showed that one of the predicted drugs, rosiglitazone, modestly reduced replication of influenza virus A/Anhui/1/2013 *in vitro.*

♦ Analysis support: Primary gene expression data processing; Differential expression analysis; Functional enrichment analysis (using Ingenuity Pathway Analysis).

**NHP models of viral hemorrhagic fever**

We used mRNA sequencing to analyze PBMC from cynomolgus macaques after VSVΔG/EBOVgp immunization and subsequent EBOV challenge. We found a controlled transcriptional response that transitioned to immune regulation as the EBOV was cleared. This observation supported the safety of the vaccine [Excluded by Requester] *et al. 2015**).

♦ Analysis support: Primary RNA-seq gene expression data processing and read mapping; Differential expression analysis (using edgeR); Functional enrichment analysis (using Ingenuity Pathway Analysis)

To identify host factors associated with arenavirus virulence, in collaboration with colleagues at RML, we used a cynomolgus macaque model to evaluate the pathogenesis of Lujo virus (LUJV), a recently emerged arenavirus that caused an outbreak of severe viral hemorrhagic fever in southern Africa [redacted] *et al. 2014**). The Division performed RNA profiling analysis on PBMC samples and detected a 72-hour delay in induction of host responses to infection during the less pathogenic LUJV infection compared to the animals infected with the more pathogenic LASV and an early differential expression of a subset of genes specific to LUJV infection that accounts for the delayed inflammatory response. Cell-type enrichment analysis suggested that host response induction delay and LUJV-specific profile may be due to a different proportion of natural killer cells responding in LUJV infection compared to the LASV-infected animals. Together, these data indicate that delayed pro-inflammatory and pro-apoptotic host responses to arenavirus infection could ameliorate disease severity.

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♦ Analysis support: Primary gene expression data processing; Differential expression analysis (using the CDS statistical test); Pairwise comparisons between series of gene expression profiles (using Pearson's coefficient of correlation); Functional enrichment analysis (using Ingenuity Pathway Analysis); Data visualizations using singular value decomposition-multidimensional scaling; Cell-type enrichment analysis (based on the Human Gene Atlas data set and computed using Enrichr).

Additional ongoing NHP studies at RML are described in the progress report for the Research Component of the Division.

**Improvements to NHP transcriptome resources**

Complex immune loci

In collaboration with [Excluded by Requester] ([Private Source]), we are developing a strategy for accurately quantifying rhesus MHC allele expression, taking into full account the complexities of the MHC class I gene family in macaques. Our strategy leverages a large collection of full-length rhesus MHC genomic sequences and a custom-developed computational pipeline. With this approach we find that the expression of both MHC class I and class II genes are highly tissue specific and there is an overall increase in the expression of class I alleles in acutely infected rhesus macaque PBMC samples.

Multiple NHP reference transcriptomes

The Nonhuman Primate Reference Transcriptome Resource (NHPRTR) is an R24-funded resource that is a collaboration involving the Division, Illumina Inc. and Cornell Medical College. There were two publications during this reporting period describing additional resources generated through this collaboration. Prior to the results described in [redacted] *et al. 2014*(J. Med Primatol.)* the genome annotations of rhesus (*Macaca mulatta*) and cynomolgus (*Macaca fascicularis*) macaques, two of the most common non-human primate animal models, were limited. Through this work, we uncovered thousands of novel isoforms and un-annotated

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intergenic transcripts including coding and non-coding RNAs, polyadenylated and non-polyadenylated transcripts [redacted] *et al. 2015** describes Phase II of the NHPRTR project in which 10.1 billion fragments of tissue-specific RNA-seq data was generated and released to the public. These data come from ~15 individual tissues from 11 NHP species and subspecies. The sequence quality was such that 88% of the reads align to human reference sequences, allowing for the full listing of expression abundance across all tissues for each species, using the reads mapped to human genes.

♦ Analysis support: Primary RNA-seq gene expression data processing and read mapping; Expression abundance analysis across tissues; Correct assignment of tissues was verified using the covariance analysis of the expression patterns provided by the Magic pipeline.

NHP cell-specific transcriptomes

In collaboration with Excluded by Requester Private Source, we are using RNA-seq to build transcriptome databases of immune cells relevant to primate models of lentivirus infection. Division infrastructure aids this project at several levels including sample processing, data processing/analysis and data disseminating to the community.

**Citations refer to the P51 supported publications that are listed elsewhere in the progress report*

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

In August, the WaNPRC hosted the first international conference on Systems Biology of Infectious Diseases (~175 attendees) that included a bioinformatics workshop (~30 attendees). The conference highlighted research aimed at understanding, treating, and preventing conditions such as respiratory infections, tuberculosis, and AIDS; and it featured presentations on the identification of emerging pathogens, the role of the host response and host genetics in determining disease outcome, and the promises of personalized care. The workshop was an introduction to cutting edge high throughput technologies and innovative analytical tools; it provided attendees fundamental concepts to manage complex data sets. The Division played a supportive role in organizing and holding both events [redacted] served as the main host to the conference and other Division personnel helped in planning and hosting the workshop.

Excluded by Requester

## C. COMPONENT PRODUCTS

### C.1 PUBLICATIONS

Not Applicable

### C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

### C.3 TECHNOLOGIES OR TECHNIQUES

Technology developments associated with the Division of Nonhuman Primate Systems Biology are described in the Progress Report for the High-Throughput Molecular Profiling Core.

### C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

### C.5 OTHER PRODUCTS AND RESOURCE SHARING

**C.5.a Other products**

NOTHING TO REPORT

**C.5.b Resource sharing**

File uploaded: WaNPRC_SAM_Core_C5b.pdf

We make all sequence data and microarray data generated by the High-Throughput Molecular Profiling Core available to the scientific community no later than the date of publication of the main findings from the final data set. Data are submitted to the following repositories:

- NCBI Sequence Read Archive (SRA)
  - Gastrointestinal microbiome data uploaded as raw paired-end Illumina MiSeq 16S rRNA reads
  - Gene expression data uploaded as raw RNA-seq reads (through the corresponding GEO submission).
- NCBI Gene Expression Omnibus (GEO):
  - Gene expression data uploaded as normalized gene expression matrix
- Virus Pathogen Resource (ViPR):
  - Expression data uploaded as normalized gene expression matrix
  - Relevant associated data, including experimental conditions and animal phenotypes
- PRIDE, the PRoteomics IDEntification database
  - Proteomics data is submitted here.

In some cases, in addition to submitting data to these repositories, data sets can be publically accessed through websites such as the Nonhuman Primate Reference Transcriptome Resource (http://nhprtr.org/), Excluded by Requester Lab (https://viromics.washington.edu/publications.html) and the NHP Functional Genomics Core (https://www.nhp-fgc.org/).

## 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*: 605799469

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

## 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 | | | | Principal Investigator - Primary | Institutional Base Salary | EFFORT | | | 8,065.00 | 1,815.00 | 9,880.00 |

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

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** **9,880.00**

## 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 | Research Scientists | 10.2 | | | 93,081.00 | 23,555.00 | 116,636.00 |
| **2** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | **116,636.00** |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | **126,516.00** |

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

# RESEARCH & RELATED BUDGET - SECTION C, D, & E

**ORGANIZATIONAL DUNS*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| **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*:** 605799469
**Budget Type*:** ● Project ● Subaward/Consortium
**Enter name of Organization:** UNIVERSITY OF WASHINGTON

**Start Date*:** 05-01-2015 **End Date*:** 04-30-2016

| 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. Iron Mountain Storage | 4,537.00 |
| **Total Other Direct Costs** | **4,537.00** |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | **131,053.00** |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1. Modified Total Direct Cost (MTDC) | 42.0 | 131,053.00 | 55,042.00 |
| | | **Total Indirect Costs** | **55,042.00** |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): U.S. Department of Health and Human Services (DHHS) Program Support Center (PSC) Division of Cost Allocation (DCA) Western Field Office Arif Karim, (415) 437-7820

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | **186,095.00** |

| J. Fee | Funds Requested ($)* |
|---|---|
| | **0.00** |

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

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

**BUDGET JUSTIFICATION: Statistical Analysis and Computational Modeling Core - 7463**

Only budget categories with significant deviations from the prior (non-competitive) year are included in this budget justification.

**OTHER**: As in the prior year, funding is requested for Iron Mountain document storage and retrieval. Significantly less funding is required this year as the work has progressed from the prior year.