PRIMATE RESEARCH CENTER GRANT **Federal Award Date:** 05/18/2015
Department of Health and Human Services
National Institutes of Health
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P51OD011092-56
FAIN: P51OD011092

Principal Investigator(s):
JOSEPH E ROBERTSON, MD

Project Title: SUPPORT FOR NATIONAL PRIMATE RESEARCH CENTER

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

Award e-mailed to: orserv@ohsu.edu

Period Of Performance:
Budget Period: 05/01/2015 – 04/30/2016
Project Period: 05/01/1997 – 04/30/2019

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $12,612,766 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to OREGON HEALTH & SCIENCE UNIVERSITY in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

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

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number P51OD011092. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

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

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

Sincerely yours,

Irene Haas
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows

SECTION I – AWARD DATA – 5P51OD011092-56

Award Calculation (U.S. Dollars)

Salaries and Wages	$5,064,041
Fringe Benefits	$1,641,249
Consultant Services	$32,726
Equipment	$331,736
Supplies	$1,269,772
Travel Costs	$60,940
Alterations and Renovations	$169,628
Other Costs	$1,393,305
Federal Direct Costs	$9,963,397
Federal F&A Costs	$2,649,369
Approved Budget	$12,612,766
Total Amount of Federal Funds Obligated (Federal Share)	$12,612,766
TOTAL FEDERAL AWARD AMOUNT	$12,612,766
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$12,612,766

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
56	$12,612,766	$12,612,766
57	$12,976,995	$12,976,995
58	$12,976,996	$12,976,996
59	$12,976,996	$12,976,996

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

Fiscal Information:

CFDA Name:	Research Infrastructure Programs
CFDA Number:	93.351
EIN:	1931176109A1
Document Number:	POD011092J
PMS Account Type:	P (Subaccount)
Fiscal Year:	2015

IC	CAN	2015	2016	2017	2018
OD	8014499	$12,263,034	$12,627,263	$12,627,264	$12,627,264
AG	8470701	$349,732	$349,732	$349,732	$349,732

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

NIH Administrative Data:
PCC: CMP01 / **OC**: 414E / **Released**: eRA Commons User Name 05/15/2015
Award Processed: 03/23/2015 01:36:12 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD011092-56

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

SECTION III – TERMS AND CONDITIONS – 5P51OD011092-56

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

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

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

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

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

Treatment of Program Income:
Additional Costs

SUBJECT FOA
This award is subject to the conditions set forth in PA-11-136, "Limited Competition: National Primate Research Centers (P51)," which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link: http://grants.nih.gov/grants/guide/pa-files/PAR-11-136.html.

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.

CO-FUNDING
This award reflects support from the NIA in the amount of $349,742 total costs and from the ORIP in the amount of $12,263,024 total costs.

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

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

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

Excluded by Requester

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

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

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

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

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

STAFF CONTACTS

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

Grants Management Specialist: Amy R Bartosch
Email: bartoschar@mail.nih.gov **Phone**: 240-276-6300

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

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011092-56

INSTITUTION: OREGON HEALTH & SCIENCE UNIVERSITY

Budget	Year 56	Year 57	Year 58	Year 59
Salaries and Wages	$5,064,041	$5,215,962	$5,215,962	$5,215,962
Fringe Benefits	$1,641,249	$1,690,486	$1,690,486	$1,690,486
Consultant Services	$32,726	$33,708	$33,708	$33,708
Equipment	$331,736	$282,677	$356,933	$304,279
Supplies	$1,269,772	$1,307,865	$1,307,865	$1,307,865
Travel Costs	$60,940	$62,768	$62,768	$62,768
Alterations and Renovations	$169,628	$223,610	$149,355	$202,009
Other Costs	$1,393,305	$1,435,105	$1,435,105	$1,435,105
TOTAL FEDERAL DC	$9,963,397	$10,252,181	$10,252,182	$10,252,182
TOTAL FEDERAL F&A	$2,649,369	$2,724,814	$2,724,814	$2,724,814
TOTAL COST	$12,612,766	$12,976,995	$12,976,996	$12,976,996

Facilities and Administrative Costs	Year 56	Year 57	Year 58	Year 59
F&A Cost Rate 1	28%	28%	28%	28%
F&A Cost Base 1	$9,462,033	$9,731,477	$9,731,477	$9,731,477
F&A Costs 1	$2,649,369	$2,724,814	$2,724,814	$2,724,814

A. OVERALL COVER PAGE

Project Title: SUPPORT FOR NATIONAL PRIMATE RESEARCH CENTER	
Grant Number: 5P51OD011092-56	**Project/Grant Period:** 05/01/1997 - 04/30/2019
Reporting Period: 08/15/2014 - 04/30/2015	**Requested Budget Period:** 05/01/2015 - 04/30/2016
Report Term Frequency: Annual	**Date Submitted:** 02/27/2015
Program Director/Principal Investigator Information: JOSEPH E ROBERTSON , MD PHD **Phone number:** 503 494-1085 **Email:** robertjo@ohsu.edu	**Recipient Organization:** OREGON HEALTH & SCIENCE UNIVERSITY OREGON HEALTH & SCIENCE UNIVERSITY 3181 SW Sam Jackson Pk Rd PORTLAND, OR 972393098 **DUNS:** 096997515 **EIN:** 1931176109A1 **RECIPIENT ID:**
Change of Contact PD/PI: No	
Administrative Official: JASON JAWORSKI 3181 S.W. Sam Jackson Park Rd L106RGC Portland, OR 972393098 **Phone number:** 503-494-7784 **Email:** jaworski@ohsu.edu	**Signing Official:** JASON JAWORSKI 3181 S.W. Sam Jackson Park Rd L106RGC Portland, OR 972393098 **Phone number:** 503-494-7784 **Email:** jaworski@ohsu.edu
Human Subjects: No	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** Yes If yes, previously reported: Yes

B. OVERALL ACCOMPLISHMENTS

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

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

Progress toward these goals was summarized in our competing renewal. In 2014, the Center leadership team led and completed another formal strategic planning process based on the Hoshin-Kanri method that we had used previously. Based on the formal SWOT analysis, we identified seven major areas of strategic focus and objectives within these areas. The seven new objectives to accomplish in the next five years are described below and are based on this renewed strategic plan.

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

Yes

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-OVERALL_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

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

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
3P51OD011092-55		Specific Aim 1. To provide funding for the viral testing, quarantine and housing per diems, husbandry and social enrichment for 25 additional Macaca mulatta from the NEPRC so that they can be integrated into the ONPRC eSPF colony. Specific Aim 2. To provide funding for the renovation and improvements to primate housing facilities for the eSPF macaques from NEPRC.	The ONPRC is working with NIH to start the work for this grant.

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?

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

Progress on our strategic objectives is provided to the Senior Vice President for Research at OHSU [Excluded by Requester] on a monthly basis. A summary of progress is provided to ORIP and the other NPRC Directors and senior staff at our fall and spring NPRC Directors' Meetings. We provide twice-yearly summaries to the External Scientific Advisory Board (ESAB).

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

The major efforts underway include completing the work of the six Strategic Task Forces by June 30, 2015. Progress toward these objectives was reviewed by an expanded leadership group of approximately 30 leaders at ONPRC on January 27th, and final reports will be provided in June 2015.

In the next several months, ONPRC leadership will analyze the progress achieved by the Task Forces and will identify the next set of priorities for advancing our breakthrough objectives for July, 2015-June, 2016. We will convene our ESAB on September 10, 2015, for our annual meeting.

OVERALL: ACCOMPLISHMENTS

We first defined our seven refined strategic objectives to assure the success of the Center as a world-class research and training institution within the OHSU research sphere that serves the mission of ORIP and NIH and results in biomedical breakthroughs to improve human health.

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

After defining these larger objectives, we assessed overall strengths and then identified which areas required breakthrough progress in the first year (July 1, 2014-June 30, 2015).

We convened six Task Forces and leaders of these Task Forces then appointed appropriate members to develop strategies to make progress toward and to accomplish these goals. Briefly, progress to date is summarized below. The overall strategic plan breakthrough objective that these tie to is in parentheses after the name of the Task Force, and the leader responsible for leading each group is noted also.

1. Faculty Retention and Collaborative Research (**COLLABORATIVE, INTERDISCIPLINARY ENVIRONMENT**) Excluded by Requester This group has developed promotion guidelines and policies that are in alignment with the OHSU School of Medicine in order to streamline and better coordinate promotions of faculty members. They also led a Center-wide scientific retreat at Proprietary Info on February 12-13, 2015. The Center invited all core faculty, DCM unit heads, and leaders of the Research Support Cores and NHP Resources, as well as key collaborating faculty and leaders at OHSU, including Excluded by Requester
2. Information Technology Task Force (**INFRASTRUCTURE** Excluded by Requester) This group has focused on the implementation and refinement of tools for data management and access, including our web-based electronic medical records and billing system (PRIMe), program usage and data storage. OHSU financed and completed a very large university-wide data center. The unique design provides a high-security, high-capacity, high-efficiency computing facility with one of the best power utilization efficiencies in the country. The new 18,000-square-foot data center contains 10 mini data centers called "pods" arranged in a wheel and spoke configuration with a central hub. At full capacity it could house thousands of data servers along with 100 petabytes of data (one petabyte is one million gigabytes).
3. Infrastructure Plan Task Force (**INFRASTRUCTURE** Excluded by Requester) This group has taken a comprehensive and in-depth examination of needs for laboratory, NHP breeding, NHP research, and administrative space, based on various growth models for the next five years for faculty and NHP growth. The plan is based on the scientific strategic needs and takes into consideration the needs of the other groups co-located on the OHSU West Campus, such as the Vaccine & Gene Therapy Institute. The group prepared a report for Excluded by Requester in January and is working to prioritize this year's capital requests to begin this plan.

4. Laboratory Space Allocation Task Force (**INFRASTRUCTURE**) Excluded by Requester This group has just begun to work on setting strategies for assignment of laboratory space that will tie to programmatic size and scientific needs. This process will be done in alignment with space assignment policies at the host institution, OHSU>

5. NHP Space and Utilization Task Force (**NHP RESOURCES**) Excluded by Requester This group has refined our animal utilization process to include an understanding not only of NHP availability per model, but also to manage space availability to better assure that we can provide NHP resources in a timely manner and that needs for infrastructure growth are identified. One of the key successes has been to identify a methodology and tools for colony modeling, based on systems science and Proprietary Info

6. NHP Resource Task Force (**NHP RESOURCES**) Excluded by Requester This group focused on the NHP Resource groups and how investments in them have led to return on investment (ROI), how to identify the current and future needs for these or different NHP resources

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 Metabolism of lutein and zeaxanthin in rhesus monkeys: identification of (3R,6'R)- and (3R,6'S)-3'-dehydro-lutein as common metabolites and comparison to humans. Comp Biochem Physiol B Biochem Mol Biol. 2008 Sep;151(1):70-8. PubMed PMID: 18582588; PubMed Central PMCID: PMC3419355.
Complete	Excluded by Requester A microarray analysis of sexual dimorphism of adipose tissues in high-fat-diet-induced obese mice. Int J Obes (Lond). 2010 Jun;34(6):989-1000. PubMed PMID: 20157318; PubMed Central PMCID: PMC3667412.
Complete	Excluded by Requester Chromosome transfer in mature oocytes. Fertil Steril. 2012 May;97(5):e16. PubMed PMID: 22542144; PubMed Central PMCID: PMC3893349.
Complete	Excluded by Requester Targeted gene silencing to induce permanent sterility. Reprod Domest Anim. 2012 Aug;47 Suppl 4:228-32. PubMed PMID: 22827375; PubMed Central PMCID: PMC3516287.
Complete	Excluded by Requester Identification of phosphodiesterase 9A as a cyclic guanosine monophosphate-specific phosphodiesterase in germinal vesicle oocytes: a proposed role in the resumption of meiosis. Fertil Steril. 2012 Aug;98(2):487-95.e1. PubMed PMID: 22704629; PubMed Central PMCID: PMC3409309.
Complete	Excluded by Requester Excluded by Requester Motif-optimized subtype A HIV envelope-based DNA vaccines rapidly elicit neutralizing antibodies when delivered sequentially. Vaccine. 2012 Aug 10;30(37):5519-26. PubMed PMID: 22749601; PubMed Central PMCID: PMC3447634.
Complete	Excluded by Requester Genetic load is associated with hypothalamic-pituitary-adrenal axis dysregulation in macaques. Genes Brain Behav. 2012 Sep 21;PubMed PMID: 22998353; PubMed Central PMCID: PMC3595329.
Complete	Excluded by Requester Impact of infection or vaccination on pre-existing serological memory. Hum Immunol. 2012 Nov;73(11):1082-6. PubMed PMID: 22902392; PubMed Central PMCID: PMC3478407.
Complete	Excluded by Requester Social rank, chronic ethanol self-administration, and diurnal pituitary-adrenal activity in cynomolgus monkeys. Psychopharmacology (Berl). 2012 Nov;224(1):133-43. PubMed PMID: 22526537; PubMed Central PMCID: PMC3469782.
Complete	Excluded by Requester Sritanaudomchai H, Masterson KR, Wolff EE, Jia Y, Mitalipov SM. X-chromosome inactivation in monkey embryos and pluripotent stem cells. Dev Biol. 2012 Nov 15;371(2):146-55. PubMed PMID: 22935618; PubMed Central PMCID: PMC3466365.

Complete	Excluded by Requester Applying gene silencing technology to contraception. Reprod Domest Anim. 2012 Dec;47 Suppl 6:381-6. PubMed PMID: 23279544; PubMed Central PMCID: PMC3598614.
Complete	Excluded by Requester Obesity: a transgenerational problem linked to nutrition during pregnancy. Semin Reprod Med. 2012 Dec;30(6):472-8. PubMed PMID: 23074005; PubMed Central PMCID: PMC3615704.
Complete	Excluded by Requester Stable liquid glucagon formulations for rescue treatment and bi-hormonal closed-loop pancreas. Curr Diab Rep. 2012 Dec;12(6):705-10. PubMed PMID: 22972416; PubMed Central PMCID: PMC3970213.
Complete	Excluded by Requester Macular lutein and zeaxanthin are related to brain lutein and zeaxanthin in primates. Nutr Neurosci. 2013 Jan;16(1):21-9. PubMed PMID: 22780947; PubMed Central PMCID: PMC3824968.
Complete	Excluded by Requester Primate follicular development and oocyte maturation in vitro. Adv Exp Med Biol. 2013;761:43-67. PubMed PMID: 24097381; PubMed Central PMCID: PMC4007769.
Complete	Excluded by Requester Excluded by Requester Towards germline gene therapy of inherited mitochondrial diseases. Nature. 2013 Jan 31;493(7434):627-31. PubMed PMID: 23103867; PubMed Central PMCID: PMC3561483.
Complete	Excluded by Requester Impact of the prostaglandin synthase-2 inhibitor celecoxib on ovulation and luteal events in women. Contraception. 2013 Mar;87(3):352-7. PubMed PMID: 22902348; PubMed Central PMCID: PMC4040982.
Complete	Excluded by Requester Stem cell potency and the ability to contribute to chimeric organisms. Reproduction. 2013 Mar 1;145(3):R81-8. PubMed PMID: 23221011; PubMed Central PMCID: PMC3678546.
Complete	Excluded by Requester Ovarian hormones and the heterogeneous receptor mechanisms mediating the discriminative stimulus effects of ethanol in female rats. Behav Pharmacol. 2013 Apr;24(2):95-104. PubMed PMID: 23399883; PubMed Central PMCID: PMC3864632.
Complete	Excluded by Requester Ovarian regulation of kisspeptin neurones in the arcuate nucleus of the rhesus monkey (macaca mulatta). J Neuroendocrinol. 2013 May;25(5):488-96. PubMed PMID: 23331967; PubMed Central PMCID: PMC3928808.
Complete	Excluded by Requester Pancreatic inflammation and increased islet macrophages in insulin-resistant juvenile primates. J Endocrinol. 2013 May;217(2):207-13. PubMed PMID: 23420316; PubMed Central PMCID: PMC3697080.
Complete	Excluded by Requester Antiviral immune response after live yellow fever vaccination of a kidney transplant recipient treated with IVIG. Transplantation. 2013 May 15;95(9):e59-61. PubMed PMID: 23648410; PubMed Central PMCID: PMC3647227.

Excluded by Requester

Complete	Excluded by Requester Effects of aromatase inhibition and androgen activity on serotonin and behavior in male macaques. Behav Neurosci. 2013 Jun;127(3):400-14. PubMed PMID: 23506438; PubMed Central PMCID: PMC3910396.
Complete	Excluded by Requester Rhesus macaque rhadinovirus-associated disease. Curr Opin Virol. 2013 Jun;3(3):245-50. PubMed PMID: 23747119; PubMed Central PMCID: PMC3780577.
Complete	Excluded by Requester Efferent projections of neuropeptide Y-expressing neurons of the dorsomedial hypothalamus in chronic hyperphagic models. J Comp Neurol. 2013 Jun 1;521(8):1891-914. PubMed PMID: 23172177; PubMed Central PMCID: PMC3618613.
Complete	Excluded by Requester The influence of fetal ethanol exposure on subsequent development of the cerebral cortex as revealed by magnetic resonance imaging. Alcohol Clin Exp Res. 2013 Jun;37(6):924-32. PubMed PMID: 23442156; PubMed Central PMCID: PMC3670687.
Complete	Excluded by Requester S. Human embryonic stem cells derived by somatic cell nuclear transfer. Cell. 2013 Jun 6;153(6):1228-38. PubMed PMID: 23683578; PubMed Central PMCID: PMC3772789.
Complete	Excluded by Requester Excluded by Requester Mechanisms of glucagon degradation at alkaline pH. Peptides. 2013 Jul;45:40-7. PubMed PMID: 23651991; PubMed Central PMCID: PMC3947653.
Complete	Excluded by Requester A system biology approach to identify regulatory pathways underlying the neuroendocrine control of female puberty in rats and nonhuman primates. Horm Behav. 2013 Jul;64(2):175-86. PubMed PMID: 23998662; PubMed Central PMCID: PMC3933372.
Complete	Excluded by Requester Plasma sphingolipids are biomarkers of metabolic syndrome in non-human primates maintained on a Western-style diet. Int J Obes (Lond). 2013 Aug;37(8):1064-70. PubMed PMID: 23207405; PubMed Central PMCID: PMC3718866.
Complete	Excluded by Requester Diurnal pituitary-adrenal activity during schedule-induced polydipsia of water and ethanol in cynomolgus monkeys (Macaca fascicularis). Psychopharmacology (Berl). 2013 Aug;228(4):541-9. PubMed PMID: 23508555; PubMed Central PMCID: PMC3715599.
Complete	Excluded by Requester Excluded by Requester Choline transporter-like protein 4 (CTL4) links to non-neuronal acetylcholine synthesis. J Neurochem. 2013 Aug;126(4):451-61. PubMed PMID: 23651124; PubMed Central PMCID: PMC3866050.
Complete	Excluded by Requester Contribution of NMDA glutamate and nicotinic acetylcholine receptor mechanisms in the discrimination of ethanol-nicotine mixtures. Behav Pharmacol. 2013 Aug 7;PubMed PMID: 23928692; PubMed Central PMCID: PMC3925192.
Complete	Excluded by Requester High-throughput screen for pharmacoperones of the vasopressin type 2 receptor. J Biomol Screen. 2013 Sep;18(8):930-7. PubMed PMID: 23640875; PubMed Central PMCID: PMC3735853.
Complete	Excluded by Requester The effect of short moderate stress on the

Excluded by Requester

	midbrain corticotropin-releasing factor system in a macaque model of functional hypothalamic amenorrhea. Fertil Steril. 2013 Oct;100(4):1111-21. PubMed PMID: 23849846; PubMed Central PMCID: PMC3961579.
Complete	Excluded by Requester Intrahepatic lipid, not visceral or muscle fat, is correlated with insulin resistance in older, female rhesus macaques. Obesity (Silver Spring). 2013 Oct;21(10):2021-8. PubMed PMID: 23408675; PubMed Central PMCID: PMC3661746.
Complete	Excluded by Requester Dehydroepiandrosterone sulfate (DHEAS) as an endocrine marker of aging in calorie restriction studies. Exp Gerontol. 2013 Oct;48(10):1136-9. PubMed PMID: 23318475; PubMed Central PMCID: PMC3641169.
Complete	Excluded by Requester The relationship between adjunctive drinking, blood ethanol concentration and plasma corticosterone across fixed-time intervals of food delivery in two inbred mouse strains. Psychoneuroendocrinology. 2013 Nov;38(11):2598-610. PubMed PMID: 23827168; PubMed Central PMCID: PMC3812349.
Complete	Excluded by Requester Causes and consequences of age-related steroid hormone changes: insights gained from nonhuman primates. J Neuroendocrinol. 2013 Nov;25(11):1062-9. PubMed PMID: 23796387; PubMed Central PMCID: PMC3883982.
Complete	Excluded by Requester Diffusion MRI of the developing cerebral cortical gray matter can be used to detect abnormalities in tissue microstructure associated with fetal ethanol exposure. Neuroimage. 2013 Dec;83:1081-7. PubMed PMID: 23921100; PubMed Central PMCID: PMC3815979.
Complete	Excluded by Requester Ovarian steroids increase PSD-95 expression and dendritic spines in the dorsal raphe of ovariectomized macaques. Synapse. 2013 Dec;67(12):897-908. PubMed PMID: 23959764; PubMed Central PMCID: PMC3975919.
Complete	Excluded by Requester Endocrine and local control of the primate corpus luteum. Reprod Biol. 2013 Dec;13(4):259-71. PubMed PMID: 24287034; PubMed Central PMCID: PMC4001828.
Complete	Excluded by Requester Ovarian germline stem cells: an unlimited source of oocytes?. Fertil Steril. 2014 Jan;101(1):20-30. PubMed PMID: 24382341; PubMed Central PMCID: PMC3926438.
Complete	Excluded by Requester Clinical and ethical implications of mitochondrial gene transfer. Trends Endocrinol Metab. 2014 Jan;25(1):5-7. PubMed PMID: 24373414; PubMed Central PMCID: PMC4005369.
Complete	Excluded by Requester Measuring cone density in a Japanese macaque (Macaca fuscata) model of age-related macular degeneration with commercially available adaptive optics. Adv Exp Med Biol. 2014;801:309-16. PubMed PMID: 24664712; PubMed Central PMCID: PMC4332712.
Complete	Excluded by Requester Excluded by Improvement of antibody responses by HIV envelope DNA and protein co-immunization. Vaccine. 2014 Jan 16;32(4):507-13. PubMed PMID: 24280279; PubMed Central PMCID: PMC3926420.
Complete	Excluded by Requester Excluded by Requester Progress in a replicated selection for

	elevated blood ethanol concentrations in HDID mice. Genes Brain Behav. 2014 Feb;13(2):236-46. PubMed PMID: 24219304; PubMed Central PMCID: PMC3923418.
Complete	Excluded by Requester A unified approach to diffusion direction sensitive slice registration and 3-D DTI reconstruction from moving fetal brain anatomy. IEEE Trans Med Imaging. 2014 Feb;33(2):272-89. PubMed PMID: 24108711; PubMed Central PMCID: PMC4271809.
Complete	Excluded by Requester A brief, critical review of research on impaired control over alcohol use and suggestions for future studies. Alcohol Clin Exp Res. 2014 Feb;38(2):301-8. PubMed PMID: 24117468; PubMed Central PMCID: PMC3946792.
Non-Compliant	Excluded by Requester Increased fibroblast growth factor 21 expression in high-fat diet-sensitive non-human primates (Macaca mulatta). Int J Obes (Lond). 2014 Feb;38(2):183-91. PubMed PMID: 23736354; NIHMSID: 659782.
Complete	Excluded by Requester Isoflurane-induced apoptosis of neurons and oligodendrocytes in the fetal rhesus macaque brain. Anesthesiology. 2014 Mar;120(3):626-38. PubMed PMID: 24158051; PubMed Central PMCID: PMC3938095.
Complete	Excluded by Requester Current trends in West Nile virus vaccine development. Expert Rev Vaccines. 2014 May;13(5):589-608. PubMed PMID: 24689659; PubMed Central PMCID: PMC4279923.
Complete	Excluded by Applications of schedule-induced polydipsia in rodents for the study of an excessive ethanol intake phenotype. Alcohol. 2014 May;48(3):265-76. PubMed PMID: 24680665; PubMed Central PMCID: PMC4016177.
Complete	Excluded by Requester Excluded by Requester Nuclear reprogramming by interphase cytoplasm of two-cell mouse embryos. Nature. 2014 May 1;509(7498):101-4. PubMed PMID: 24670652; PubMed Central PMCID: PMC4124901.
Complete	Excluded by Requester ER. Vitamin C supplementation for pregnant smoking women and pulmonary function in their newborn infants: a randomized clinical trial. JAMA. 2014 May;311(20):2074-82. PubMed PMID: 24838476; PubMed Central PMCID: PMC4296045.
Non-Compliant	Excluded by Requester Limitations of preimplantation genetic diagnosis for mitochondrial DNA diseases. Cell Rep. 2014 May 22;7(4):935-7. PubMed PMID: 24856294; NIHMSID: 666583.
Non-Compliant	Excluded by Requester Excluded by Requester Monkey alcohol tissue research resource: banking tissues for alcohol research. Alcohol Clin Exp Res. 2014 Jul;38(7):1973-81. PubMed PMID: 24942558; NIHMSID: 663598.
Complete	Excluded by Requester Could moderate alcohol intake be recommended to improve vaccine responses?. Expert Rev Vaccines. 2014 Jul;13(7):817-9. PubMed PMID: 24872009; PubMed Central PMCID: PMC4245072.
Complete	Excluded by Requester Renal Pigmentation Due to Chronic Bismuth Administration in a Rhesus Macaque (Macaca mulatta). Vet Pathol. 2014 Jul 2;PubMed PMID: 24990482; PubMed Central PMCID: PMC4285376.

Excluded by Requester

Complete	Excluded by Requester Adrenal steroid hormones and ethanol self-administration in male rhesus macaques. Psychopharmacology (Berl). 2014 Sep;231(17):3425-36. PubMed PMID: 24781519; PubMed Central PMCID: PMC4135005.
Complete	Excluded by Requester Full genome sequence analysis of a novel adenovirus of rhesus macaque origin indicates a new simian adenovirus type and species. Virol Rep. 2014 Sep;3-4:18-29. PubMed PMID: 25530944; PubMed Central PMCID: PMC4266990.
Complete	Excluded by Requester Expression of the oestrogen receptor GPER by testicular peritubular cells is linked to sexual maturation and male fertility. Andrology. 2014 Sep;2(5):695-701. PubMed PMID: 25052196; PubMed Central PMCID: PMC4134690.
In Process at NIHMS	Excluded by Requester Selective targeting of GnRH-II neurons to block ovulation. Contraception. 2014 Sep 28;PubMed PMID: 25444718; NIHMSID: 631796.
Complete	Excluded by Requester Chronic alcohol self-administration in monkeys shows long-term quantity/frequency categorical stability. Alcohol Clin Exp Res. 2014 Nov;38(11):2835-43. PubMed PMID: 25421519; PubMed Central PMCID: PMC4244650.
Complete	Excluded by Requester Excluded by Requester Development and validation of a SNP-based assay for inferring the genetic ancestry of rhesus macaques (Macaca mulatta). Am J Primatol. 2014 Nov;76(11):1105-13. PubMed PMID: 24953496; PubMed Central PMCID: PMC4319213.
In Process at NIHMS	Excluded by Requester Null Mutation of 5-Reductase Type I Gene Alters Ethanol Consumption Patterns in a Sex-Dependent Manner. Behav Genet. 2014 Nov 23;PubMed PMID: 25416204; NIHMSID: 644436.
Complete	Excluded by Requester Quantification of dynamic changes to blood volume and vascular flow in the primate corpus luteum during the menstrual cycle. J Med Primatol. 2014 Dec;43(6):445-54. PubMed PMID: 24948037; PubMed Central PMCID: PMC4232987.
Complete	Excluded by Requester Hepatic abscesses in five outdoor-housed rhesus macaques (Macaca mulatta). J Med Primatol. 2014 Dec;43(6):503-6. PubMed PMID: 25041124; PubMed Central PMCID: PMC4232975.
Non-Compliant	Excluded by Requester Phosphodiesterase 3 (PDE3) inhibition with Cilostazol does not block in vivo oocyte maturation in rhesus macaques (Macaca mulatta). Contraception. 2015 Jan 30;PubMed PMID: 25645461.
In Process at NIHMS	Excluded by Requester Mitochondrial replacement therapy in reproductive medicine. Trends Mol Med. 2015 Feb;21(2):68-76. PubMed PMID: 25573721; NIHMSID: 653648.
In Process at NIHMS	Excluded by Requester 3D structure tensor analysis of light microscopy data for validating diffusion MRI. Neuroimage. 2015 Feb 7;PubMed PMID: 25665963; NIHMSID: 662062.
In Process at NIHMS	Excluded by Requester Excluded by Requester Nicotinic receptors in non-human primates: Analysis of genetic and functional conservation with humans. Neuropharmacology. 2015 Feb 7;PubMed PMID: 25661700; NIHMSID: 661887.

PMC Journal - In process	Excluded by Requester Direct actions of androgens on the survival, growth and secretion of steroids and anti-Müllerian hormone by individual macaque follicles during three-dimensional culture. Hum Reprod. 2015 Mar;30(3):664-74. PubMed PMID: 25567619.
In Process at NIHMS	In Preparation
In Process at NIHMS	In Preparation

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

http://www.ohsu.edu/xd/research/centers-institutes/onprc/
This is the publicly available home website for the Center within the OHSU website.

http://nprcresearch.org/primate/
The purpose of this website is to provide investigators, collaborators and program managers from funding organizations such as the NIH with an informative resource to help facilitate research collaborations.

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?

Yes

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? Yes

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

NOTHING TO REPORT

C.5.b Resource sharing

File uploaded: RPPR-OVERALL_ResourceSharing.pdf

OVERALL: RESOURCE SHARING

All materials that are produced as part of published scientific research are made freely available via Material Transfer Agreements between OHSU and the requesting organization.

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	ROBERTSON, JOSEPH E			PHD,MD	PD/PI	EFFORT						NA
	N	Excluded by Requester		DOB		Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Cost Accountant					Core-6102 (Business Services)		NA
	N					Admin Coordinator					Core-6107 (Division of Comparative Medicine)		NA
	N					Unit Manager					Core-6113 (Surgical Services Unit)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Unit Supervisor					Core-6103 (Facilities)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Clinical Technician					Core-6115 (Clinical Medicine Unit)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Admin Coordinator					Core-6103 (Facilities)		NA
	N				PhD	Sr. Research Informatics					Core-6127 (Primate Genetics)		NA

	N	Excluded by Requester		DOB		Programmer/Analyst	EFFORT		Core-6104 (Information Systems)		NA
	N					Sr Res Asst			Core-6121 (Endocrine)		NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Unit Manager			Core-6104 (Information Systems)		NA
	N					Admin Coordinator			Project-6130 (Division of Pathobiology & Immunology)		NA
	N					Unit Supervisor			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Admin Coordinator			Project-6129 (Division of Reproductive &...ntal Sciences)		NA
	N					Facilities Technician			Core-6103 (Facilities)		NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Assistant			Core-6125 (Molecular Virology)		NA
	N					Business Analyst			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Assistant			Core-6116 (Obese NHP Resource)		NA
	N				DVM	Assoc Vet			Core-6112 (Pathology Services)		NA
	N					Animal Technician			Core-6111 (Resources,		NA

											Facilities, and Operations)		
	N	Excluded by Requester		DOB		Financial Analyst	EFFORT				Core-6102 (Business Services)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Resident					Core-6107 (Division of Comparative Medicine)		NA
	N					Computer Analyst					Core-6104 (Information Systems)		NA
	N					Office Specialist					Core-6102 (Business Services)		NA
	N					Research Assistant					Core-6114 (Behavioral Services Unit)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Assistant					Core-6116 (Obese NHP Resource)		NA
	N					Facilities Technician					Core-6103 (Facilities)		NA
	N					Research Assistant					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Facilities Technician					Core-6103 (Facilities)		NA
	N					Animal Technician							NA
	N					Asst Vet					Core-6115 (Clinical Medicine Unit)		NA
	N					Transporter /Laborer					Core-6103 (Facilities)		NA

	N	Excluded by Requester			PhD	Asst Vet	EFFORT		Core-6112 (Pathology Services)	NA
	N			DOB		Facilities Technician			Core-6103 (Facilities)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Occupational Health Nurse			Core-6106 (Research Safety)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N				PhD	Staff Scientist			Core-6121 (Endocrine)	NA
	N					Research Assistant			Core-6112 (Pathology Services)	NA
	N					Laborer			Core-6103 (Facilities)	NA
	N					Admin Coordinator			Admin Core-8016 (Director's Office)	NA
	N					Research Assistant			Core-6118 (Infectious Disease Resource)	NA
	N					Admin Coordinator			Core-6102 (Business Services)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Sr Res Asst			Core-6117 (Primate Aging Resource)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Research Assistant			Core-6125 (Molecular Virology)	NA
	N					Business			Core-6111	NA

		Excluded by Requester				Analyst					(Resources, Facilities, and Operations)		
	N			DOB		Financial Analyst		EFFORT			Core-6102 (Business Services)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Associate					Core-6118 (Infectious Disease Resource)		NA
	N					Asst Facilities Technician					Core-6103 (Facilities)		NA
	N					Research Assistant					Core-6112 (Pathology Services)		NA
	N					Unit Manager					Admin Core-8016 (Director's Office)		NA
	N				PhD	Staff Scientist					Core-6120 (Assisted Reproductio n Technology)		NA
	N					Research Assistant					Core-6127 (Primate Genetics)		NA
	N					Admin Assistant					Project-6128 (Division of Neuroscienc e)		NA
	N					Facilities Technician					Core-6103 (Facilities)		NA
	N					Research Assistant					Core-6112 (Pathology Services)		NA
	N					Clinical Technician					Core-6115 (Clinical Medicine Unit)		NA
	N					Admin Coordinator					Project-6129 (Division of Reproductiv e &...ntal		NA

										Sciences)	
	N	Excluded by Requester		DOB		Clinical Technician		EFFORT		Core-6115 (Clinical Medicine Unit)	NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)	NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)	NA
	N					Sr. Research Assoc				Core-6119 (Japanese Macaque Resource)	NA
	N					Unit Supervisor					NA
	N					Clinical Technician				Core-6115 (Clinical Medicine Unit)	NA
	N					Sr Res Asst				Core-6114 (Behavioral Services Unit)	NA
	N					Research Associate				Project-6131 (Division of Diabetes, Obes... & Metabolism)	NA
	N					Sr Res Asst				Core-6113 (Surgical Services Unit)	NA
	N					Laboratory Aide				Core-6121 (Endocrine)	NA
	N					Research Associate				Core-6124 (Molecular & Cell Biology)	NA
	N					Asst Vet				Core-6111 (Resources, Facilities, and Operations)	NA
	N					Research Assistant				Core-6114 (Behavioral Services Unit)	NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and	NA

											Operations)	
	N	Excluded by Requester		DOB		Animal Technician	EFFORT			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Business Data Analyst				Core-6104 (Information Systems)		NA
	N					Grant Manager				Core-6102 (Business Services)		NA
	N					Unit Supervisor				Core-6107 (Division of Comparative Medicine)		NA
	N					Chief Operating Officer				Core-6102 (Business Services)		NA
	N				PhD	Unit Head				Core-6116 (Obese NHP Resource)		NA
	N					System/Application Analyst				Core-6104 (Information Systems)		NA
	N					Clinical Technician				Core-6115 (Clinical Medicine Unit)		NA
	N					Financial Analyst				Core-6102 (Business Services)		NA
	N					Research Assistant				Core-6112 (Pathology Services)		NA
	N					Clinical Technician				Core-6115 (Clinical Medicine Unit)		NA
	N					Mgr, Res Informatics				Other-6136 (NPRC Consortium-Based Activities)		NA
	N					Admin Coordinator				Project-6129 (Division of Reproductive &...ntal Sciences)		NA
	N					Project Manager				Core-6118 (Infectious Disease Resource)		NA
	N					Animal Technician				Core-6111 (Resources,		

											Facilities, and Operations)	
	N	Excluded by Requester		DOB		Research Assistant	EFFORT				Core-6112 (Pathology Services)	NA
	N					Research Assistant					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Research Associate					Core-6126 (MRI)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Custodian					Core-6103 (Facilities)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Unit Manager					Core-6114 (Behavioral Services Unit)	NA
	N					Research Associate					Core-6126 (MRI)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Asst Vet					Core-6113 (Surgical Services Unit)	NA
	N					Research Associate					Core-6112 (Pathology Services)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities,	NA

										and Operations)		
	N	Excluded by Requester		DOB		Asst Vet	EFFORT			Core-6115 (Clinical Medicine Unit)		NA
	N					Unit Manager				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Assistant				Core-6122 (Flow Cytometry)		NA
	N					Unit Manager				Core-6114 (Behavioral Services Unit)		NA
	N					Facilities Technician				Core-6103 (Facilities)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Assistant				Core-6125 (Molecular Virology)		NA
	N					Unit Manager				Core-6103 (Facilities)		NA
	N					Clinical Technician				Core-6115 (Clinical Medicine Unit)		NA
	N					Unit Manager				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Research Assistant				Core-6121 (Endocrine)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Financial Analyst				Core-6102 (Business Services)		NA
	N					Research Assistant				Core-6112 (Pathology Services)		NA
	N					Unit Manager				Core-6115 (Clinical Medicine		NA

									Unit)		
	N	Excluded by Requester		DOB		Facilities Technician	EFFORT		Core-6103 (Facilities)		NA
	N					Sr Res Asst			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)		NA
	N				PhD	Staff Scientist			Core-6127 (Primate Genetics)		NA
	N					Research Subject Protection Analyst			Admin Core-8016 (Director's Office)		NA
	N					Program Coordinator			Core-6107 (Division of Comparative Medicine)		NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Admin Coordinator			Project-6128 (Division of Neuroscience)		NA
	N					Unit Manager			Core-6112 (Pathology Services)		NA
	N				DVM	Assoc Vet			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Unit Supervisor			Core-6126 (MRI)		NA
	N					Research Associate			Core-6127 (Primate Genetics)		NA
	N					Research Assistant			Core-6116 (Obese NHP Resource)		NA
	N					Research Assistant			Core-6120 (Assisted Reproduction Technology)		NA
	N					Program			Core-6114		NA

		Excluded by Requester				Technician				(Behavioral Services Unit)		
	N			DOB		Unit Supervisor		EFFORT		Core-6113 (Surgical Services Unit)		NA
	N					Financial Analyst				Core-6102 (Business Services)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Sr Res Asst				Core-6114 (Behavioral Services Unit)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Clinical Technician				Core-6115 (Clinical Medicine Unit)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					HR Manager				Core-6102 (Business Services)		NA
	N					Animal Technician				Core-6111 (Resources, Facilities, and Operations)		NA
	N					Training Lead				Core-6107 (Division of Comparative Medicine)		NA
	N					Grants/Contracts				Project-6128 (Division of		NA

						Coord					Neuroscienc e)	
	N	Excluded by Requester		DOB		HR Coordinator	EFFORT				Core-6102 (Business Services)	NA
	N					Surgical Technician					Core-6113 (Surgical Services Unit)	NA
	N					Facilities Engineer					Core-6103 (Facilities)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Surgical Technician					Core-6113 (Surgical Services Unit)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N					Clinical Technician					Core-6115 (Clinical Medicine Unit)	NA
	N					Research Assistant					Core-6114 (Behavioral Services Unit)	NA
	N					Animal Technician					Core-6111 (Resources, Facilities, and Operations)	NA
	N				DVM	Unit Head					Core-6115 (Clinical Medicine Unit)	NA
	N					Sr. Research Assoc					Core-6125 (Molecular Virology)	NA
	N					Research Associate					Core-6124 (Molecular & Cell Biology)	NA
	N					Office Specialist					Project-6130 (Division of Pathobiology	NA

									& Immunology)		
	N	Excluded by Requester		DOB		Clinical Technician	EFFORT		Core-6115 (Clinical Medicine Unit)		NA
	N				DVM	Asst Vet			Core-6115 (Clinical Medicine Unit)		NA
	N					Research Assistant			Core-6127 (Primate Genetics)		NA
	N					Surgical Technician			Core-6113 (Surgical Services Unit)		NA
	N					Clinical Technician			Core-6115 (Clinical Medicine Unit)		NA
	N					Admin Assistant			Core-6103 (Facilities)		NA
	N					Research Assistant			Core-6114 (Behavioral Services Unit)		NA
	N				PhD	Staff Scientist			Core-6118 (Infectious Disease Resource)		NA
	N					Clinical Technician			Core-6115 (Clinical Medicine Unit)		NA
	N					Facilities Engineer			Core-6103 (Facilities)		NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Admin Coordinator			Core-6111 (Resources, Facilities, and Operations)		NA
	N					Sr. Research Assoc			Core-6125 (Molecular Virology)		NA
	N					Facilities Technician			Core-6103 (Facilities)		NA
	N					Research Librarian			Core-6105 (Research Library)		NA

	N	Excluded by Requester		DOB		Animal Technician	EFFORT		Core-6111 (Resources, Facilities, and Operations)	NA
	N					Project Manager			Admin Core-8016 (Director's Office)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Custodian			Core-6103 (Facilities)	NA
	N					MRI Technician			Core-6126 (MRI)	NA
	N					Unit Supervisor			Core-6103 (Facilities)	NA
	N					Office Specialist			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Research Assistant			Core-6123 (Imaging and Morphology)	NA
	N					Asst Facilities Technician			Core-6103 (Facilities)	NA
	N					Research Associate			Core-6127 (Primate Genetics)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Research Assistant			Core-6121 (Endocrine)	NA
	N					Unit Supervisor			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Facilities Engineer			Core-6103 (Facilities)	NA
	N					Animal Technician			Core-6111 (Resources, Facilities, and Operations)	NA
	N					Animal Technician			Core-6111 (Resources,	NA

											Facilities, and Operations)		
	N	Excluded by Requester		DOB	DVM	Asst Vet	EFFORT				Core-6115 (Clinical Medicine Unit)		NA
	N					Research Assistant					Core-6112 (Pathology Services)		NA
eRA Commons User Name	N				PhD	Sr. Staff Scientist					Core-6123 (Imaging and Morphology)		NA
	N				DVM	Unit Head					Core-6111 (Resources, Facilities, and Operations)		NA
	N				PhD	Assoc Scientist					Project-6130 (Division of Pathobiology & Immunology)		NA
	N				PhD	Staff Scientist					Core-6118 (Infectious Disease Resource)		NA
	N				PhD	Senior Scientist					Project-6129 (Division of Reproductiv e &…ntal Sciences)		NA
	N				PhD	Sr. Staff Scientist					Core-6125 (Molecular Virology)		NA
	N				PhD	Unit Head					Core-6114 (Behavioral Services Unit)		NA
	N				PhD	Staff Scientist					Admin Core-8016 (Director's Office)		NA
	N				PhD	Assistant Scientist					Project-6131 (Division of Diabetes, Obes… & Metabolism)		NA
	N				PhD	Assoc Scientist					Core-6119 (Japanese Macaque Resource)		NA
	N				PhD	Assistant Scientist					Project-6129 (Division of Reproductiv e &…ntal Sciences)		NA

eRA Commons User Name	N	Excluded by Requester		DOB	PhD	Unit Head	EFFORT		Core-6120 (Assisted Reproductio n Technology)		NA
	N				PhD	Interim Division Chief			Project-6129 (Division of Reproductiv e &…ntal Sciences)		NA
	N					Unit Head			Core-6113 (Surgical Services Unit)		NA
	N				PhD	Assistant Scientist			Project-6130 (Division of Pathobiology & Immunology)		NA
	N				PhD	Division Chief			Project-6128 (Division of Neuroscienc e)		NA
	N					Division Chief			Core-6107 (Division of Comparative Medicine)		NA
	N					Senior Scientist			Project-6130 (Division of Pathobiology & Immunology)		NA
	N				PhD	Unit Head			Core-6117 (Primate Aging Resource)		NA
	N				PhD	Unit Head			Core-6126 (MRI)		NA
	N				PhD/DV M	Unit Head			Core-6112 (Pathology Services)		NA
	N				PhD	Assistant Scientist			Core-6127 (Primate Genetics)		NA
	N				PhD	Assistant Scientist			Project-6128 (Division of Neuroscienc e)		NA
	N				PhD	Senior Scientist			Project-6129 (Division of Reproductiv e &…ntal Sciences)		NA
	N				PhD	Assoc Scientist			Project-6130 (Division of Pathobiology &		

eRA Commons User Name	N	Excluded by Requester		DOB	PhD	Senior Scientist	EFFORT		Immunology)		
	N				PhD	Senior Scientist			Project-6128 (Division of Neuroscience)		NA
	N				PhD	Senior Scientist			Project-6130 (Division of Pathobiology & Immunology)		NA
	Y				PhD	Center Director			Admin Core-8016 (Director's Office)		NA
	N				PhD	Senior Scientist			Project-6128 (Division of Neuroscience)		NA
	N				PhD	Senior Scientist			Project-6130 (Division of Pathobiology & Immunology)		NA
	N		SSN		PHD	Senior Scientist			Admin Core-8016 (Director's Office)		NA
	N				PhD	Faculty			Core-6126 (MRI)		NA
	N				PhD	Assistant Scientist			Project-6129 (Division of Reproductive &...ntal Sciences)		NA
	N				PhD	Senior Scientist			Project-6128 (Division of Neuroscience)		NA
	N				PhD	Assoc Scientist			Project-6129 (Division of Reproductive &...ntal Sciences)		NA
	N				PhD	Senior Scientist			Project-6128 (Division of Neuroscience)		NA
	N					Senior Scientist			Project-6129 (Division of Reproductive &...ntal Sciences)		NA
	N				PhD	Senior Scientist			Project-6128 (Division of Neuroscience)		NA

eRA Commons User Name	N	Excluded by Requester		Excluded by Requester	PhD	Assistant Scientist	EFFORT		Core-6127 (Primate Genetics)		NA
	N				PhD	Interim Division Chief			Project-6130 (Division of Pathobiology & Immunology)		NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: P51 OD011092-56 Other Support.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

Excluded by Requester

OTHER SUPPORT

Changes in Other Support (D.2.c)

ACTIVE

R01AI111851 Excluded by Requester (PI) 05/06/2014 – 04/30/2018 EFFORT
NIH/NIAID $9,739 (subcontract)
Targeting neutralizing epitopes in the MPER of HIV Env
The goal of this project is to develop an effective vaccine strategy to induce bNAbs against the conserved epitopes in the membrane-proximal external region (MPER) of the HIV envelope glycoprotein (Env).
(**New Project)**

P51 OD11092 Robertson (PI) 05/01/14 - 04/30/19 EFFORT
NIH/NCRR
Support for Oregon National Primate Research Center
Salary support only as administrative leader to achieve the goals of the P51

P01 AI078064 Excluded by Requester (PI) 07/16/09 – 06/30/15 EFFORT
NIH/NIAID $1,709,074
Programming HIV Immunity for Broadly Neutralizing Antibodies by Vaccination
The overall goal is to design novel vaccines based on env genes derived from virions (plasma RNA) from HIV-infected subjects who develop broad Nabs in an accelerated fashion (<3 years). The focus of the program project is on subtype B infected individuals. Collaborators include Excluded by Requester Excluded by Requester

R44AI091546-03 Excluded by Requester (MPI-contact) 09/15/2013-08/31/2015 EFFORT
NIH/NIAID $339,481 (subcontract)
Oral, replicating Ad4-HIV vaccine development & evaluation in NHP challenge model
This Phase II SBIR grant will test the efficacy of Adenovirus-4 based vaccines in rhesus macaques, challenged with SHIV. The Excluded by Requester laboratory will receive adenovirus and proteins from PaxVax and work with the ONPRC animal care staff and Excluded by Requester to deliver the vaccines in vivo and to perform the mucosal repeated low dose SHIV challenges as well as to evaluate immunity pre- and post-challenge Excluded by Requester will evaluate T cell responses.

R21 AI104392 01A1 Excluded by Requester (PI) 04/05/2013 – 03/31/2015 EFFORT
DHHS NIH/NIAID $150,000
HIV Envelope-based Vaccines from Superinfection to Elicit Neutralizing Antibodies
The major goals of this project are to investigate the potential for using HIV-1 Envelope genes from superinfected individuals and to develop HIV Envelope-based vaccines that induce strong cross-clade neutralizing antibodies.

Research contract Excluded by Requester (PI) 5/5/2014 – 3/31/2015 EFFORT
IAVI (USAID) $387,019
Passive transfer studies in rhesus macaques to investigate the efficacy of protection of anti-V2 HIV-1 mAb 697D
The objective of this study is to determine the protection efficacy of a human monoclonal antibody directed against an epitope on the V2 region of HIV-1 gp120 Envelope glycoprotein.

(New Project)

P01AI100151 Excluded by Requester (PI) 08/01/2013-07/31/2018 EFFORT
NIH/NIAID $85,554 (subcontract)

Epitope-targeted vaccines for HIV-1 prevention: Macaque Core C

The goal of the macaque core for this P01 project is to provide expertise and nonhuman primates to determine the immunogenicity of novel HIV vaccines.

(New Project)

1R01HD080459-01 Excluded by Requester (PI) 08/01/2014 – 6/30/2019 EFFORT
NIH/NICHD $543,361

Reducing Latent Viral Reservoirs in Infant Macaques

The objective of this project is to adapt an established model of persistent pathogenic SHIV infection in newborn rhesus macaques to study the effects of very early therapies with or without ART.

(New Project)

R01AI112546-01A1 Excluded by Requester 09/01/2014-08/31/2019 EFFORT
NIH/NIAID $251,000

Protective role of V2 antibodies induced at mucosal tissues in macaques

The main goal of this project is to induce anti-V2 antibodies at the mucosal tissue in rhesus macaques and challenge the immunized animals by vaginal inoculation of SHIV virus to observe whether anti-V2 antibodies can protect directly or need cooperation with other anit-HIV-1 envelope antibodies.

(Effort in Years 2-5 of project)

(New Project)

R01 research grant Excluded by Requester (PI) 03/01/2015-02/28/2019 EFFORT
NIH $21,551

Targeting IgM memory to establish protective B cell responses to HIV

The overall goal of the research project is to develop and test vaccines in rhesus macaques that will induce robust HIV-1 Env-specific IgM memory immune responses.

(New Project)

INACTIVE

Private Source Excluded by Requester (PI) 02/01/2014 – 01/31/2015 EFFORT
$180,000

Reducing Latent Viral Reservoirs in Infant Macaques

The goal of this research is to determine the effectiveness of HIV-1 neutralizing human monoclonal antibodies to limit or eliminate latent viral reservoirs.

R21 AI096977 Excluded by Requester (PI) 05/01/12-04/30/14 EFFORT
NIH/ NIAID $68,657

Induction of HIV neutralizing antibodies by targeting macaque B cell receptors

The role of the Excluded by Requester laboratory is to develop novel proteins based on the mimotopes, to vaccinate macaques with these plus DNA, and to determine the immunogenicity of these novel immunogens, followed by collection of blood and tissue samples for antibody cloning and characterization.

OVERLAP

None

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

OTHER SUPPORT

ROBERTSON, J.E

ACTIVE

P51 OD011092-55 Robertson (PI) 05/01/14 - 04/30/19
NIH/ORIP
EFFORT

Support for the Oregon National Primate Research Center
The major goal of this project is to provide the support for specialized facilities, scientific and technical personnel, and NHP species needed for the conduct of biomedical research.

Oregon Health & Science University – Host Institution 07/01/08 – 06/30/15
EFFORT

OVERLAP

No overlap

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

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

File(s) uploaded:
SpecialReportingRequirements.pdf

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: Oregon National Primate Research Center	096997515	OR-001	505 NW 185th Ave Beaverton OR 97006
Oregon Health Sciences & University	096997515	OR-003	3181 SW Sam Jackson Park Rd Portland OR 97239

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

Yes

Anticipated Amount	Source(s)
18761270	F&A, animal lease, per diem, support core fees

G.12 F&A COSTS

Not Applicable

1. SPECIAL REPORTING REQUIREMENTS

A. Colony Statistics

Genus, species	Breeding Colony			Not in Breeding Colony			Total Colony Census
	Male	Female	Total	Male	Female	Total	
Papio anubis				8		8	8
Macaca fascicularis	2		2	49	65	114	116
Macaca fuscata	66	128	194	43	80	123	317
Macaca mulatta	1196	2207	3403	565	456	1021	4424
Total	1264	2335	3599	665	601	1266	4865

U42 and U24 included in P51 grant numbers							
U42	436	217	653				653
U24	122	76	198				198

B. Tissue Distribution Program Information

As part of the NHP TDP, 33 ONPRC/OHSU investigators received 5,263 tissue specimens and 12 non-OHSU investigators received 581 specimens prepared according to their specifications. An additional 285 tissues were distributed for use in tissue banks administered at ONPRC. Of 6,129 total tissue samples distributed, 4,631 tissues were received by investigators from animals assigned to them as part of terminal research protocols. The majority of specimens are in the form of whole or partial organs/tissues (5497); a smaller portion of specimens are body fluids including blood, cerebrospinal fluid, and more rarely urine and bile (632). Requests from 12 external investigators were filled, the majority of which represented multiple tissues from multiple animals. Similarly, requests from 22 ONPRC/OHSU investigators were fulfilled with tissues from animals not assigned to them.

C. Project Summary Table

Research	156
Pilots	11
Other	5
Total	172

D. AIDS Statement

P51 supports 30% AIDS sponsored projects.

E. Breakdown of Investigators

Core Scientists	48
Affiliate Scientists	182
Total	230

F. Publications Summary Table

Excluded by Requester

A statement or table showing: i) the number of peer-reviewed journal articles supported by activities directly attributable to the P51 grant (reviews that are peer-reviewed should be included here); ii) the number of book chapters; iii) other publications (e.g., non-peer reviewed reviews). Do not include abstracts. Note that the papers in item i) will also be listed in the publication list (see item 3, below).

Peer-Reviewed Journal Articles	130
Books & Chapters	14
Other publications	7
Total	151

G. Training Tables

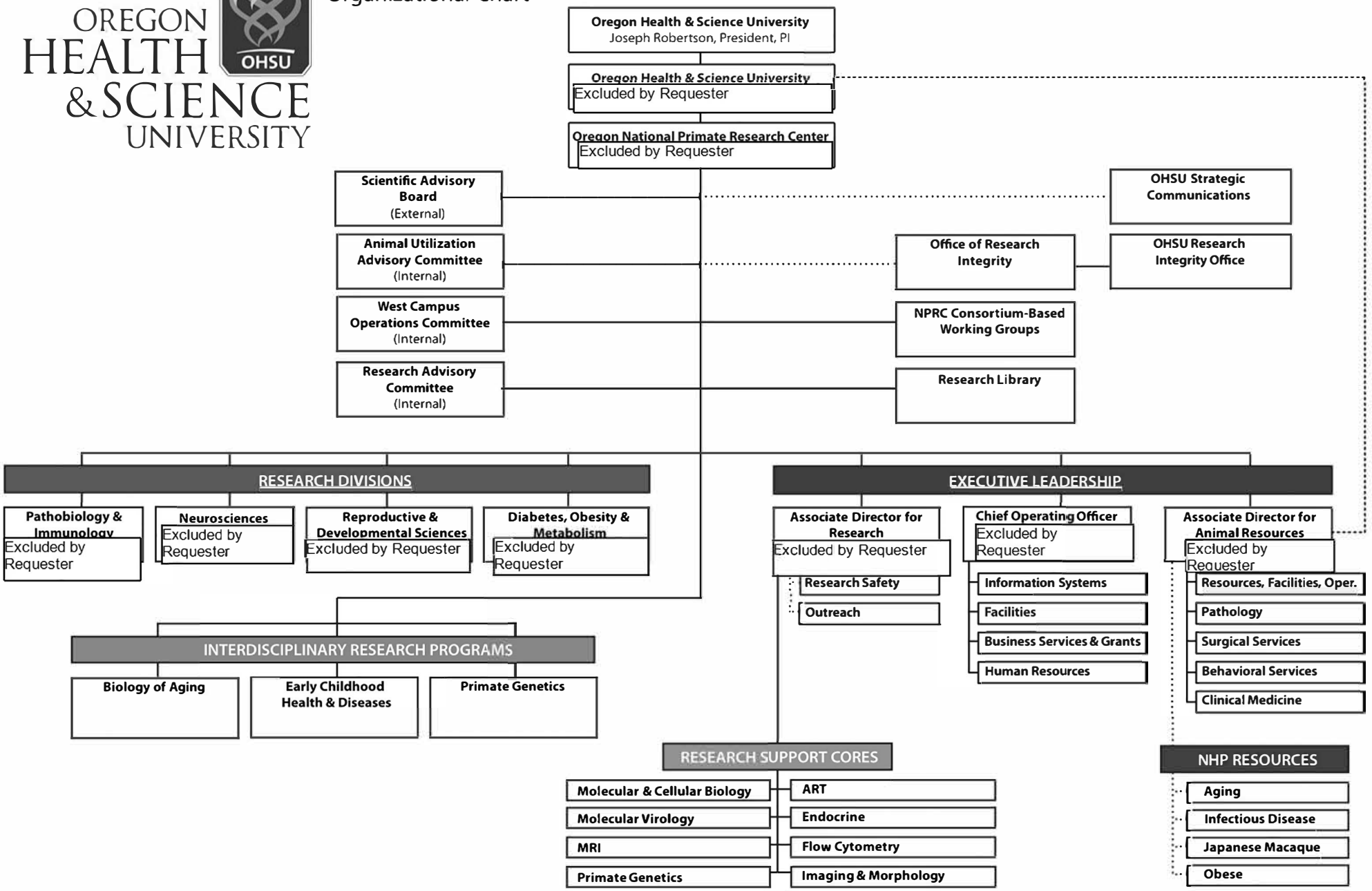
Training Summary	
Postdoc Trainees	7
Postdoc Researchers	15
Graduate Students - TG	12
Graduate Students	5
Undergrads	18
School Teachers	3
Total	60

H. Org Chart

OREGON HEALTH & SCIENCE UNIVERSITY

Oregon National Primate Research Center

Organizational Chart



2. INDIVIDUAL PROJECTS

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

Project Title: Summer Internship Program: Primate Center

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: ONPRC's Summer Internship program is a core component of the Center's multi-faceted education outreach program. In addition to conducting authentic research under the direction of a Primate Center scientist for 8 weeks, interns are intentionally immersed in the culture of science. They attend lab meetings and journal clubs, and are required to attend weekly seminars presented by Center scientists. At the close of summer, they are required to make a presentation of their research at the Summer Science Symposium.

Project Progress: During the summer of 2014, 17 undergraduate students and 5 high school students were supported in 8-week apprenticeships. Funding was secured to support an equal or greater number of apprentices during the summer of 2015.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: ASB1 Containment Expansion

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: AIDS related research is a major focus of the Division of Pathobiology and Immunology at the Oregon National Primate Research Center (ONPRC). The nonhuman primate (NHP) resource and disease models for AIDS at the ONPRC have contributed importantly to the search for effective vaccines and therapies, however, the ONPRC AIDS research program is currently limited due to a lack of sufficient bio-containment space. Annual usage of bio-containment space has increased from 50 NHPs in 2005 to 330 NHPs in 2010. This tremendous growth in demand for space has resulted in project delays in 2010 of up to six months. Although improved operating procedures are making effective and efficient use of existing bio-containment space, the physical space limitation cannot be overcome by operating procedures alone. This project proposes to construct an addition to the Animal Services Building (ASB) bio-containment space that will add six animal rooms and a kitchen. The addition of the animal rooms will add 96 cage spaces for the conduct of AIDS related research, and the kitchen will ensure that all services for research and animal welfare can be provided within the bio-containment barrier.

Project Progress: Final funding details have been completed and final design package expected to be sent to NIH for final approval mid-February 2015 and construction expected to start March 2015. Expected completion is fall of 2015. Project design expanded to include a totally independent and redundant HVAC system for these new animal rooms.

Funding Sources: NIH 1C06RR032703

Percent P51 Dollars: 0%

Project Title: Extramural Research Facilities Program

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: Oregon Health & Science University (OHSU) seeks funds to construct new outdoor group housing and a clinic and hospital support facility at the Oregon National Primate Research Center (ONPRC). The proposed outdoor group housing will be called the Primate Enclosures in a Natural Setting (PENS). Rapid research growth, expansion of Specific Pathogen Free (SPF) breeding colonies, and compliance with the USDA "Draft Policy on Environment Enhancement for Nonhuman Primates" necessitate additional social housing for nonhuman primates (NHPs) and increased animal central support space. Our long-term objectives are to: 1) provide housing for NHPs in social groups in a natural setting; 2) protect growing populations of SPF Indian origin rhesus macaques; 3) free-up cage space for the growing number of research projects; and 4) provide state-of-the-art central clinic and hospital support facilities to benefit all NHPs at ONPRC. To accomplish these objectives, we are proposing to construct outdoor group housing, called PENS, to provide a natural setting in which to raise NHPs in social groups and to accommodate the need for expansion of the SPF Indian-origin rhesus macaques, which are an invaluable resource for biomedical research. The design incorporates innovative features that will offer animals multiple environmental choices. Specific Animal Location ENS will consist of a [redacted] grassy Outdoor Area Enclosure to simulate a natural setting and a Specific Animal Location nclosed Area Shelter that provides excellent protection against inclement weather and also serves as a feed and catch area. Each of the 6 individual PENS will provide housing for 40 - 60 rhesus monkeys. We are also proposing to construct an important and much needed Clinic and Hospital Support Facility located adjacent to the six PENS. This will add an additional 80 cages to the current 60-cage clinic located on the opposite side of the campus. Specific Aim 1: Construct 6 PENS for SPF rhesus macaque breeding colonies. Providing a heated Enclosed Area Shelter connected to a large grassy Outdoor Area Enclosure is thought to be the best means possible for the ONPRC to raise healthy, naturally enriched SPF rhesus macaques. Specific Animal Location c Aim 2: Construct [redacted] Clinic and 80-cage Hospital Support Facility adjacent to the proposed (Specific Aim 1) to provide much needed clinical/support space. In addition to providing medical facilities for up to 360 rhesus to be housed in the six PENS, it will also provide much needed hospital support space for the approximately 1,000 rhesus located in corrals adjacent to the proposed PENS site.

Project Progress: Project was completed and occupancy approved October 2013.

Funding Sources: NIH 1C06RR022120

Percent P51 Dollars: 0%

Project Title: Establishment of Specific Free Rhesus and Pigtail Macques Colonies

Core Scientists Associated with Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

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

Project Progress:

The colony census at the close of 2014 was 198 and comprised of 124 adult breeding animals, 54 juveniles and 20 infants. Ten animals were assigned to research projects. Serologic screening of the colony was completed using a multiplex protein assay, Intuitive Biosciences, Inc. that we have been beta testing for the past two years. The colony remains free of the nine expanded SPF definition agents with the exception of lymphocryptovirus (LCV). The LCV component of this assay is quality control evaluated with the assistance of

Excluded by Requester Private Source

Twenty-five expanded SPF adults were obtained from the New England Primate Research Center. These animals will provide the colony additional breeding capacity and genetic diversity. Initial testing of the U24 ESPF breeding groups Crib Shelter housing units has been completed, but further evaluation will be needed to determine adequate biosecurity measures prior to occupation. These units will provide critically needed housing space for maintaining and expanding the ESPF colony and represents a long term, major investment to providing characterized NHPs for biomedical research, in particular for AIDS research.

Funding Sources: NIH 5U24OD010850

Percent P51 Dollars: 0%

Project Title: Establishment of Specific Pathogen-Free Rhesus Macaque Colonies

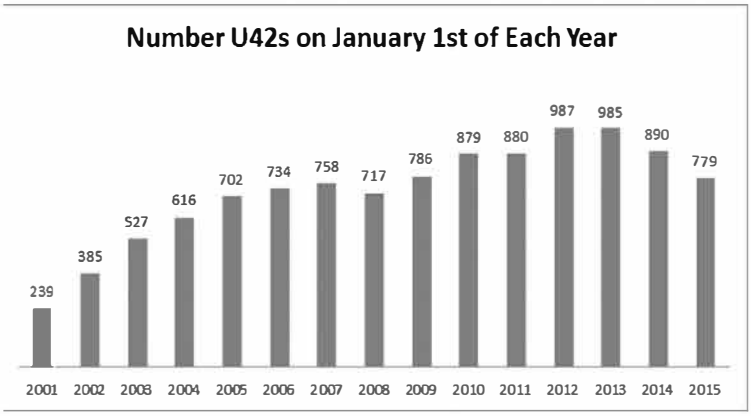
Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The projected need for Indian rhesus macaques for AIDS-related research exceeds availability from current domestic breeding programs and there continues to be an urgent need for breeding programs for future AIDS vaccine and pathogenesis studies. Rhesus macaques with defined major histocompatability complex (MHC) genotypes and known pedigree are becoming increasingly important for research to understand biologic variation in host immune responses and its effects on vaccine strategies and the pathogenesis of AIDS. The objective of this project is to expand the Oregon National Primate Research Center's specific pathogen-free (SPF) Indian rhesus macaque resource and sufficiently characterize their MHC haplotype to permit selected pedigree breeding for MHC class I alleles useful in AIDS research. Specific aims for accomplishing this objective include intensively managing a subpopulation of the Center's SPF Indian rhesus macaque breeding colony to maximize production of genetically diverse females to expand the breeding capacity of the colony. The breeding colony is typed for ten MHC alleles and managed for the production of MHC-defined offspring of known parentage. Both selective breeding of MHC-typed animals and assisted reproduction technology are used to enhance production of future breeder males that are homozygous for the MAMU-A*01 and other alleles important for assessing virus-specific cell-mediated immune function in simian immunodeficiency virus vaccine models for preventing AIDS virus infection.

Project Progress: One hundred eighty-two U42 animals were assigned to HIV/AIDS projects nationally throughout the funding year. The development of an algorithm designed to create maximally diverse breeding groups from a set of available animals ranked by genetic value has resulted in increased genetic diversity. We also produced expressed MHC allele data for 153 members of the U42 colony. MHC allele analysis of all U42 animals completed identifies a distribution of Mamu-A and Mamu-B alleles that approximates that found in our other rhesus macaque breeding colonies, with the majority of the animals falling within 18 different haplotypes. Access to animal pedigree information and parentage assignment is now readily accessible by ONPRC investigators through the PRIMe electronic database. Over the next year, we are transitioning to the use of single nucleotide polymorphism (SNP) genotype data for parentage analysis and pedigree data curation, and the incorporation of this genetic data into the PRIMe records is already underway. The U42 colony was downsized this year and will continue to be adjusted to better match actual grant-specific funding and lessen the financial burden on the P51 core grant.



Funding Sources: NIH 2U42OD010426

Percent P51 Dollars: 0%

Project Title: Use of novel advanced non-invasive imaging techniques to understand acute placental adaptations to injury

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: It is well established that clinical conditions of pathophysiological abnormalities in the placenta cause a wide range of health complications for the mother and child. Specifically, structural abnormalities of the placenta, or impaired utero-placental blood supply are both significant underlying causes of adverse human pregnancy complications and poor fetal outcomes. The hemochorial placenta of the rhesus monkey is analogous to the human placenta with the added feature of a secondary lobe. Surgical ligation of the inter-placental bridging vessels results in the loss of functional capacity to the secondary lobe, removing ~40% of the surface area for nutrient exchange. Our published study using this model demonstrates that the placenta has the ability to adapt to this injury to conserve fetal growth, yet the mechanisms underlying this adaptive capability are unknown. The acute disruption to the 'supply and demand' exchange between mother and baby in this NHP model affords a unique and novel means to investigate the fetal-maternal signaling mechanisms mediating placental adaptations to injury. A vital unanswered question is how does the placenta sense and adapt to vascular compromise? Human studies are limited by the inability of current diagnostic modalities to assess placental injury and perfusion, as well as the lag between the timing of vascular injury and collection of tissue thus limiting investigation of acute *in vivo* modifiers of placental growth and development. Therefore, a major weakness in our understanding of the fetal-placental adaptive response to injury is that assessments of placental function (both clinical and research) are limited by an inability to directly link *in vivo* placental perfusion to *in vitro* functional outcomes. We have developed a novel Dynamic-Contrast Enhanced (DCE) MRI technique that quantifies blood flow directly to the transfer unit of the placenta, the cotyledon. Our objectives are to understand the acute placental adaptive responses to vascular injury in a relevant animal model where there is a mismatch between maternal and fetal blood flow. DCE-MRI has been validated in the NHP but this proposal will be the first to pair this novel technology with the unique ligation model, allowing us to image and understand *in vivo* placental vascular adaptations. In addition, the ability to correlate *in vitro* expression of nutrient transporters, vascular growth factors and stereological outcomes with *in vivo* blood flow makes this a truly exceptional model for the study of placental vascular insufficiency. Secondarily, it is our intention to simultaneously utilize Contrast Enhanced-Ultrasound (CE-US) as a complementary imaging technique to DCE-MRI that can be more readily implemented in the clinical setting as a diagnostic tool for placental dysfunction.

Project Progress:
All imaging has been completed and analysis of the imaging is in process. Analysis of samples by stereology and molecular biology techniques is in process.

Funding Sources: NIH P51OD011092

Percent P51 Dollars: 0%

Project Title: Scaffold-based vaccines targeting conserved regions of dengue virus (DENV)

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: The dengue virus (DENV) E glycoprotein domain III (EDIII) is known to elicit potent DENV neutralizing antibodies when delivered as individual recombinant protein subunits. This project will assess the overall immunogenicity and protection provided by EDIII when delivered into rhesus macaques using the E2DISP protein scaffold antigen display platform. This study will evaluate the following after EDIII-E2 vaccination in macaques: 1) Immunogenicity in macaques of EDIII-E2 vaccination at 10 and 28 days using DENV neutralization assays against both homotypic and heterotypic DENV, 2) Protection against DENV viremia in macaques following homotypic virus challenge.

Project Progress: This project has progressed well, and we have found that the DNA and protein combination vaccination was highly immunogenic in rhesus macaques. After three immunizations, the vaccine elicited high titers of DENV neutralizing antibodies. The animals were challenged with a homotypic DENV-2 strain and we are currently evaluating the results of this challenge.

Funding Sources: NIH P51OD011092, NIH UL1 RR024140

Percent P51 Dollars: 0%

Project Title: Total Blood Volume of Rhesus Macaques

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description (one paragraph): Total blood volume (TBV) is commonly estimated for the purpose of determining institutional limits on blood sampling to prevent animal morbidity and experimental confounds that may result from overbleeding. TBV estimation formulas vary widely among biomedical facilities that use nonhuman primates (NHPs) and there are no current scientific studies that provide validation or guidance for TBV estimation. This pilot study will compare the feasibility of two alternative methodologies for determining TBV and generate preliminary data in support of an NIH application to expand the study to include a diverse subject population. The goal of the larger study is to derive an accurate means of estimating TBV that uses practical measurements and may be applied across a wide range of rhesus monkey demographics and phenotypes.

Project Progress (one paragraph):
This project was completed in the fall of 2014. The experiment successfully answered the questions that it was designed to answer. A manuscript that includes a detailed description of the experiment and the findings was recently Submitted

Funding Sources: NIH P51OD011092

Percent P51 Dollars: 0%

Project Title: Targeting oviductal epithelium with Proprietary Info

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: Our broad goal is to create a new reagent using Proprietary Info technology that can be applied clinically for gynecologic therapy. Oviductal Glycoprotein-1 (OVGP-1, MUC9) is a naturally-occurring mucin with a very specific pattern of expression. OVGP-1 is produced by the estrogen-stimulated fallopian tube, some malignant ovarian epithelial tumors and rarely, in endometrial cancer. Proprietary Info

Proprietary Info

Proprietary Info and thereby cause tubal blockade for the purpose of permanent contraception. In theory, Proprietary Info could also be used to target and ablate ovarian carcinoma cells. This is a 'proof of concept' study to demonstrate the synthesis of Proprietary Info

Proprietary Info

Project Progress:

Experiments evaluating localization of the Proprietary Info demonstrated low level binding to the target region. When mice treated with the Proprietary Info we did not observe any evidence of tissue damage. Proprietary Info Proprietary Info Proof-of-concept was not demonstrated in these experiments.

Funding Sources: NIH P51OD011092

Percent P51 Dollars: 0%

Project Title: Eliminating the latent SIV reservoir in rhesus macaques (RM) using Alemtuzumab

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

Vaccine & Gene Therapy Institute

Project Description:

Despite the great success of antiretroviral therapy (ART) in reducing morbidity and mortality associated with HIV infection, treatment must be taken life-long and there is no widely available means to cure HIV. The main reason why ART is unable to cure HIV is because HIV integrates into the host cellular DNA, and persists in long-lived $CD4_+$ memory T cells. Recently, the relative success of allogeneic transplants for hematological malignancies from CCR5 and non-CCR5 homozygous donors to HIV-infected patients on ART have suggested that elimination of existing T cells and immune reconstitution in the presence of ART may be key to reducing the number of latently infected cells, potentially allowing patients to safely stop ART and achieve what is now referred to as a "functional" cure. Allogeneic transplants are clearly impractical as a strategy for HIV cure, however oral or intravenous agents capable of inducing complete stem cell or T cell depletion would be of major interest. Alemtuzumab is a previously licensed humanized anti-CD52 monoclonal antibody, used in chronic lymphocytic leukemia, pre-transplant conditioning and cutaneous T cell lymphoma. It has recently been licensed for relapsing-remitting multiple sclerosis. Alemtuzumab acts via antibody dependent cell-mediated cytotoxicity and complement dependent cytotoxicity, and neutrophils are thought to support Alemtuzumab-induced T-cell depletion. We hypothesize that Alemtuzumab will deplete long-lived latently infected $CD4_+$ memory T cells in the presence of optimally suppressive ART. Thus, $CD4_+$ T cell reconstitution following Alemtuzumab treatment may allow for safe cessation of ART and potentially lead to a functional cure for HIV.

Project Progress:

The study has been delayed due to slow contract negotiations between OHSU and the pharmaceutical companies that will be supplying the reagents for the study. We have just recently obtained agreements with Proprietary Info and Proprietary Info We are still working on obtaining a Proprietary Info transfer agreement (MTA) with Proprietary Info healthcare for use of their drug Proprietary Info The study will begin as soon as the necessary MTAs are in place.

Funding Sources: NIH P51OD011092

Percent P51 Dollars: .689%

Project Title: Use of advanced non-invasive imaging to understand altered placental hemodynamics and injury following prenatal alcohol exposure

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description:

A prospective study utilizing advanced imaging techniques in combination with *in vitro* analysis of markers of hypoxia, oxidative stress, and angiogenesis in a relevant prenatal alcohol exposure NHP model to address fetal outcomes of maternal adverse behavior. The non-invasive imaging techniques utilized will be Doppler-ultrasound, dynamic contrast enhanced magnetic resonance imaging, and blood oxygen level-dependent MRI.

Project Progress:

We have had 2 control animals and 1 treatment animal that we have collected imaging data, placental tissue, and performed placental villous explant experiments along with molecular analyses for. In total we are hoping to have 6 controls and 6 treatment animals.

Funding Sources: NIH P51OD011092

Percent P51 Dollars: .256%

Project Title: The role of JM rhadinovirus (JMRV) infection of vascular endothelial cells in the pathogenesis of Japanese macaque encephalomyelitis (JME)

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: JME is a spontaneous inflammatory demyelinating disease with clinical, MRI, and pathologic similarities to multiple sclerosis (MS) that occurs in the ONPRC's Japanese macaque (JM; M. fuscata) colony. The disease appears to track with specific matrilineages, implying genetic predisposition, and appears to be associated with a novel simian herpesvirus, JM rhadinovirus (JMRV)[1]. Experimental intracranial injection of JMRV into the JM brain leads to the development of acute white matter lesions that resemble those seen in the spontaneous disease, suggesting that JMRV is a viral trigger for disease initiation and/or progression. Thus, JME is an attractive model for demyelinating conditions for which a viral and/or autoimmune component is indicated. To properly utilize the JME model, however, the role of JMRV in JME needs to be defined. Endothelial cell (EC) dysfunction is implicated in MS pathogenesis, and key findings implicating EC include: (i) breakdown of blood-brain (BBB) and blood-spinal cord (BSCB) barriers and (ii) elevated levels of EC-derived biomarkers in plasma and CSF. This project will focus on the EC that form these two critical blood-CNS barriers, and determine if JMRV infection of, or interaction with, these EC is important for disease. The hypothesis to be tested is that JMRV contributes to the pathogenesis of JME in part via infection of brain or spinal cord-associated EC and disruption of blood-CNS barriers.

Project Progress:
We have successfully isolated, purified and cryopreserved low passage stocks of primary spinal cord endothelial cells from JM tissue for use in future experiments. CNS-derived EC were derived from the same JM, which will enable direct comparison of interaction of JMRV with the critical cellular elements of the BBB and BSCB. We have begun to characterize JMRV infection of spinal cord-derived EC: the cells are highly susceptible to infection and exhibit barrier malfunction even prior to overt destruction of the monolayer. Further studies will involve a detailed analysis of infection of this cell type, including comparisons with CNS-derived EC.
Funding Sources: NIH P51OD011092

Percent P51 Dollars: 0%

Project Title: Inducing donor-specific tolerance through clonal deletion

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

University of California, Riverside
Oregon Health & Science University

Project Description: Each year there are approximately 16,000 kidney transplants performed in the U.S. The outcomes of transplantation are dependent upon the continuous use of immuosuppressive drugs, which can increase susceptibility to infections and cancers as well as nephrotoxicity. There is therefore an urgent need to discover novel approaches to induce donor specific tolerance, thus eliminating the need for long-term immunosuppression. Our long-term goal is to induce donor-specific tolerance in a rhesus monkey model of kidney transplantation using a novel approach to specifically eliminate allospecific lymphocytes. The working hypothesis of this proposal is that sensitizing a recipient using a donor specific lymphocyte transfusion (DST) will induce the activation of alloreactive lymphocytes that can subsequently be depleted using agents targeting activation markers. We will first identify the dose of PBMC needed to induce effective optimization of the recipient. We will use an adaptive study design starting with 1 x 108 cells followed by dose escalation or de-escalation by a factor of 10. The development of the alloresponse will be monitored by measuring the generation of donor specific T cells and alloantibodies by the recipient. We will then optimize the timing of administration of Brentuximab vedotin, an FDA approved drug that targets activated T and B cells, which upregulate CD30. We will deliver this agent day -1, the peak, and 1 week after the peak of T/B cell activation. The success of this approach will be evaluated by repeating the DST 3 weeks after the last Brentuximab vedotin administration.

Project Progress:
We were able to demonstrate that transferring non-syngeneic PBMC resulted in a allo-reactive T cell response as evidenced by increased expression of Ki67 in naïve and central memory CD4 and CD8 T cells. Interestingly, no B cell proliferation was observed. We also determined that re-challenge resulted in increased proliferation of CD8 T cells primarily. Importantly, we were able to detect increased expression of CD30 and CD70 on both CD4 and CD8 T cells. We are now continuing our analysis of in T cell activation by focusing on changes in gene expression associated with the development of alloresponses.

Funding Sources: NIH P51OD011092

Percent P51 Dollars: 0%

Project Title: Unconventional secretion from adipose tissue regulating metabolism

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: Extracellular vesicles are secreted from a variety of cell types and tissues and deliver protein and RNA cargo to target cells to alter phenotype. Preliminary mouse data suggest that this novel more of intercellular communication is involved in adipose tissue induction of insulin resistance in obesity. This project will determine if a similar mechanism is operant in nonhuman primates as a foundation for more in-depth analysis of this mechanism in the non-human primate model of diet-induced obesity and pre-diabetes developed at the ONPRC. The specific aims are to: 1) determine the effects of adipose tissue-derived vesicles on insulin action in a cellular model; 2) evaluate the effect of vesicles on macrophage cytokine expression; and 3) assess the microRNA profile of adipose vesicles.

Project Progress:
We have completed studies in support of specific aim 1 and in the current funding period are completing the experiments on cytokine secretion and microRNA profiling.

Funding Sources: NIH P51OD011092 and NIH UL1 RR024140

Percent P51 Dollars: 0%

Project Title: Examining the roles of microRNAs (miRNAs) in Japanese macaque encephalomyelitis (JME), a model for Multiple Sclerosis (MS)

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Vaccine & Gene Therapy Institute

Project Description:

JME is a chronic, inflammatory demyelinating disease with clinical and pathological characteristics comparable to MS that spontaneously occurs in JM (*M. fuscata*) at ONPRC. A novel gamma (g)-herpesvirus, JM rhadinovirus (JMRV), has recently been identified in JME lesions. Notably, experimental intracranial injection of JMRV leads to acute white matter lesions resembling JME, lending to the hypothesis that *JMRV infection contributes to the induction and/or progression of JME.* All primate g-herpesviruses examined to date encode viral miRNAs and can perturb the cellular miRNA environment during acute and chronic infection. miRNAs are small, non-coding RNAs that post-transcriptionally inhibit gene expression, and cellular miRNAs, in particular, regulate many key biological processes including cell signaling, proliferation, and the development of immune responses. Aberrant miRNA patterns have been linked to disease states and clinical outcomes. miRNA profiling studies of MS patients show dysregulated miRNAs in circulation and in active MS lesions; such miRNAs are hypothesized to modulate pro-inflammatory events contributing to disease. Little is known about the molecular biology of JME, and thus, gaining insight into the molecular mechanisms involved in JME pathogenesis is critical in developing JME as a model for MS and related inflammatory diseases—particularly given the implications of miRNAs as biomarkers and novel therapeutic targets. This project aims to characterize the miRNAs and mRNAs expressed during JMRV infection and in JME lesions utilizing next-generation sequencing methods. In addition to generating novel genetic information about JME and JMRV, these studies will importantly increase the genomic resources available for research involving nonhuman primates.

Project Progress:

We have identified both the JMRV-associated miRNAome and the transcriptome by deep sequencing that is present during lytic infection *in vitro;* importantly, many of the viral miRNAs and transcripts are also detectable *in vivo* >15 months post intracranial infection in JMRV-derived white matter lesions. Our analysis has revealed a handful of cellular miRNAs that are significantly altered during JMRV infection and we are currently characterizing these miRNAs—as well as their targets-- in JME lesions. Lastly, we have an extensive annotation of >400 miRNAs expressed in the JM brain and are using these data to identify additional novel miRNAs in non-human primates.

Funding Sources: NIH P51OD011092

Percent P51 Dollars: .497%

G. L (SpecialReportingRequirements.pdf)

Project Title: Proprietary Info

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health and Science University
Oregon Health and Science University
Oregon Health and Science University

Project Description: Increasing evidence suggests that anti-Müllerian hormone (AMH), which is produced by granulosa cells of the follicle, plays a major role in follicle growth and maturation. During our preliminary study, AMH ablation by the AMH antibody during the preantral stage negatively impacted the survival and growth of follicles in vitro. The data indicate that AMH may have a stimulatory role in early development of preantral follicles in primates. However, studies regarding the direct action of AMH on preantral follicle growth are limited due to the endogenous AMH production by the growing follicles, which prevents further effect by exogenous AMH treatment. Therefore, translational studies are proposed to (1) develop a molecular approach to knock down endogenous AMH expression (AMH-) by short hairpin (sh) RNAs in vitro, (2) examine the direct actions of AMH on primate follicle survival/growth, steroidogenic potential, and oocyte maturation in vitro via AMH addition to AMH- follicles in vitro, and (3) evaluate the role of AMH in regulating primate follicular development in vivo by knocking down endogenous AMH during the follicular phase of the natural menstrual cycle.

Project Progress:

Proprietary Info

Proprietary Info The preliminary data contributed to the Pending Support

Pending Support

Funding Sources: Oregon National Primate Research Center

Percent P51 Dollars: .547%

Project Title: Self-Injurious Behavior and Primate Well Being

Principal Core Scientist Associated with Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

University of Massachusetts Amherst
Washington NPRC, University of Washington
Southwest NPRC, Texas Biomedical Research Institute

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

Project Progress: This grant was transitioned to the University of Massachusetts and has been closed as a part of the transition.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Self-Injurious Behavior and Primate Well Being

Principal Core Scientist Associated with Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

University of Massachusetts Amherst
Washington NPRC, University of Washington
Southwest NPRC, Texas Biomedical Research Institute

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

Project Progress: In the past year, we found a positive correlation between hair cortisol (a measure of chronic stress) and alopecia in indoor housed rhesus macaques. We also found a correlation between some measures of anxiety and alopecia. Interestingly, there were large facility effects on behavior with the anxiety test we utilized. In the past year, this project has resulted in one published paper and one symposium at the 2014 American Society of Primatologists meeting.

Pending Publication

Pending Publication

Funding Sources: NIH 7R24OD011180

Percent P51 Dollars: 0%

Project Title: CDI-Type I: Computational Models for the Automatic Recognition of Non-Human Primate Social Behaviors

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Private Source

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

Project Progress: The ultimate goal of this study is to create an algorithm to automatically code the behavior of NHPs living in a social group. To date, we have successfully collected continuous audio and video recordings of five groups of 4-6 monkeys (n=24). We recently finished scoring behavior manually from the videotapes, which will be used for evaluating our algorithms. This analysis is being performed by our colleagues at Private Source Results from this study were presented at several conferences, and manuscripts are In Preparation

Funding Sources: National Science Foundation BCS-1027834

Percent P51 Dollars: 0%

Project Title: Anesthesia Toxicity in Neonatal Primate Brain

Principal Core Scientist Associated with Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

Oregon Health & Science University

Oregon Health & Science University

Project Description: A decade ago, the applicant and colleagues discovered that drugs that have either NMDA antagonist or GABAA agonist properties, a description that fits alcohol and all general anesthetics, trigger widespread death of nerve cells in the developing animal brain. In order to maximize the translational significance of our anesthesia toxicity studies, we applied for and were awarded a grant (start date Jan 2007) to study this phenomenon in the developing non-human primate (NHP) brain. The present application is a request for renewal of funding for ongoing studies pertaining to the apoptogenic properties of anesthetic drugs in the developing NHP brain. This work is being performed in collaboration with colleagues at Private Source Private Source and Oregon Health & Science University and Oregon National Primate Research Center. In the first 4 years of the grant period we have developed a valuable data base documenting susceptibility of the developing fetal and neonatal NHP brain to apoptotic death of brain cells (both neurons and oligodendrocytes) induced by clinically relevant exposure to each of three anesthetic drugs (isoflurane, ketamine, propofol). In this renewal application we are proposing to conduct additional NHP studies to further clarify the potential neurotoxicity of anesthetic drugs for the developing NHP brain and explore ways of modifying anesthesia protocols to enhance their safety for the developing brain. We have already developed a valuable data base, and now want to build upon that base toward the goal of achieving improved safety in the clinical application of anesthetic drugs in pediatric and obstetric medicine. The aims of the proposed research are to determine: 1) If there is a significant positive correlation between duration of anesthesia exposure and the number of neurons and/or oligodendrocytes that undergo apoptotic cell death; 2) How anesthesia without surgery compares in toxic impact with anesthesia with surgery; 3) How long into the post natal period does the brain remain vulnerable to significant neuronal or glial loss following clinically relevant exposure to anesthesia; and 4) Can the apoptotic response to anesthesia be prevented or significantly mitigated by adjunctive administration of neuroprotective drugs.

Project Progress:

In the last year we have completed the neonatal groups treated with 3 h, 7 h and 9 h of Isoflurane. The tissues from these experimental groups are still being evaluated histologically. In addition we performed experiments wherein pregnant time-mated dams were treated with an anesthetic agent and caffeine; the anesthetic agents were Isoflurane, Ketamine and Midazolam. A control/untreated 90 day fetal animal was also performed. After the treatment, the fetuses were collected by C-section and the tissues are being processed for histological analysis.

Funding Sources: NIH 5R01HD052664

Percent P51 Dollars: 0%

Project Title: Long-term Effects of Early Post Natal Isoflurane Anesthesia on Behavior, Learning and Memory in Non-Human Primates

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

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

Project Progress:

There were 24 animals enrolled in this study divided into 4 cohorts. The first cohort completed the battery of behavioral and cognitive testing during this year. The remaining 3 cohorts will complete the same tests later this year. In preliminary findings we have found a dose dependent delay in motor development, changes in behavioral response to stress, and exhibition of anxiety-typical behavior in animals that received anesthesia during early life.

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: Factor XI inhibitors

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excludedby Requester — Oregon Health & Science University

Project Description:

Proprietary Info

Project Progress:

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Hemocompatibility testing of stent coatings

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description:

Proprietary Info

Project Progress:

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

G.1 (SpecialReportingRequirements.pdf)

Project Title: Proprietary Info

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description:

Proprietary Info

Project Progress:

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Therapeutic Protein C Activator for Myocardial Ischemia

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description:

Proprietary Info

Project Progress:

Proprietary Info

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: Vascular tissue engineering: rational design using modeling

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: Tissue engineering holds promise for the treatment of cardiovascular disease. For tissue-engineered cardiovascular constructs it is widely believed that a nonthrombogenic endothelial cell (EC) surface will be advantageous. Many studies have therefore attempted to characterize the reactivity of EC with blood, i.e., EC "thrombogenicity". Unfortunately, most in vitro studies with EC have employed anticoagulated blood, static or nonphysiologic blood flow conditions, and relatively short blood exposure times. Consequently, the relevance of these results for in vivo applications remains uncertain. Similarly, in the development of tissue-engineered constructs there have been few studies of EC reactivity in vivo, and no systematic studies have been reported that correlate the properties of ECs that are measurable in vitro with in vivo responses. Nonetheless, it is now recognized within the tissue engineering community (and medical device and drug industries in general) that a key impediment to further progress is the lack of predictive animal models that will enable the rational design of constructs, i.e., preclinical models that will enable optimization of construct performance in vivo based on the identification and selective manipulation of key cellular activities in vitro.

Project Progress:

This project has concluded. The full scientific results were reported in the following articles:

a. Excluded by Requester "Engineering an endothelialized vascular graft: a rational approach to study design in a non-human primate model." PLoS One, 9(12):e115163, 2014. PMC4272299.

b. Excluded by Requester "Thrombotic responses of endothelial outgrowth cells to protein-coated surfaces." Cells Tissues Organs, Epub Jan 16, 2015. NIHMS631246, PMC number is pending.

Funding Sources: NIH 5R01HL095474

Percent P51 Dollars: 0%

Project Title: Ultrasound-Targeted Therapy for Acute Myocardial Infarction

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Private Source
University of Nebraska
Cedars-Sinai, University of California, Los Angeles
Oregon Health & Science University

Project Description: Acute myocardial infarction is one of the leading causes of death in the developed world and is fast becoming a leading cause of death even in the developing world. If a patient has access to a hospital with interventionalists on 24 hr a day call, the chances of opening an infarct-related artery (IRA) within 90-120 minutes of the onset of chest pain is 85%. Most patients, even in the US, do not have access to such facilities and if they arrive at a regional hospital are likely to receive thrombolytic therapy that has a success rate of 60% in opening the infarct-related artery. If some other non-invasive and easily applied treatment could enhance the success of thrombolytics alone and bring it closer to the 85% that can be achieved with percutaneous coronary interventions, it could have a major public health impact. The overall aim of this proposal is to develop novel ultrasound device technologies for microbubble-ultrasound mediated treatment of acute myocardial infarction. The specific aims of this proposal are to develop an integrated in vivo therapy-imaging system to: 1. Determine the optimal ultrasound parameters that cause successful thrombolysis in vivo using a vascular shunt model in baboons. 2. Develop therapy probe(s) that can deliver appropriate ultrasound energy to the thrombus in order to dissolve it and reduce microthromboembolism after reperfusion. 3. Integrate the therapy probe(s) with a 4D ultrasound imaging system that can image microbubbles in vivo and gate ultrasound pulses to automatically dissolve the thrombus. 4. Determine the mechanisms of myocardial microcirculation during acute coronary occlusion and prevent microthromboembolism after reperfusion by treating the myocardium with ultrasound. This proposal is for a Biomedical Research Parternership that involves the leaders in the country in their specific fields Excluded by Requester (OHSU) is an expert on thrombosis and has used innovative baboon models to study thrombolysis Excluded by Requester (University of Nebraska) is a pioneer in the use of microbubbles and ultrasound for arterial thrombus dissolution Excluded by Requester (Cedars-Sinai, UCLA) has described the novel findings of direct myocardial protection by und during acute coronary occlusion that is independent of its effect on the thrombus. Excluded by Requester (OHSU) has pioneered the field of MCE and has developed sophisticated techniques to assess the microcirculation, including measurement of no reflow, quantifying regional myocardial perfusion, and molecular Private Source Excluded by Requester is a leader in transducer technology, and GE is a world leader in und systems Excluded by Requester (OHSU) is an authority on deterministic tracking algorithms that can assist in of ultrasound to the correct target in a beating heart.

Project Progress:
We have conducted non-invasive *in vivo* experiments in order to investigate the possibility of ultrasound and ultrasound contrast agent be used as an adjuvant therapy to an FDA-approved thrombolytic rt-PA. We have results suggesting that ultrasound and ultrasound contrast agent combined with low dose of rt-PA reduce significantly the formation of *ex vivo* thrombi in an AV shunt.

Funding Sources: NIH 5R01HL095868

Percent P51 Dollars: 0%

Project Title: Molecular Imaging of Inflammation in Atherosclerosis

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: The development of techniques for molecular imaging of disease will likely lead to improvements in patient care through early diagnosis and customized phenotype-based treatment. Much of the recent progress in molecular imaging has been technology refinement whereby novel targeted probes and imaging algorithms have been tested in various models of disease. For cardiovascular applications, there is has been particular interest on imaging immune responses that play a critical role in atherosclerosis, ischemic injury, and heart failure. In the initial funding period of this award, we demonstrated that the severity of inflammation in murine models of atherosclerosis could be assessed with contrast-enhanced ultrasound and contrast agents targeted to endothelial cell adhesion molecules (ECAMs). These studies provided important information on binding characteristics, sensitivity of targeting ligands for disease processes. In this competitive renewal we will evaluate the relative clinical utility of this approach. We will determine whether molecular imaging of ECAMs provides unique diagnostic information that could positively impact patient care by guiding therapeutic decisions. One aim is to determine whether CEU targeted to VCAM-1 or P-selectin can detect the earliest stages of atherosclerosis prior to significant lesion development. This capability may be of critical value for assessing risk at a very early stage when novel potent anti-inflammatory therapies would be most effective. Hence, a second aim is to determine whether interventions aimed at the inflammatory response (immunotherapy against oxidized LDL or exercise) are most effective when given at the earliest sign of disease detected by molecular imaging. Sequential imaging studies will be used to determine whether suppression of ECAM expression predicts therapeutic response to treatment. These studies will be performed in two models of disease. The first is a reproducible murine model of atherosclerosis, the LDL-receptor and ApoBec editing peptide knockout, which will provide high-throughput and histologic confirmation. The second will be a novel non-human primate (rhesus macaque) model of obesity, inflammation and atherosclerosis which more closely resembles human disease. This model will be useful for determining the safety and feasibility for imaging with probes that are easily adaptable for human use.

Project Progress:
The non-human primate studies have now been completed and published in a high-impact cardiovascular journal (*Circulation* 2014,129:471). These studies showed that rhesus macaques fed a high fat diet developed very gradual increase in carotid intimal medial thickening (CIMT) which was statistically significant from baseline after 2 years. Despite the very subtle morphologic phenotype, we demonstrated that obesity and insulin resistance was associated with a progressive increase in carotid endothelial cell adhesion molecule expression (Figure). These data are important for understanding that the endothelial activation processes responsible for atherosclerosis (1) are related to the duration of IR, (2) precede by years any morphologic change, and (3) could be used as a biologic readout for new therapies. These data were key to the successful competitive renewal of this grant.

Funding Sources: NIH 5R01HL078610

Percent P51 Dollars: 0%

Project Title: Development of Toll-Like Receptor Agonists as Neuroprotectants in Brain Ischemia

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

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

Project Progress:

We have successfully demonstrated efficacy with Proprietary Info Proprietary Info Proprietary Info These studies are ongoing at our contract laboratories and we will file documentation with the FDA at the end of next year for permission to conduct human studies.

Funding Sources: NIH 1U01NS064953

Percent P51 Dollars: 0%

Project Title: Dynamic contrast-enhanced MRI of placental circulation

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: Maternal obesity during pregnancy is common and is associated with increased obstetric, neonatal, and childhood risks. Of growing concern is maternal nutrition during pregnancy due to the global obesity epidemic and the availability and consumption of a high calorie/high fat Western style diet (HFD). The nonhuman primate (NHP) shares developmental ontogeny similar to human fetuses including placental function, and the full spectrum of metabolic disease when placed on a HFD diet making it an invaluable model for translatable studies. In this animal model we are able to distinguish the relative contribution of maternal diet and metabolic health, something that is difficult in human cohorts. Our recent studies directly link HFD consumption in this well characterized NHP model with a reduction in uteroplacental perfusion and increased placental injury suggesting that a Western style diet may have a significant independent impact on the adverse obstetric and neonatal consequences reported in the obese human population. Since the placenta regulates nutrient exchange from mother to fetus, it occupies a central role in mediating the adverse obstetric risks associated with the obese gravidae. Current assessments of placental function, both clinical and research are limited by an inability to link placental perfusion with placental pathology and nutrient transport. Our objectives are to understand the consequences of altered placental blood flow on placental development and lipid transport in our NHP model.

Project Progress:
In the past year, we have successfully completed our in vivo assessment of placental blood flow in the NHP. We have found that consumption of a high fat diet during pregnancy reduces maternal perfusion of the placenta and that regions of underperfusion can be identified both by ultrasound and MRI. Our ongoing studies are linking blood flow to lipid and amino acid transport across the placenta.

Funding Sources: NIH 1R21HD076265

Percent P51 Dollars: 0%

Project Title: Control of Gonadotropin Secretion During Lactation

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

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

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

Project Progress:
In the last 12 months, we have explored the potential role glucagon-like peptide 1 (GLP-1) in signaling conditions of negative energy balance to kisspeptin and GnRH neurons in the brain. GLP fibers arising from a brainstem population appear to make close contacts to both kisspeptin and GnRH neurons, and a GLP-1 agonist is capable of depolarizing kisspeptin neurons in electrophysiological recordings. However, add back of GLP-1 during a 48-hr fast did not restore inhibited luteinizing hormone levels, indicating that other signals likely play a role in the inhibition of GnRH release during negative energy balance. In addition, we also explored the role of fibroblast growth factor-19 (FGF-19) in signaling negative energy balance states to reproductive neuroendocrine circuits by examining c-Fos activation after acute central administration.

Funding Sources: NIH 5R01HD014643

Percent P51 Dollars: 0%

Project Title: Determination of the Ability of Novel Targets to Activate Brown Adipose Tissue Thermogenesis for the Treatment of Diet Induced Obesity

Core Scientists Associated with the Project:
Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:
Excluded by Requester
Oregon Health & Science University

Project Description:
The study focused on investigating a novel therapy for weight loss via promotion of beige fat within adipose tissues to increase energy expenditure. This study involved several advanced techniques such as Dixon analysis via MRI and indirect calorimetry studies using metabolica chambers. In addition, this project will monitor changes in body compostion and glucose homeostasis.

Project Progress:
The treatment did not result in significant changes in body weight when compared to a control group and did not seem to provide a great improvement in glucose homeostasis

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Developmental programming of leptin signaling in arcuate neuropeptide Y neurons

Core Scientists Associated with the Project:
Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: The incidence of preventable diseases such as obesity among children has markedly increased during the last 20 years. This emerging epidemic of childhood obesity is partially due to the availability of highly palatable and calorically rich diets. Obese children and adolescents are considered at high risk for the development of type 2 diabetes and heart disease. Currently, there is little information regarding how overnutrition at a young age may alter the function of regulatory systems in the brain that control feeding behavior. The proposed studies will use a transgenic rodent model to investigate how leptin, a hormone produced by fat tissue, regulates brain pathways that modulate food intake during important periods of development. The second objective of this proposal will focus on the impact of early overnutrition on the development of abnormalities in the leptin signaling. It is hypothesized that leptin regulation of feeding circuits in the brain may have differential functions during development than it does in adults. It is expected that overnutrition during development will disrupt the mechanisms of leptin regulation in the brain, increasing the animals' susceptibility to metabolic diseases such as diabetes. These studies will provide important insights about the role of leptin in early nutritional reprogramming. These insights may help further our understanding of childhood obesity and its long-term impact on the development of diabetes.

Project Progress:
During this funding period, we demonstrated that leptin is an excitatory signal in NPY neurons throughout the first three weeks of postnatal development. As pups initated autonomic feeding behavior, we observed that leptin signal in NPY neurons transition from stimulatory to inhibitory. These changes in leptin signaling are due to a delay in the expression of KATP channels in NPY neurons. Furthermore, our studies in undernourished neonatal mice have revealed that leptin stay as an stimulatory signal until the 5th week of development in NPY neurons. Together, our results suggests that leptin actions in NPY neurons are important for the normal development of hypothalamic circuits that control food intake.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Drug Study in the Non-Human Primate Model of Diet-Induced Obesity

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description:

For these studies, we propose testing the efficacy of a proprietary drug in a non-human primate (NHP) model of obesity. We propose using pre-diabetic diet-induced obese (DIO) cynomolgus macaques that have a unique metabolic profile that model the human disease. With over-nutrition the animals get obese, hyperinsulinaemic, insulin resistant, pre-diabetic and also have increased inflammatory and cardio-vascular markers in the circulation. We will explore whether the effect of this proprietary drug to increase energy expenditure translates to higher species and also determine the impact of treatment on the body weight and insulin resistance phenotype of the DIO NHPs.

Project Progress:

The treatment did not result in significant changes in body weight when compared to a control group and did not seem to provide a great improvement in glucose homeostasis

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Effects of a novel leptin sensitizer, on food intake and body weight of obese Rhesus macaques

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Private Source

Project Description:

The current study focuses on investigating a novel leptin sensitizer that suppressed appetite and increases energy expenditure in mice and led to a significant weight loss. It has been demonstrated that a sustained reduction in caloric intake in obese individuals can produce steady weight loss. As such, treatments with compounds that are known to reduce food intake (anorexigenic) have long been pharmaceutical targets for the treatment of obesity. In this study, we will test an anorexigenic compound in its ability to suppress food intake and decrease body weight. This project tests a novel leptin sensitizer as a potential for weight loss therapy.

Project Progress:

This study demonstrated that a novel leptin sensitizer can result in a reduction in food intake in a short treatment plan. Longer treatment phases have been shifted to later studies.

Funding Sources: Private Source

Percent P51 Dollars: 0%

G.1 (SpecialReportingRequirements.pdf)

Project Title: Effects of Proprietary Info compounds on cardiovascular responses and glycemic control in lean Cynomolgus Macaques

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health and Science University

Project Description: The current therapy for acromegaly is somatostatin analogues, but these are only effective in 50-75% of patients, which means there is a significant population that does not respond. Several clinical studies have demonstrated that the combination of somatostatin analogues and dopamine agonists is more effective than somatostatin analogues alone in reducing GH levels in patients resistant to somatostatin analogues. The purpose of the present study is to test these Proprietary Info compounds in a species closer to humans to evaluate effects on normal pituitary secretion, pancreatic secretion and cardiovascular function with the goal of advancing one or more of the compounds into full development activities to support clinical development.

Project Progress:

The study clearly identified an effect of Proprietary Info compounds on heart rate, blood pressure and pancreatic function. The study aided in compound selection for future trials in humans.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Gestational Malnutrition: A Preventable Cause of Cognitive Impairment in Children

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description:

Oregon Health & Science University (OHSU) and the Oregon National Primate Research Center (ONPRC) are recognized as world leaders in child health research, especially in regards to the impact of maternal health and diet on the long-term health outcomes in children. These include behavioral outcomes, such as social anxiety, depression, and cognition, as well as increased risks for numerous other complications such as metabolic, cardiovascular and infectious disease. While increased metabolic disease risks have a significant impact on long-term survivability and dramatically increase health care costs, it is the effect on neurological and psychiatric health that have the largest impact on quality of life. Impairments in cognition and increased anxiety and depression impact the whole family and community and hinder a person's ability to develop quality social relationships, learn, and establish a successful career. To better understand the mechanisms linking maternal nutrition and child health, we propose to establish a multidisciplinary team of experts to develop a new highly relevant and translational nonhuman primate (NHP) model in which to systematically dissect the complex physiological and behavioral outcomes in offspring associated with maternal malnutrition. This team consists of highly productive senior and young investigators with proven track records in their fields of expertise. This team will enable a broad, complimentary, integrated approach that will be able to quickly establish the model and critically judge its application towards an important human health epidemic. This group has a strong focus on translational research, with the ultimate goal of preventing health complications before they start. We believe that specifically improving gestational health and nutrition will result in significant reductions in costly health complications in infants, allowing them to grow into productive individuals that will be better able to benefit their entire community. The long-term objective of these studies is to establish a highly translation NHP model in which to test specific intervention strategies that effectively prevent the developmental abnormalities caused by maternal malnutrition and that are logistically viable.

Project Progress:

This project initiated in September 2014. To date the adult animals have been assigned and placed on their respectives diets and allowed to breed naturally. To date we have over 14 pregnancies that we will follow through delivery and during the early post-natal period.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Immune Therapy of Insulin Resistance in Diet Induced Obese (DIO) Rhesus Macaques with Humanized Antibody in Proprietary Info a Natural Killer Cell Activating Receptor

Core Scientists Associated with the Project:
Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:
Excluded by Requester Oregon Health & Science University

Project Description:
The purpose of this study is to examine a novel compound in the treatment of diabetes. Recent studies have indicated that obesity can alter the immune system, and it is this alteration that plays a big role in the development in the co-morbidities of obesity, such as diabetes and cardiovascular problems. The compound used in this study targets a specific population of immune cells. Using rodent models, this compound has been demonstrated to prevent the onset of diabetes and atherosclerosis.

Project Progress:
This study has progressed and currently is investigating different compounds in the ability to improve body weight, insulin resistance, and immune function. This study is still ongoing.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: The Impact of Maternal Health and Diet on Development of Fetal Metabolic Systems

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

University of Colorado, Denver
University of Oregon
Oregon Health & Science University
Oregon Health & Science University

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

Project Progress:
In the last year, members of our group were invited to speak at numerous national and international meetings to present results from our studies, including at the International Conference on Obesity (Sydney AU), and the Australian Endocrine Society meeting in Melbourne AU. We also published two review articles on the topic area and four publications on specific science projects in high impact journals, including *Nature Communications*, *FASEB Journal,* and *Diabetes*.

Funding Sources:
NIH 5R24DK090964

Percent P51 Dollars: 0%

Project Title: Maternal High Fat Diet and Melanocortin System in Offspring

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

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

Project Progress:
In the last year, members of our group were invited to speak at numerous national and international meetings to present results from our studies, including at the International Congress of Neuroendocrinology, (Sydney, Australia), and the annual meeting of the Society for the Study of Ingestive Behavior (Seattle, WA). We also published two review articles on the topic area in the *Journal of Chemical Neuroanatomy* and *Neuroendocrinology*.

Funding Sources: NIH 5R01DK079194

Percent P51 Dollars: 0%

Project Title: Strategic Partnership for the Development of Novel Therapeutics for Diabetes and Obesity

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Private Source

Project Description:

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

Project Progress:

To date, tissue samples from various animal models have ben generated and shipped to collaborators. In addition, a molecular screening of initial targets has been performed.

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: Validation of brain protein systems associated with sensitivity and resistance to diet-induced obesity

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Private Source

Project Description: It is well recognized that the brain is critically involved in the regulation of food intake and energy expenditure and that dysregulation of several brain regions are associated with obesity and diabetes, from humans down to zebra fish. In spite of extensive study for more than a decade of several neuropeptide and neurotransmitter systems there has been very limited success in the development of a treatment of obesity. A primary reason for the limited success in developing new therapies for this indication has been the heavy reliance on rodent models for target discovery and preclinical validation; as there are key species differences in the circuits and mechanisms for the regulation of metabolic systems. Our overall strategy is to use the sophisticated and highly translational nonhuman primate (NHP) model of diet induced obesity and diabetes for discovery of novel targets for the treatment of metabolic diseases. Using cerebrospinal fluid (CSF) samples obtained from our NHP models we used proteomics to identify a number of novel proteins associated with various degrees of metabolic complications (i.e., obesity and insulin resistance). The overall goal of this project is validate and further characterize that these proteins are involved in the regulation of energy homeostasis. Our strategy is to identify protein systems that engage multiple orexigenic and anorexic systems simultaneously. By modestly engaging several systems simultaneously there should be improved therapeutic efficacy. Furthermore, we are particularly interested in target candidates that may have peripheral actions as well. These studies will identify several novel targets for the treatment of obesity and/or diabetes that will be relevant and translational to humans.

Project Progress:

This award was closed and rolled over into the Private Source

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Targeting hypothalamic kisspeptin neurons in the brain to regulate reproductive neuroendocrine function and energy metabolism

Core Scientists Associated with the Project:

Excluded by Request er

Affiliate or Visitina Scientists with Institutional Affiliation:

Excluded by Request e — Oregon Health & Science University

Project Description:

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

Project Progress:

The transgenic animals for these studies are currently breeding. We are also in the process of packaging a plasmid with a designer receptors exclusively activated by designer drugs (DREADD) construct into an adeno-associated virus (AAV) which will enable us to specifically activate ARC Kiss1 neurons. A new digital stereotax and nanoinjection system have been purchased that will enable us to more accurately and consistently inject the AAV virus into the ARC of the transgenic mice.

Funding Sources: Privat eSource

Percent P51 Dollars: 0%

Project Title: Effect of an FXR antagonist on food intake, body weight, glucose homeostasis, and body composition in the nonhuman primate model of diet-induced obesity

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description:

The Obese NHP Resource at the Oregon National Primate Research Center is focused on advancing the understanding of obesity, diabetes, and other related metabolic diseases by providing access to well characterized diet-induced obese nonhuman primates (NHP) to improve research in clinically translational disease models.

Our group has been using the NHP model of obesity for more than 6 years. Animals are maintained on a diet high in fat (35% of calories from fat), whereas normal NHP are maintained on chow (15% of calories from fat). This energy excess intake results in diet-induced obesity (DIO) with many clinical similarities to obesity in humans. Insulin resistance, hyperglycemia, hyperlipidemia, cardiovascular abnormalities, and other metabolic disruptions have been observed in these animals.

This study will test whether treatment with a novel compound in obese Rhesus macaques (DIO-NHP) will result in improvements in body weight, insulin resistance, and hepatic liver deposition. The initial study will establish the starting amount to be administered to DIO-NHP. The main proof of concept study will treat 8 animals and it is expected, based on previous results in rodent obesity models that significant improvement in body weight and insulin resistance will be observed.

Project Progress:

This study is currently in progress. We have identified the starting dose and will initiate treatment soon.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Effects of inhibitor in diet induced obese (DIO) Rhesus macaques.

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Request er — Oregon Health & Science University

Project Description:

The purpose of this study is to examine a novel compound in the treatment of obesity and associated diseases such as diabetes, hypertriglyceremia and nonalcoholic hepatosteatosis (NASH). This compound targets the initial and rate-limiting enzyme Propriet ary Info Propri et aryInfo have an important role in the regulation of insulin resistance and the formation of NASH. Obesity Propri et aryInfo in increasing levels of which in turn modify the direct interaction between the insulin receptor and nstream signaling cascades. This interference with insulin action at the liver results in lipid accumulation and liver failure. Using obese rodent models, inhibitors of the enzyme demonstrated to improve ins Propri et aryInfo sensitivity and liver functions. This study is the first to determine whether inhibiting in NHP can res similar improvements in insulin sensitivity and lipid accumulation in the liver..

Project Progress:

This project is currently ongoing. We have established half lives of the compound in obese animals and the dosing parameters that reduces enzyme activity. The next phase will be an efficacy study with these established dose levels.

Funding Sources: Pri vat eSource

Percent P51 Dollars: 0%

Project Title: Molecular Mechanisms of Human and Murine Beta Cell Proliferation and Regeneration

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

Project Description: The mission of the Beta Cell Biology Consortium (BCBC) is to generate functional human glucose-responsive, insulin-producing (-cells and to promote (-cell regeneration or proliferation of existing (-cells. While current research has identified many transcription factors and inductive signals that promote critical steps in mouse islet development, and that knowledge is guiding efforts to generate human beta cells from stem and progenitor cells, we have also learned that mouse and human islets differ significantly in terms of cellular composition, function, replication, regenerative capacity, and gene expression. These distinctive features of human islets and the need to translate emerging findings from rodent islet biology to human islets serve as the basis of our proposal. Our broad-based, interdisciplinary scientific team, consisting of experts in pancreatic islet and stem cell biology, islet regeneration, developmental biology, and "humanized" mice, will test the overall hypothesis that key genes and/or environmental stimuli which promote rodent (-cell proliferation can similarly induce the proliferation or regeneration of human or non-human primate (NHP) (-cells. We propose three specific aims: 1) Determine if signals that induce mouse (-cell proliferation also induce human and NHP (-cell proliferation in vivo and evaluate the effect of local inflammation on human and NHP (-cell proliferation. 2) Define the gene expression profile of proliferating human and NHP (-cells and build on these findings to induce proliferation of adult human (-cells. 3) Identify and characterize the regulators allowing and limiting postnatal islet (-cell proliferation in rodents, NHPs, and humans. Importantly, our investigative team will enhance the BCBC's team science-based efforts by: 1) focusing on human islet biology to complement and synergize with investigators working on either mouse pancreas and islet biology and/or human ES or iPS cells; 2) adding considerable expertise in the molecular mechanisms underlying (-cell development, cell fate determination, and proliferation; and 3) bringing and developing valuable research tools and technologies such as "humanized" mouse models, in vitro and in vivo models to study the proliferation and regeneration of fetal, juvenile, and adult human and NHP islets, and unique mouse models of (-cell proliferation and regeneration.

Project Progress:

Funding Sources: 5 U01-DK089572-04 (Vanderbilt)

Percent P51 Dollars: 0%

Project Title: The Impact of High-fat Diet Exposure During the Pre-and Perinatal Period

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: This study examines the effect of exposure to high fat diet during the pre and perinatal period on childhood behavioral disorders. We focus specially on a range of behaviors relevant to autism spectrum disorders (ASD). ASD are a group of neurodevelopmental conditions that manifest during early childhood. They are characterized by impairments in social behavior and communication, and often include the presence of stereotyped, repetitive behaviors. These disorders have a potentially complex range of associated symptomatology, including abnormalities in sensory integration, fine and gross motor skills, anxiety, aggression and obsessive compulsive behaviors. ASD are an important public health concern as their prevalence has risen dramatically in recent years. Currently, little is known about the etiology or underlying pathology of ASD. There is strong evidence that the perinatal environmental influences brain development and impacts autism risk. Maternal infection is a well-documented environmental risk factor for autism as it exposes the developing fetus to increased inflammatory factors. Moreover, there is evidence that individuals with ASD have persistent neural inflammation. Metabolic status during the perinatal period has also been associated with autism risk. Children born either small or large for gestational age are at increased risk for autism. Maternal obesity and increased weight gain during pregnancy are reported to increase the risk of children developing autism. As maternal obesity and overnutrition are associated with increased circulating inflammatory cytokines, we hypothesize that exposure to a high fat diet (HFD) and maternal obesity during fetal development impacts neural development and increases the risk of developing ASD. The proposed study will utilize behavioral tests, adapted from tests commonly used in psychiatric clinics to examine the ASD-like behavior of juvenile offspring from mothers that consume either a healthy diet or a HFD, which allow the findings to be directly translatable to humans. At the same time, we will use the pilot funds to broaden our repertoire of valid behavioral measurements to better mimic measures of attention deficits, hyperactivity, and externalizing behaviors in human children. Success on this front will open multiple routes for extramural funding to identify developmental origins of these behaviors that will not be available to any other institution.

Project Progress:

In the last year, members of our group were invited to speak at numerous national and international meetings to present results from our studies, including at the International Congress of Neuroendocrinology, (Sydney, Australia), and the annual meeting of the Society for the Study of Ingestive Behavior (Seattle, WA). We also published two review articles on the topic area in the *Journal of Chemical Neuroanatomy* and Neuroendocrinology.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Attenuation of androgen deprivation therapy-induced metabolic syndrome by diet

Percent P51 Dollars: 0%

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

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

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

Project Progress:
The first year study is complete, showing significant effects of androgen deprivation on muscle loss, reduced bobe density and persisting insulin resistance. Tissue samples from fat, liver and muscle biopsies were collected and are undergoing histological and gene expression analysis. In addition, activity patterns and physical activity are being analyzed.

Funding Sources: NIH 1R21AG047543

Project Title: Neuroscience Imaging Center at OHSU

Core Scientists Associated with Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: We propose to establish a Neuroscience Imaging Center at OHSU that will provide state-of-the-art instrumentation for electron, fluorescent, and confocal microscopy as well as expertise in designing and analyzing imaging experiments. The Neuroscience Imaging Center will have 3 cores: 1) a Live-cell Imaging Core, 2) a Confocal Core, and 3) an EM Core. The major instrumentation and expertise necessary for establishing these cores exist already at OHSU. However, the lack of fully staffed cores for these microscopes prevents efficient and reliable use of these instruments by NINDS investigators. The Neuroscience Imaging Center will provide the dedicated staff for these microscopes to enhance and facilitate the research by NINDS investigators at OHSU. An advisory committee, aided by an administrative core, will oversee the operations of the Center, review and optimize the effectiveness of the component cores, and manage the fiscal aspects of the Center. The three cores will function together as a truly integrated facility from experimental design, to performance, to data analysis. Instrumentation resources will be located on both the West and Marquam Hill campuses, thereby serving the entire OHSU neuroscience community. Excluded by Requester will serve as co-Directors of the Center; each Director brings unique scientific and technical qualifications and experience in managing shared facilities. The Center Directors will provide front-end consultation with the investigators, refining experimental questions and formulating optimal technical approaches for individual experiments. Three Core Managers and technical staff will operate the major instrumentation, train new users, and provide full service experiments for some investigators. Training opportunities will be available to serve principal investigators, postdoctoral fellows, and graduate students. Neuroscience is the centerpiece of research at OHSU, the Imaging Center will bring cutting-edge imaging to the 23 NINDS-funded research programs identified in this proposal, as well as our NINDS-funded trainees. The Neuroscience Imaging Center will catalyze focused interactions within our entire neuroscience community.

Project Progress: This project has offered NINDS investigators and other neuroscientists access to the instruments and expertise of the ONPRC Imaging and Morphology Support Core. Eight principal investigators were supported during the last year, and their work resulted in six publications within the same year. Single cell genomics based on Laser Capture Microsdissection of GFP labeled cells was among the new protocols developed within this grant.

Funding Sources: NIH 5P30NS061800

Percent P51 Dollars: 0%

Project Title: Gaining insight into brain circuitry using designer receptors exclusively activated by designer drugs in rhesus macaque monkeys

Core Scientists Associated with Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: To understand the functional role of brain micro- and macro-circuitry, it is critical to clarify the relationship between the activity of specific neuronal subtypes and behavior. The ability to manipulate brain regions/neuronal subtypes allows for assessing their contribution to behaviors and pathologies. A key step toward this goal is to use non-human primate models, both as a tool for analyzing neural function in more sophisticated models of behavior and as a potential use in clinical applications. However, the use of techniques in non-human primates to dissect neural circuitry has trailed behind that of c-elegans, drosophila, and rodents. Existing methods for manipulating neural activity in non-human primate models differ in their degree and speed of reversibility as well as factors that influence their utility for in vivo manipulation.

The first method used lesions or $GABA_A$ receptor specific drugs to "knock out" a region of interest. This method did not allow for cell-type specificity or temporal resolution. The most widely used method is electrical stimulation that activates cells in a precise temporal manner, but lacks cell-type specificity and does not allow for inhibition of brain circuitry. The third technique used viral-based expression of a Drosophila allatostatin r that enabled neuronal silencing (Excluded by Requester 2006). The use of viral constructs and cell-type specific ers allows for cell-expression specificity. However the ligand, allatostatin, does not readily cross the blood brain barrier and hence requires delivery through in-dwelling catheters for local administration. The most recent method is optogenetics that uses light-activated ion channels that either increases or decreases neural with high temporal and spatial precision (Excluded by Requester 2009; Excluded by Requester 2011). Cell-type s ers allows for expression of these light-activated channels within specific population of cells (Excluded by Requester 2011 Excluded by Requester 2012 Excluded by Requester 2012). Optical stimulation to elicit or al activity offers extremely fast temporal control, as they are only limited by the speed and efficiency of light delivery. However delivering light to deep tissue is difficult due to light dispersal, limiting its use to cortical areas. Also, despite strong neuronal responses to light, little to no motor behavior changes was elicited with light stimulation as were observed with electrical stimulation of the same regions (Excluded by Requester 2009; Excluded by Requester al., 2011 Excluded by Requester 2012 Excluded by Requester 2012).

Here we test the hypothesis that the newest form of pharmacogenetic technology currently used in rodent models can be functionally employed in monkeys. This model uses designer receptors that are exclusively activated by designer drugs (DREADDs) which are naturally mutated muscarinic receptors that have lost their sensitivity to their native ligand, acetylcholine, while gaining a greater affinity to clozapine and its metabolite clozapine-n-oxide (CNO; Excluded by Requester 2007). Currently there are 4 types of DREADDs: two that increase neuronal activity (Gs-DREADD; Gq-DREADD), one that decreases it (Gi-DREADD), and one that couples to (arr-DREADD; reviewed by Excluded by Requester et al., 2010 Excluded by Requester 2011 Excluded by Requester 2013). Excluded by Requester cogenetic tools allows for the reversible manipulation of brain circuitry since they are only activ the presence of CNO/clozapine, which bypasses the pitfall of lesions. The use of cell-specific promoters allows for the expression and subsequent investigation of neuronal subpopulations that are otherwise difficult to examine in vivo due to their limited numbers (interneurons) or their similarities with other neuronal subtypes that making cell distinctions difficult (e.g. D1-expressing medium spiny neurons versus D2-expressing MSNs), which addresses the pitfalls of lesions, $GABA_A$ receptor specific drugs, and electrical stimulation. CNO and clozapine readily crosses the blood brain barrier and shown to accumulate in the brain. This is an advantage over the previous use of the Drosophila allatostatin receptor. Also since there are a few varieties of DREADDs, it allows for the flexibility to either promote or inhibit cell excitability that was lacking in the use of the allatostatic receptors, lesions, and electrical stimulation. We will focus our initial studies on the manipulation of brain circuitry within the putamen, area implicated to play a role in habit formation and is suggested to be altered in Huntington's disease, Parkinson's disease, Tourette syndrome, obsessive-compulsive disorder, and that we have previously demonstrated to be altered in addiction and fetal alcohol syndrome. Since the putamen is a deep brain structure it will allow us to bypass the limitation of optogenetic technology to superficial brain structures such as the cortex.

Project Progress: We are currently performing the characterization of two viral constructs (AAV1-hSyn-Gq-DREADD-mCherry; AAV1-CaMKIIα-Gq-DREADD-mCherry) using immunohistochemistry and whole-cell patch clamp electrophysiology. Immunohistochemistry is used to examine the viral spread and to determine which cell types were infected by the virus (i.e. the hSyn promoter leads to expression of only neurons in the putamen and the CaMKIIα promoter leads to expression of only the medium spiny projection neurons of the putamen). Whole-cell patch clamp electrophysiology in mCherry-expressing neurons located in the putamen was used to examine action potential firing and membrane properties before, during and after the application of clozapine-n-oxide (CNO; 500nM) to activate DREADDs. We also performed a pharmacokinetic study to determine the concentration and timing of CNO (0.2-2.0mg/kg) that reaches the brain and blood stream after an intramuscular.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Gestational Ethanol Effects on Dorsal Striatal Function and Associated Behaviors

Core Scientists Associated with Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: The objective of the proposed research plan is to investigate the effects of gestational ethanol (EtOH) exposure on dorsal striatal circuitry that contribute to some of the behavioral abnormalities, such as impaired decision making, increased impulsivity, and motor deficits that observed in Fetal Alcohol Spectrum Disorder (FASD). Using a mouse model, we will expose individuals via a vapor chamber to ethanol throughout the embryonic and early postnatal period in order to mimic the three trimesters of human development (gestational EtOH) and examine the disposition of dorsal striatal circuitry and associated behaviors during adulthood. Preliminary findings to date indicate that in adult mice that were exposed to gestational EtOH display decreased GABAergic transmission in the dorsal lateral striatum (DLS) that appears to involve increased modulation by endocannabinoids. We observed no gestational EtOH-induced effect of glutamatergic transmission. Gestational EtOH also impairs habit learning; a type of associative instrumental conditioning that involves the DLS. 1 will determine the mechanisms underlying these gestational EtOH effects by accomplishing the following specific aims: 1) Determine the synaptic specificity of aberrant GABAergic microcircuits in the DLS of mice exposed to gestational EtOH. To accomplish this 1 propose viral, optogenetic, and electrophysiological experiments to examine the three major GABAergic synapses onto striatal medium spiny neurons (MSNs), those formed by parvalbumin interneurons, those formed by other MSNs, and those formed by low-threshold spiking somatostatin interneurons. 2) Rescue of gestational EtOH exposure on associative learning and striatal neurotransmission: possible avenues for treatment. Using the information gained in specific aim 1,1 will use pharmacological agents to decrease endocannabinoid tone to rescue the impaired habit learning and GABAergic neurotransmission.Taken together, the completion of this project will lay the groundwork for assessing how disruptions of the GABAergic microcircuitry of the striatum underlie many of the behavioral abnormalities seen in FASD and suggest approaches to compensate for these effects.

Project Progress: In the past year we have focused our studies on examining the effects of our gestational ethanol exposure paradigm on the synapse between parvalbumin-expressing fast-spiking interneurons to medium spiny projection neurons. Data obtained suggests a decrease in neurotransmitter release specifically in the parvalbumin-to-MSN synapse. We have had much difficulty in rescuing the loss of habit learning in those exposed to gestational ethanol exposure as the use of cannabinoid receptor 1 knockout and diacylglycerol lipase alpha knockout mice were unable to yield any litters after the vapor chamber exposure. Our latest attempt was to increase the release of GABA specifically from the parvalbumin-expressing fast spiking interneurons in the DLS by expression of h3MDq DREADD-mCherry. However activation of DREADDs did not restore habit formation in gestational ethanol exposed mice.

Funding Sources: NIH 4R00AA02176002

Percent P51 Dollars: 0%

Project Title: Genetic and Epigenetic Analysis of Alcohol Self-Administration in Monkeys

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: This proposal investigates the implication of both genetic variation and epigenetic modification on HPA axis regulation and excessive alcohol consumption in primates. These studies will draw upon the rhesus macaque ethanol self-administration model, which will enable a longitudinal study design examining genomic DNA methylation before and after 12 months of ethanol consumption, accurate measure of ethanol intake and endocrine levels, and access to both blood and brain tissue samples for the comparison of epigenetic changes in both tissues. We will use whole-genome approaches to measure CpG methylation levels in the tissues before and after chronic ethanol consumption. We will test whether changes in methylation levels are associated with corresponding changes in gene expression. We will also test whether changes in methylation patterns in the blood parallel those found in the brain. Also taking advantage of the high efficiency of next generation sequencing technology, we will sequence neurotransmitter genes from the HPA axis and monoamine signaling pathways in a large cohort of animals. We will test the association between common variants and endocrine dysfunction, and will evaluate potential additive effects and interactions between "risk" alleles in multiple signaling pathways. We will also explore whether there is an association between specific alleles or haplotypes and changes in methylation following chronic alcohol consumption (allele-specific methylation). Together, these approaches will provide a comprehensive basis for evaluating the cumulative genetic vulnerabilities that contribute to excessive alcohol use. Owing to the close evolutionary relationship of non-human primates, these studies will have a high-degree of translational relevance to human alcoholism, potentially 1) identifying alcohol-linked epigenetic modification of genes, 2) determining the relevance of epigenetic modifications in a clinically accessible tissue (blood) to those in the brain and 3) suggesting novel targets for the future treatment of alcohol use disorders.

Project Progress: We completed the whole genome analysis of the effect of chronic alcohol use on CpG methylation levels within the Nucleus accumbens Proprietary Info

Proprietary Info

Funding Sources: NIH 5U01AA020928

Percent P51 Dollars: 0%

Project Title: Washington National Primate Research Center - Collaborative Genetics Resource Unit

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester University of Washington

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

Project Progress: We used RNAseq methods to establish the MHC expressed allele composition of 170 WaNPRC pigtail macaques. Data were reported to the WaNPRC for upload into the ARMS database. We also provided consultation to the WaNPRC global health program, meeting with visiting scholars to discuss genetic approaches that can be implemented in Indonesia to monitor population diversity. We also worked with Excluded by Requester to identify genotype compatible rhesus macaques at the ONPRC that would be appropriate for use in her transplantation studies at the WaNPRC.

Funding Sources: NIH OD010425

Percent P51 Dollars: 0%

Project Title: Monkey Alcohol Tissue Research Resource (MATRR)

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Description: Excessive alcohol ingestion, occasionally or chronically, is co-morbid with medical disorders affecting the brain and behavior as well as other organ damage. Much of what is known about risk for and the consequence of heavy alcohol consumption, including mechanisms of organ damage, is derived from rodent studies or retrospective human accounts. This application proposes establishing a unique resource for alcohol research, a Monkey Alcohol Tissue Research Resource (MATRR). From this resource both tissue and associated bioinformatics tools will be made readily available to the wider alcohol research community. The tissue is derived from a standard protocol of ethanol self-administration in 3 species of monkeys. This resource provides novel data for hypothesis testing relating the risk for and consequences of alcohol consumption and serve to bi-directionally bridge the gap between rodent and human studies. The basis of the MATRR is that nonhuman primates, specifically monkeys, show a range of drinking excessive amounts of alcohol (>3.0 g/kg or a 12 drink equivalent/day) over long periods of time (12-30 months) with concomitant pathological changes in endocrine, hepatic and central nervous system (CNS) processes. These longitudinal designs span "stages of drinking" from ethanol-nai've to early alcohol exposure to chronic abuse. The CNS and peripheral organs from these animals comprise a unique translational resource for mechanistic and genetic studies of ethanol-induced pathologies. The state-of-the-art necropsy protocol will provide fresh, fixed and frozen tissue that are appropriate for ex vivo electrophysiology and neurochemical recordings, histological studies and genomic, proteomic and metabolomic approaches, respectively.

Project Progress: Overall, the MATRR resource has exceeded all expectations in terms of tissue generation, inventory control, tissue requests, tissue utilization, data analytics, novel data generated, publications, newly funded projects and new research directions. We have provided over 1532 tissue samples or RNA/DNA extractions from 241 tissue requests, with MTAs filed prior to sending and timely progress reports automatically requested. The users of this resource have generated 36 publications since the MATRR was funded and 25 additional studies have received funding that directly resulted from utilization of MATRR tissue and resources. In terms of tissue generation, currently there are tissues and data from 13 cohorts of monkeys (5 cynomolgus, 6 rhesus, 2 vervet) available for request.

Funding Sources: NIH 5R24AA019431

Percent P51 Dollars: 0%

Project Title: INIA: Stress and Ethanol Self-Administration in Monkeys

PI, with Institutional Affiliation:

Excluded by Requester | Oregon Health & Science University

Core Scientists Associated with the Project:

Excluded by Requester | Ph.D.

Excluded by Requester | Ph.D.

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester | Ph.D. | Oregon Health & Science University

Project Description:

The self-administration of ethanol assessed under "open-access" conditions allows the characterization of how chronic ethanol intoxication pushes the organism beyond the normal limits of homeostasis (a constant internal environment) and into chronic, variable, stress responses (allostasis) and disease states. A critical barrier to understanding the apparent reciprocal relationship between stress and excessive ethanol drinking is the availability of within-subject comprehensive, longitudinal data sets on the neurogenetic, neurochemical, neurophysiological, neuroendocrine, and behavioral adaptations to chronic ethanol. The macaque monkey that self-administers high doses of ethanol for >20 months can provide these data sets; optimally within a highly collaborative and integrative environment such as the Integrative Neuroscience Initiative on Alcoholism (INIA) consortium. In this project we provide a nonhuman primate model to address fundamental aspects of what is known (or suspected) in humans with respect to stress, anxiety and excessive alcohol drinking. The studies show longitudinal adaptations to excessive ethanol self-administration in cynomolgus and rhesus monkeys (pedigree population at the ONPRC). The studies address fundamental questions of stress and risk for excessive drinking including consumption patterns following stressful provocations and repeated periods of prolonged abstinence from alcohol. Translational variables include changes in the patterns of drinking alcohol as monkeys transition from moderate to heavy drinking, specific prefrontal cortical epigenetic adaptations, circulating endocrine and peptide markers, and functional connectivity MRI (fcMRI) studies. In addition, the research designs allows for unprecedented opportunities to investigate underlying synaptic changes in key regions of an integrative neural circuitry associated with the consequences of chronic alcohol self-intoxication.

Project Progress: One cohort of rhesus monkeys is currently enrolled in the experimental design and the next cohort of monkeys were leased and are being trained in the initial procedures. All is progressing on time.

Funding Sources: NIH 5U01AA013510

Percent P51 Dollars: 0%

Project Title: Symposium on Data Integration from the Monkey Model of Alcohol Drinking

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description:
The primary goal of the conference is to customize an informatic platform to produce new knowledge in the long-term adaptation of multiple organ systems to chronic, excessive, voluntary alcohol self-administration in order to understand the dynamic contributions of these adaptations to adverse biomedical outcomes. We will accomplish this goal by bringing together scientists that have collaborated and used the resources within the Monkey Alcohol Tissue Research Resource (www.MATRR.com) and the Integrative Neuroscience Initiative on Alcoholism (INIA): Stress, anxiety and excessive alcohol (www.INIAstress.org). The data sets that have been generated on the tissue to date are cross-disciplinary and cross-institutional, but all have the common factor of the same alcohol self-administration procedure, same antecedent and subsequent longitudinal genomic, endocrine, imaging and behavioral protocols. Indeed, the monkey model of alcohol self-administration has produced novel data for hypothesis testing relating the risk for and consequences of alcohol consumption and serve to bi-directionally bridge the gap between rodent and human studies. The symposium will focus on datasets generated from two species of monkeys (cynomolgus and rhesus macaques), particularly the rapid expansion of the data from different disciplines in the past 3 years. An outcome of the meeting will be to further understand from the users how to develop an informatics system that can accept summarized experimental outcomes across many disciplines and experimental protocols in order to integrate the analysis of genomic, genetic and phenotypic information and produce a comprehensive picture of dynamic interactions of risk factors, alcohol exposure, and adverse biomedical outcome. The gathering of geneticists, molecular biologists, neurophysiologists, endocrinologists, immunologists, osteopathologists, in vivo imagers, and behaviorists for a two day meeting will efficiently accomplish this goal.

Project Progress: We held the meeting and 65 attending, including the entire external advisory board attended. We set in place new policies for requesting tissue and submitting data.

Funding Sources: NIH R13AA023725

Percent P51 Dollars: 0%

Project Title: Modeling stroke in the female nonhuman primate to evaluate gender difference

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: This project will examine the neuroprotective effects of Proprietary Info Proprietary Info This model was created through a Proprietary Info Proprietary Info Proprietary Info will be evaluated between negative controls and E-treated animals with Neurological examinations and with MR imaging.

Project Progress: Currently Proprietary Info Proprietary Info Proprietary Info the study will enter the analysis phase of the study.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Characterizing the FASD Cerebral Cortex in Utero with DTI

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of Washington

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

Project Progress: There have been no modifications to the Specific Aims, or the Timeline of the original proposal. Currently, a 16-cage room is dedicated to this project, and difficulties are not anticipated in generating the planned number of animals within the stated timeline. Fetal brain MRI data analysis procedures we have developed for this project, which we have begun to apply to 7 G110 and G135 fetuses that have undergone imaging and necropsy.

Funding Sources: NIH 1R01AA021981

Percent P51 Dollars: 0%

Project Title: Bev Hartig Huntington's Disease Foundation

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Progress: This project has just begun and we have just obtained plasmids that will be used for rAAV vector production.

Funding Sources: Oregon Health & Science University

Percent P51 Dollars: 0%

Project Title: Biodistribution and dosing of an AAV expressing RNAi construct for Huntington's disease: a pre-clinical collaboration

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Progress: To date we have injected 3/18 animals using the novel Clearpoint MRI Compatible surgical system. We have collected tissue at 4 weeks post injection into the putamen and sectioned brains in preparation for immunohistochemical studies.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Determining the Feasibility of Gene Transfer to Ventricular Lining Cells of the Non-Human Primate Brain for Widespread Distribution of TPP1 and SGSH Lysosomal Enzymes following Intra- Cisterna Magna Delivery

Core Scientists Associated with the Project:
Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: This study investigates the biodistribution in the CNS and peripheral tissues of 2 different gene therapy vectors (AAV-CLN2 encoding TPP1 and AAV-SGSH encoding SGSH) aimed at treating Batten's disease and Sanfilippo A Disease, respectively, when administered into the cisterna magna.

Project Progress: All animals have been injected into the cisterna magna and tissues have been collected. Molecular and histological studies are planned for the next two months.

Funding Sources:
Private Source

Percent P51 Dollars: 0%

Project Title: RNAi dosing study for human HDS clinical trial

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: This project investigates the dosing, biodistribution and safety RNAi-mediated HTT suppression in the rhesus macaque putamen using the ClearPoint surgical device.

Project Progress: This project is now complete and an extension of this study is now being funded by Private Source

Private Source

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: RNAi Therapy for Huntingtons Disease: Safety & Efficacy in the Nonhuman Primate

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: This project investigates the creation of a viral vector-mediated non-human primate model of Huntington's disease and the subsequent assessment of RNA interference to prevent motor and cognitive deficits induced by the model.

Project Progress: This project has demonstrated clear motor, cognitive and temperament changes in rhesus macaques injected with AAV-mHTT into the caudate and putamen. Animals are still being evaluated on this study and it is set to end in the next 3-4 months.

Funding Sources: NIH 5R00NS069798

Percent P51 Dollars: 0%

Project Title: Temperament, functional connectivity, and ethanol self-administration in monkeys

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: Aim 1: Identify the functional neural correlates of an aggressive temperament. Hypothesis: Amygdala-dorsolateral prefrontal cortex (dlPFC), amygdala-orbitofrontal cortex (OFC), and amygdala-dorsal anterior cingulate cortex (dACC) connectivity will be reduced in monkeys with an aggressive temperament and will correlate with aggressive behavior. Monkeys with an aggressive temperament will have reduced modular organization (i.e. large-scale network organization) of regulatory systems, which will relate to aggression. Aim 2: Determine behavioral and functional connectivity predictors of heavy drinking in a monkey self-administration model. Hypothesis: Aggressive behavior at baseline will positively correlate with future ethanol self-administration. The atypical differences in functional connectivity (reduced connectivity between the amygdala and prefrontal cortical areas; reduced regulatory systems modular organization) associated with an aggressive temperament at baseline will also be predictive of future ethanol consumption. Aim 3: Measure the changes in functional connectivity and aggressive behavior following exposure to ethanol. MRI scans and behavioral testing will be performed (in a non-intoxicated state) following 6 and 12 months of exposure to ethanol, in order to characterize changes in both behavior and neural networks. Hypothesis: dependent an aggressive baseline temperament, chronic heavy alcohol intake (≥3.0g/kg/d) will increase aggressive behavior elicited during the HIT. Connectivity between the amygdala and prefrontal cortical areas will be further decreased from baseline levels in heavy drinkers compared to non-heavy drinkers. Independent of temperament, large-scale network organization is expected to be impaired to a greater extent in heavy drinkers versus non-heavy drinkers.

Project Progress: This small grant helped pay for five scans in these monkeys

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: VitC to Decrease Effects of Smoking in Pregnancy on Infant Lung Function-CCCLead

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

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

Project Progress: Patient recruitment continues on or slightly ahead of schedule. Study is progressing as planned and treatment groups are still blinded.

Funding Sources: NIH 5R01HL105447

Percent P51 Dollars: 0%

Project Title: Cognitive Nutrients and the Brain: Production of Isotopically Labeled Nutrients and Development of Animal Models

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
University of Illinois

Private Source

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

Project Progress: Brain tissue from a series of areas relevant to cognitive function was collected from 16 rhesus monkeys. From each sample membrane fractions were isolated, including synaptic, mitochondrial, nuclear and myelin membranes. Proprietary Info

Proprietary Info

Proprietary Info Methods were developed for the production of 13C-labelled lutein to be used in short-term dosing studies. MRI scans were obtained from a cohort of 15 monkeys fed life-long carotenoid-free diets as well as a reference group fed a standard carotenoid-rich diet.

Funding Sources: University of Illinois, Center for Nutrition, Learning and Memory

Percent P51 Dollars: 0%

Project Title: Development of a Japanese Macaque Model of Macular Disease

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: Age-related macular degeneration (AMD) is the most frequent cause of blindness in the elderly, but treatments are lacking. Higher primates are the only animals that closely resemble humans with respect to retinal anatomy and visual function. In particular, only monkeys, apes, and humans have a highly centralized retina with a macula and cone-rich fovea, the specializations underlie a high level of visual acuity. Thus only nonhuman primates can provide an optimal model for macular degenerations. Approximately 25% of the Japanese macaque population at ONPRC is affected by a naturally-occurring macular degeneration that potentially provides an ideal model for AMD. Over the last ten years we identified this syndrome and ascertained phenotypes in over 200 individuals. Distinct advantages of this model are that it is transmitted as a simple Mendalian, dominant trait, can be propagated through selective breeding, and is detectable in juveniles as young as 1-3 years old. This project has characterized this model, including its rate of progression and the influence of dietary factors, and is attempting to identify the underlying gene mutation. We examined effects of a Western diet high in saturated fat and sugar and low in carotenoids and omega-3 fatty acids, all factors believed to increase risk for AMD in humans. The resulting data lays the groundwork for use of this model to test the efficacy of potential treatments for AMD. Monkeys with naturally-occurring macular disease provide a valuable resource for evaluating macular disease pathogenesis and risk factors and for preclinical testing of AMD therapies. Furthermore, macaques have naturally-occuring macular disorders that can serve as an ideal translational model for AMD.

Project Progress: We quantified the extent and rate of progression of macular disease. We developed a machine learning algorithm to quantify the extent of drusen, the subretinal deposits that are the hallmark of early AMD, in retinal photographs. Nine macaques fed the Western diet showed a significantly accelerated rate of progression over 18 months, compared with nine fed a standard diet. Indices of systemic inflammation were also elevated. Thus, this study demonstrated that a Western diet accelerates the progression of macular disease in a naturally-occurring nonhuman primate model under controlled conditions.

Funding Sources: Oregon Health & Science University

Percent P51 Dollars: 0%

Project Title: Evaluation of Stem Cell-derived Retinal Pigment Epithelial Cells for Retinal Disease Therapy

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
National Eye Institute

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

Project Progress: New optimized protocols were implemented for the differentiation of RPE cells from rhesus monkey induced pluripotent stem cell lines, resulting in the successful production of viable RPE cells as verified by protein expression and functional assays. These cells will be used to test the viability of transplants delivered as allografts or autografts. Monkeys used to generate the stem cell lines are available to serve as autograft hosts.

Funding Sources: NIH 5R01EY021214

Percent P51 Dollars: 0%

Project Title: Impact of Infant Formula on Brain and Eye Development

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Oregon Health & Science University
University of Illinois

Private Source

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

Project Progress: An initial pilot study was completed to optimize methods for multiple modes of noninvasive retinal imaging and magnetic resonance brain imaging, and to determine appropriate levels of lutein supplementation.

Funding Sources: University of Illinois

Percent P51 Dollars: 0%

Project Title: Leber Hereditary Optic Neuropathy: Gene Therapy Trial

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University
Private Source
University of Florida

Project Description Mutations in mitochondrial DNA are responsible for a number of serious untreatable disorders affecting the eye, nervous system and heart. Strategies for effective therapies have now been developed, based on evolving understanding of these diseases and new techniques for targeting mitochondria with gene therapy. We chose to focus on one of the most severe of these diseases, Leber Hereditary Optic Neuropathy (LHON). This disease causes blindness in later childhood and early adulthood and results from mutations in the mitochondrial gene ND4, leading to impaired cellular respiration. Since no technology exists to introduce DNA directly into mitochondria, we overcame this deficiency by constructing a "nuclear version" of the mitochondrial gene and then targeting the cytoplasmically synthesized protein to the mitochondria with a targeting sequence appended to the reading frame (allotopic expression). This gene therapy restored respiratory function to cultured cells containing a mutant ND4, and restored visual abnormalities in a mouse model of LHON. This project takes the next step toward genetic therapy for LHON by testing the safety of this gene therapy method in nonhuman primates, which have an ocular structure and immune system most closely resembling humans. An AAV viral vector is being used for allotopic delivery of the ND4 gene to the retina, and its safety is being evaluated by a comprehensive series of assessments. If it proves safe, this gene therapy will move to a clinical trial in LHON patients to test its ability to prevent and reverse visual loss.

Project Progress: The AAV-ND4 viral vector was delivered intravitreally and was well tolerated. No adverse effects were seen in clinical observations, body weights, hematology and serum clinical chemistries, or in a series of assessments of ocular structure and function. No abnormalities were found in complete histopathological evaluations, and there was minimal spread of the virus to other tissues. Studies of the expression of a marker gene transduced by the viral construct showed robust and wide-spread expression in retinal cells. Study results have been submitted to the FDA and a clinical trial is being organized. Thus this study has paved the way for a novel and potentially effective gene therapy to preserve vision in patients with LHON.

Funding Sources: NIH 5R24EY018600

Percent P51 Dollars: 0%

Project Title: Module II: Nonhuman Primate Models of Retinal Disease

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: Age-related macular degeneration (AMD) is the leading cause of vision loss in adults over 60 years of age. The macula, the specialized area of the retina that underlies sharp central vision, is present only in human and nonhuman primates, so that only nonhuman primates can provide an accurate model for this complex disease. Furthermore, both rhesus and Japanese macaques develop syndromes closely resembling human AMD, and in rhesus we have confirmed two genetic risk factors that are shared with humans. Availability of these nonhuman primate models of AMD makes possible tests of several promising therapeutic approaches, including gene therapy, stem cell therapy, growth factors and nutritional interventions, as well as studies of the mechanisms underlying retinal degeneration. This project's objective is to continue to characterize these models using several complementary approaches: 1) identifying monkeys with naturally-occurring macular disease in the ONPRC macaque colonies; 2) determining the genetic mutations or susceptibility factors and gene expression changes underlying this disease; 3) testing the feasibility, safety and efficacy of retinal gene therapies and stem cell therapies; and 4) testing the effects of long-term, controlled dietary interventions that may protect the macula from macular degeneration.

Project Progress: We continued our efforts to screen the ONPRC colony to identify both rhesus and Japanese macaques with retinal disease and characterize their syndromes with multiple state-of-the-art modes of retinal imaging and have continued to follow the retinal status of groups of rhesus monkeys fed diets lacking dietary xanthophylls and n-3 fatty acids, two nutrients thought to lower the risk of AMD. These animals have developed hallmark signs of early AMD at early ages and show increased levels of retinal lipofuscin accumulation as measured in vivo by fundus autofluorescence. Furthermore, some have progressed to the more advanced form of atrophic AMD, which has not been previously reported in macaque monkeys. Ocular evaluations have also been extended to monkeys fed high fat diets leading to prediabetic and diabetic status, with the goal of establishing a nonhuman primate model of diabetic retinopathy. In addition, we have continued collaborative efforts to develop and test improved viral vectors for gene therapy.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: rAAV-CNGB3 Gene Therapy for Achromatopsia: Translational Research Studies

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Description: This project is aimed at developing a gene therapy for the CNGB3 form of achromatopsia, by providing the preclinical data necessary to enable a clinical trial. We have developed novel recombinant adeno-associated virus (rAAV) gene delivery reagents as "first in class" therapeutic agents to address the unmet vision needs of patients with CNGB3-related achromatopsia. To achieve this goal we propose six Specific Aims. Aim 1 will optimize the rAAV-CNGB3 vector by systematically modifying each of the components (promoter, intron, cDNA and polyA) so that the vector does not exceed its optimal packaging capacity, is able to target all three cone subclasses, and has optimized codons that enable maximal efficacy at a minimum dose. Aim 2 will produce rAAV-human CNGB3 vectors for use in animal studies in order to identify an optimal vector construct, which will then be produced for use in GLP safety studies and in clinical trials using a scalable, recombinant herpes simplex virus-based production method we developed that meets GMP standards and FDA requirements. Aim 3 will evaluate alternative serotype capsids and cone promoters for efficacy in a CNGB3-/- mouse model of achromatopsia. This will refine preliminary results suggesting that intravitreal administration of vector may lead to relevant transduction of cone photoreceptors. The optimal vector construct expressing human CNGB3 and ocular site of delivery will then be used to perform preliminary safety studies in nonhuman primates. Aim 4 will evaluate CNGB3 achromatopsia patients using a battery of state-of-the-art methods to establish natural history, appropriate inclusion/exclusion criteria and endpoints appropriate for the clinical trial. Aim 5 will use the optimal vector from Aim 2 to perform GLP-compliant toxicology and biodistribution studies in rats and nonhuman primates. Prior to initiating these studies, we will conduct a pre-IND meeting with the FDA to review the proposed study design and manufacturing/release testing methods, to reach agreement on the studies that will satisfy IND requirements. Based on these data, in Aim 6 we will prepare and submit an IND to the FDA. The IND will include a protocol for a Phase 1/2 clinical trial whose design will be guided by results from the previous five Specific Aims.

Project Progress: The ONPRC subproject of this grant is attempting to determine the optimal route of delivery, AAV serotype and promoter to deliver the CNGB3 gene to retinal photoreceptors in the nonhuman primate eye. To date, two serotypes and three promoters delivering a marker gene have been tested after subretinal delivery, and two of these showed strong transduction leading to marker gene expression in cone photoreceptors. Additional studies will evaluate newly developed vectors for their ability to transduce retinal cells by the less invasive route of intravitreal delivery.

Funding Sources: NIH 1R24EY022023

Percent P51 Dollars: 0%

Project Title: AAV Capsid Functions, Immune Evasion and Neuronal Targeting in Mice and NHP

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: Adeno-associated virus (AAV) is the most promising in vivo viral gene delivery vector currently available. However, there still remain various issues to be resolved, including the high prevalence of pre-existing anti- AAV neutralizing antibodies (NtAbs) in humans, efficacy-limiting host immune responses against viral proteins, and promiscuous viral tropism. In addition, there are species-specific differences in AAV-mediated immune responses and tropism, which often make it difficult to predict clinical outcomes from small animal studies and underscore the importance of nonhuman primate (NHP) studies. As for gene therapy for the central nervous system (CNS) diseases, the inability of AAV to efficiently cross the blood-brain barrier (BBB) poses an additional obstacle to be overcome. Therefore, to ensure a greater success for gene therapy, there is an urgent need to thoroughly address these issues. The ultimate goal of this project is to acquire a large dataset of AAV capsid amino acid sequence-phenotype relationships in cultured cells, mice and NHPs~ utilize the data to understand how the multifaceted AAV capsid phenotypes are determined in each different context~ establish means to overcome the current limitations~ and create NtAb escape AAV vectors that specifically target CNS neurons via the intravenous (IV) route in mice and NHPs. To achieve this goal, we have devised a novel next generation sequencing-based approach, termed AAV Barcode-Seq, which allows us to investigate an array of viral capsid phenotypes of hundreds of different AAV species in a high-throughput manner using only a small number of replicates. We will fully utilize our unique ability to conduct AAV research using this contemporary technology in order to achieve four specific aims. In Aim 1, we will draw high-resolution functional maps of the liver, heart, muscle and CNS-tropic robust serotype capsids (AAV8 and 9) and determine functional roles of each amino acid in manifesting a spectrum of phenotypes including cell surface binding, transduction, tropism and clearance. This analysis will allow us to identify amino acids important for CNS targeting. In Aim 2, we will map epitopes of anti-AAV NtAbs using a novel type of peptide libraries expressed on viral capsids in a native 3-D structure, and establish a means to create NtAb escape mutants. In Aim 3, we will investigate how AAV crosses the BBB using in vitro and in vivo models, and establish a means to create AAV mutants with increased BBB penetrability. In Aim 4, by combining the experimental outcomes of Aims 1-3 and utilizing a novel knowledge-based directed evolution approach, we will create novel NtAb escape AAV capsids that specifically and efficiently target neurons throughout the mouse and NHP brain by IV injection. Successful completion of this proposed project will 1) yield an abundance of insightful data on viral capsid amino acid sequence-host interactions that further our understanding of the AAV capsid biology~ 2) yield novel neuron- specific NtAb escape AAV vectors that can cross the BBB efficiently and readily be used in clinically relevant animal models~ and 3) provide valuable tools and data resources for the entire gene therapy community.

Project Progress: In this first year of funding, we have worked simultaneously on achieving the goals proposed under Aim 1-3. To this end, we have generated a library of AAV8 capsid double alanine mutants, and are currently working on a virus library to characterize viral phenotypes in vitro and in mice. In Aim 2, we have produced a hexapeptide scanning AAV capsid mutant library to map anti-AAV2 capsid antibody epitopes. Now we have a set of libraries to map anti-AAV1, 2, 6, 7, 8 and 9 antibody epitopes by IP-Seq (Immunoprecipitation followed by barcode-seq). In Aim 3, we are currently producing AAV1 and 9 chimeric mutants to understand the mechanism of the slowed blood clearance of AAV9 and developing novel AAV capsids that exhibit slow blood clearance, cross the BBB and transduce the brain better than AAV9.

Funding Sources: NIH R01NS088399

Percent P51 Dollars: 0%

Project Title: Altering Energy Balance by Systemic Delivery of RNAi to the Neuroendocrine Brain

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: To date, manipulating hypothalamic function mostly relies on the use of conditional knockout mice or transgenic overexpression. The major limitation to these approaches is that they do not take into account the complexities in the development of neuroendocrine neurons and their projections, and the compensatory adaptations that occur when these neurons are manipulated during early life. Alternatively, microinjections of adeno-associated viruses (AAV) delivering siRNAs have been used to modify hypothalamic function in adulthood. The greatest limitation of this technique is the invasiveness and relative inefficiency of the procedure. The present application intends to circumvent these limitations by developing a novel, minimally invasive method to manipulate hypothalamic neuronal function in a temporally defined and cell-specific manner. Among the hypothalamic systems that can be used as a prototype for these studies, the melanocortin system of the arcuate nucleus (ARC) stands out as an ideal candidate. It has been extensively studied and shown to play a critical role in regulating energy balance through modulation of food intake, body weight and glucose homeostasis. It is composed of two major populations of neurons with opposite functions; neurons containing pro-opiomelanocortin (POMC) inhibit the drive to eat and stimulate energy expenditure, neurons containing neuropeptide Y/Agouti-related peptide (NPY/AgRP) stimulate feeding behavior and inhibit energy expenditure. The consequences of altering the functions of either neuronal subset can be reliably assessed non-invasively, by measuring food intake and body weight. From the human health standpoint, developing new tools to study this system has an enormous value; the dramatic increase in childhood and adult obesity resulting from nutritional alterations during early life makes it urgent to develop novel methods to better understand the central mechanisms underlying the control of feeding behavior and energy homeostasis. This is a particularly important issue because energy balance can be permanently affected by nutritional challenges taking place during the critical period of "developmental programming" that in humans occurs during late gestation and in rodents, during the early postnatal period. A major advantage of the technology we propose to develop is that it can be used to modify ARC function after the developmental programming of energy balance is complete.

Project Progress: This project has now ended. We were able to develop modified adeno-associated viruses (AAVs), which were engineered to incorporate into their capsid proteins peptides that facilitate delivery of the virus to the hypothalamus after a single intravenous administration.

Funding Sources: NIH 5R21NS081611

Percent P51 Dollars: 0%

Project Title: Engineering viral vectors to target the cat hypothalamus with sterilizing molecules

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

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

Project Progress: We have now completed the first phase of our screening protocol by analyzing the serum of 30 cats for the presence of antibodies against a total of 11 different AAV serotypes (AAV1 through 11). The results showed that most of the serum samples are negative for antibodies against the different AAV serotypes except for AAV6. However, this result appears to be due to cross-reactivity of the antibodies against feline panleukopenia virus with the AAV6 capsid. Thus, essentially no AAV antibodies are present in the blood of these cats.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Inducing stable infertility by RNA interference - Proof-of-principle studies - YR 2

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: The aim of this grant is to develop a novel approach to permanently sterilize dogs and cats. We proposed to use rats to provide proof-of-principle for the overall validity of this approach. With this purpose, we are using two complementary methodologies: One employs a process known as RNA interference (RNAi) that can be used to silence genes involved in the control of reproduction; the other is intended to deliver RNAi selectively to the hypothalamus (where these genes are expressed) via systemic injection of an adeno-associated virus (AAV) engineered to target this brain region. We selected the hypothalamus because it contains neurons expressing Kiss1, a gene essential for reproduction and fertility. We proposed to use a phage display library and a technique called bio-panning to identify peptide sequences able to target the hypothalamus.

Project Progress: We have now identified and isolated peptides that confer phage particles the ability to target the hypothalamus selectively without homing to the heart, other peripheral organs, and non-neuroendocrine regions of the brain. We also identified sequences in the cat and dog Tac2 mRNA that are common to both species and that, therefore, can be targeted by the same miRNA construct.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: The Systems Biology of Mammalian Puberty

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Oregon Health & Science University

Project Description: The main goal of this research project is to use a systems biology strategy to investigate the existence of a layer of repressive gene regulation that – operating within the hypothalamus – may play a fundamental role in controlling the timing of mammalian puberty at the transcriptional level. Two aims are testing the general validity of this concept: Aim 1 uses a combination of computational biology, systems biology and molecular verification approaches to test the hypothesis that transcriptional repression is a central mechanism involved in the hypothalamic control of female puberty. Aim 2 uses an RNA interference (RNAi)-based loss-of function approach to disrupt putative upstream "central hubs" predicted *in silico* to repress key downstream nodes of the network, and therefore, to be important for the initiation of the pubertal process.

Project Progress: During the third year of NSF support, we have made substantial progress toward achieving the objectives of Aim 1, and have advanced significantly in our efforts to accomplish the objectives of Aim 2. We have identified three regulatory gene networks operating in the hypothalamus to regulate puberty. One is controlled by the micro RNA repressor Lin28, another is controlled by tumor suppressor genes, and the third is composed of two opposite forces of epigenetic regulation: the repressive component is provided by the Polycom group silencing complex and the antagonistic stimulatory component is provided by genes of the Trithorax family of transcriptional activators. We also found that while the Poycomb silencing complex is regulated by members of the POK family of transcriptional repressors, the actions of the Trithorax complex is regulated by Zinc finger protein with transcriptional repressive activity.

Funding Sources: National Science Foundation IOS-1121691

Percent P51 Dollars: 0%

Project Title: Behavioral Genomics of Alcohol Neuroadaptation

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Oregon Health & Science University

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

Project Progress: The cynomolgus monkeys of this project are advancing trough the protocol on schedule. The new touch screens are working outstandingly in the home cage environments.

Funding Sources: NIH 5P60AA010760

Percent P51 Dollars: 0%

Project Title: Dynamin-related protein I and neurodegeneration in Alzheimer's disease

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: The long-term goal of our proposed research is to understand molecular basis of mitochondrial dysfunction Alzheimer's disease (AD) in pathogenesis and to develop neuroprotective strategies to delay or prevent the onset of AD. Increasing evidence suggests that amyloid beta (Ab), hyperphosphorylated tau and mitochondrial structural and functional abnormalities are critically involved in the loss of synapses and cognitive decline, in patients with Alzheimer's disease (AD). Evidence suggests that Ab and hyperphosphorylated tau are directly responsible for causing mitochondrial dysfunction and oxidative stress in AD pathogenesis. 1) Several studies found Ab and N-terminal tau in mitochondrial membranes and causing mitochondrial dysfunction in neurons affected by AD; 2) recent studies found increased mRNA and protein levels of the mitochondrial fission genes and decreased fusion genes in AD postmortem and transgenic mouse models and cell-lines that express Ab, causing abnormal mitochondrial dynamics; 3) several other studies found that Ab reduces total motile mitochondria, impairs mitochondrial axonal transport, particularly anterograde transport; inhibits synaptic ATP production; and causes synaptic degeneration in AD neurons and 4) further, GTPase protein, Drp1 interacted with Ab and hyperphosphorylated tau in neurons from AD patients and transgenic mouse models of Ab and tau. These findings lead to the hypothesis that the interaction of Drp1 with Ab and hyperphosphorylated tau triggers mitochondrial fission by enhancing Drp1 enzymatic activity and causes excessive mitochondrial fragmentation, and ultimate neuronal dysfunction selectively in AD neurons.

Project Progress: This project has moved to another institution.

Funding Sources: NIH 5R01AG042178

Percent P51 Dollars: 0%

Project Title: Voltage-Dependent Anion Channel and Neurodegeneration in Alzheimer's Disease

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: The long-term goal of the proposed research is to understand the role of the voltage-dependent anion channel 1 (VDAC1) protein in Alzheimer's disease (AD) pathogenesis. Recent studies using postmortem AD brains, brain tissues from 6-, 12-, and 24-month-old A¿PP transgenic mice, and primary neurons from A¿PP and tau mice revealed that age, amyloid beta (A¿)-, and phosphorylated (phospho) tau-induced mitochondrial dysfunction and oxidative stress are key factors involved in neuronal dysfunction in AD pathogenesis. Researchers have reported that A¿ is associated with mitochondria localized at synapses and with synaptic damage and mitochondrial dysfunction. Preliminary research revealed that VDAC1, located in the outer membrane of mitochondria, was higher in the cortical tissues from AD patients and was also higher in the cerebral cortices of the 6-, 12-, and 24-month-old A¿PP mice. Research also revealed VDAC1 interacting with A¿ and phospho tau in the AD postmortem brains and in the cerebral cortices from APP, APPxPS1, and 3xAD.Tg mice. Mitochondrial functional analysis indicated increased free radicals, lipid peroxidation levels, and fission-linked GTPase activity, and decreased cytochrome oxidase and ATP levels in the APP transgenic mice. Preliminary research also indicated that A¿-induced activated glycogen synthase kinase 3¿ (GSK3¿) reduced hexokinases 1 and 2, and enhanced VDAC1 phosphorylation, leading to defects in mitochondrial structure/function. However, the links between A¿ and VDAC1 and between phospho tau and VDAC1 are unclear, and the relationship between GSK3¿ and VDAC1 phosphorylation to mitochondrial dysfunction are unclear. One hypothesis is that A¿ and phospho tau interact with VDAC1, which disrupts the transport of proteins/metabolites, resulting in defects in oxidative phosphorylation and in ATP synthesis. Another hypothesis is that a partial deficiency of VDAC1 maintains the mitochondrial pore activity in neurons producing A¿ and phospho tau, which in turn reduce mitochondrial dysfunction/synaptic damage in AD neurons. The proposed research objective is to determine the role of VDAC1 in mitochondrial dysfunction in relation to A¿ and phospho tau in AD pathogenesis. To this end, the proposed specific aims are: 1) to determine the physiological relevance of the interactions between VDAC1 and A¿, and between VDAC1 and phosphorylated tau in relation to VDAC1 phosphorylation and hexokinase reductions in AD neurons, 2) to determine whether reduced VDAC1 maintains mitochondrial pore activity and mitochondrial function in neurons producing A¿ and 3) phosphorylated tau. The outcomes of the experiments for these aims will provide new insights into the physiological relevance of increased levels of VDAC1 and its interactions with A¿ and phosphorylated tau in AD pathogenesis~ and will provide critical information that can be used to develop therapies for reducing A¿- and phosphorylated tau-induced mitochondrial damage and neuronal dysfunction in AD patients.

Project Progress: This project has moved to another institution.

Funding Sources: NIH R01AG047812

Percent P51 Dollars: 0%

Project Title: Reproductive Biology-Multidisciplinary

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: The primary goal of this training program is to provide multidisciplinary predoctoral and postdoctoral training in reproductive biology for those who wish to pursue an academic career in research and teaching in this area of biological science. This application requests funds to continue a training grant which has been funded for the past 30 years. Trainees will be selected based on their academic merit and potential for a productive research career in reproductive biology. The training faculty have expertise in many areas of reproductive biology including: neuroendocrine regulation of sexual development and mature reproductive function, hormonal control of the pituitary, the molecular biology of GnRH action, endocrine and paracrine control of gonadal function, regulation of the reproductive tract, and identification of genes involved in ovarian function and early embryogenesis. Many of the training faculty have a strong molecular orientation, and virtually all use molecular techniques into their research. Predoctoral students will be trained in one of three graduate programs at the Oregon Health and Science University: the Program in Molecular and Cellular Biosciences, the Dept. of Behavioral Neuroscience, or the Neuroscience Graduate Program. They will meet the course, seminar, and laboratory research requirements of the graduate council of OHSU and the specific requirements of the program in which they are training. Postdoctoral fellows will have access to the same courses and seminars, but emphasis will be placed on laboratory research. The unique features of this training program reside in the roster of faculty who study a wide range of areas within reproductive biology; the close ties between the research laboratories within the training program which facilitate co-mentoring of students; free access by students to expertise and equipment in all of the laboratories of the training program; regular meetings of journal clubs and research discussion groups; and the accessibility of performing reproductive research with nonhuman primates at the Oregon National Primate Research Center, and the presence of a number of collaborative interactions that include clinicians and basic scientists interested in reproductive biology. Programs for recruitment of minority trainees and formal instruction in the principles of scientific conduct and practice are in place.

Project Progress: We continue to be successful in recruiting outstanding students and fellows into the laboratories of our training faculty. All three positions were filled during the past year with new trainees. They are Excluded by Requester (graduate student, Program in Cell & Molecular Biology) working with Excluded by Requester Ph.D. and Excluded by Requester (postdoctoral fellow; Private Source working with Excluded by Requester. (postdoctoral fellow; Univ. Illinois Chicago) working with Excluded by Requester

Funding Sources: NIH T32HD007133

Percent P51 Dollars: 0%

Project Title: Novel hyaluronidase inhibitors for the promotion of remyelination

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Description: The Excluded by Requester lab previously demonstrated that a hyaluronidase, called PH20, digests hyaluronan in demyelinating lesions into digestion products that inhibit the maturation of oligodendrocyte progenitors, leading to remyelination failure. The goal of this project is to test novel compounds for their ability to specifically inhibit PH20 in vitro, in cultures of oligodendrocyte progenitors, and in experimental models of demyelinating disease, and determine if any of these compounds can restore high speed conduction velocity in affected white matter. Our long-term goal is to identify compounds that can be assessed for safety and efficacy in Japanese macaques with Japanese macaque encephalomyelitis and then in a clinical trial.

Project Progress: We have identified several compounds, including derivatives of the flavonoid apigenin,that effectively block PH20 activity and promote oligodendrocyte maturation both in vitro and in mice. We are currently testing the best of these compounds in mice with lysolecithin-induced demyelinating lesions for their ability to increase conduction velocities. A number of additional compounds are also being tested.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Regulation of remyelination by hyaluronan-regulated pleiotrophin signaling

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: We previously discovered that an enzyme, called the PH20 hyaluronidase, is elevated in areas where myelin is damaged in MS patients and mice with demyelinating lesions. PH20 breaks down a sugar molecule called hyaluronan (HA), which accumulates in areas of nervous system damage. The breakdown products of HA generated by PH20 prevent progenitor cells in areas of demyelination from becoming myelin-forming cells. Blocking all hyaluronidase activity promotes remyelination in an animal model of demyelination. However, the drugs available that block hyaluronidase activity have serious side effects and no specific PH20 inhibitors have been described. An alternative to blocking PH20 to promote remyelination would be to prevent the HA breakdown products generated by PH20 from signaling in cells. One of the signals that is affected by HA breakdown products in cells outside the nervous system is a protein called pleiotrophin. Recent studies indicated that pleiotrophin is a key regulator of the differentiation of myelin-forming cells. Here, we will test if PH20 activity and HA breakdown products influence pleiotrophin expression and activity in nervous system progenitor cells, and whether altering pleiotrophin expression or activity can reverse the effects of HA breakdown products on remyelination. These studies have the potential to reveal a new therapeutic target for the promotion of remyelination in MS.

Project Progress: This pilot project was recently completed. We found that HA, which inhibits progenitor cell proliferation, blocks pleiotrophin expression while hyaluronidase induced pleiotrophin expression. Furthermore, we found that the activity of a downstream mediator of pleiotrophin signaling, the Src family kinase Fyn, is transiently induced by HA. This finding is interesting because Fyn has been implicated in regulating neural progenitor cell expansion and differentiation. In support of a role for this pathway in demyelinating disease, we have observed that pleiotophin is low wherever HA is elevated in demyelinating lesions from Japanese macaques with Japanese macaque encephalomyelitis. These data support a role for the pleiotrophin signaling cascade in HA-mediated remyelination failure. We plan to use these data in a future grant focused on testing ways promote remyelination.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Study of Receptor-Mediated Remyelination Failure

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Myelin surrounds nerve fibers and increases the speed of nerve impulses. Myelin damage occurs in many conditions including multiple sclerosis, leading to nerve cell conduction deficits. The Sherman lab found that the activity of an enzyme, called PH20, promotes remyelination failure. PH20 breaks down a polysaccharide called hyaluronan. Fragments of hyaluronan block the differentiation of myelin-forming cells, called oligodendrocytes, in the brain and spinal cord. A recent study found that hyaluronan fragments activate a protein called P2X7 that is found on the surface of oligodendrocytes. Here, we will test the hypothesis that PH20 blocks remyelination in a P2X7-dependnet manner.

Project Progress: This project, funded by the Private Source supports high school science teachers in laboratories over the course of two summers. This project, now completed, trained a local high school biology teacher through testing the hypothesis that P2X7 signaling was linked to remyelination failure. The teacher learned a number of techniques including primary cell culture, Western blotting and immunocytochemistry. She found that P2X7 is expressed on oligodendrocyte progenitors at all stages of differentiation but did not find definitive evidence that its activity is altered by PH20. However, several technical issues arose during these studies and members of the Excluded by Requester lab are following up on these findings.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: White Matter Damage in Age-Related Cognitive Decline

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

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

Project Progress: We have optimized protocols for the extraction of hyaluronan from aged white matter using archived tissues from old rhesus macaques. We have also now collected tissues from a large cohort of patients and examined the size distribution of hyaluronan in these samples. We are now quantifying hyaluronan in the same samples and examining the relationship between hyaluronan accumulation and progenitor cell maturation. These data will be co-registered with histopathological, biochemical, and magnetic-resonance imaging data.

Funding Sources: NIH/NIA R01 AG031892

Percent P51 Dollars: 0%

Project Title: Prenatal Nicotine and Lung Development: Role of CHRNA5, Addiction and Epigenetics

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: Maternal smoking during pregnancy remains a major cause of perinatal morbidity and causes lifelong decreases in pulmonary function and increased risk of asthma in offspring. Despite significant efforts to reduce maternal smoking through public health campaigns and smoking cessation interventions, approximately 13% of all women self-report smoking during pregnancy and this effects the lifelong respiratory health of over 400,000 infants each year. Nicotine addiction is clearly a driving force in the inability of some women to quit smoking during pregnancy and both GWAS and genotyping studies have identified a common polymorphism (rs16969968) in the α5 nicotinic acetylcholine receptor (nAChR) that is associated with heavier cigarette use and reduced smoking cessation. Remarkably, our preliminary data suggests that this same polymorphism that increases the likelihood of maternal smoking during pregnancy also increases the degree to which maternal smoking during pregnancy adversely affects offspring pulmonary function. Thus, the primary objective of this proposal is to determine the mechanism by which alterations in the α5 nAChR subunit mediate the effects of maternal smoking during pregnancy on lung development and to assess the relative contribution of nicotine addiction versus the direct effects of nicotine on lung. This fundamental question of the role of nicotine addiction versus direct consequences of nicotine on cellular processes is applicable to all smoking related diseases and ultimately must be addressed to prevent and treat smoking related diseases. To decipher between addiction mediated effects and direct end organ mediated effects of perinatal nicotine, we will employ transgenic mouse models combined with both addiction and lung development paradigms. Specifically, we will first use α5 knockout mice to delineate the role of α5 in lung development. Next we will use mice expressing the wild-type α5 subunit and mice with a knockin for the polymorphic α5 subunit to compare the effects of a set dose of nicotine to that of the higher doses of nicotine that are self-administered by mice with the polymorphic α5 subunit. Lastly, we will examine the role of DNA methylation in the regulation of target genes so as to understand the mechanisms by which in utero nicotine induces persistent changes in lung. This goal will be met by performing quantitative CpG methylation analysis by pyrosequencing within the promoter regions of select genes involved in pulmonary structure and function and in nAChR genes in both mouse and human tissues. The objectives and training components of this proposal will be met by learning basic approaches to studying lung development and function in mice and basics of clinical research. The proposed research project will additionally introduce concepts and models of addiction to successfully unravel the mechanism by which nAChR polymorphisms influences lung development within the setting of heightened addiction. This research has great public health significance to potentially identify the molecular mechanisms by which specific genotypes increase the consequences and likelihood of maternal smoking during pregnancy.

Project Progress: Initial analysis of alpha5 knockout mice shows that loss of alpha5 blocks some of the effects of prenatal nicotine exposure on lung development. This supports a direct effect of alpha5 in the lung on lung development. Combined with our human studies on effects of smoking during pregnancy on infant lung function, this finding emphasizes the importance of alpha5 in modulating the effects of maternal smoking during pregnancy on infant development.

Funding Sources: NIH F32HL123246

Percent P51 Dollars: 0%

Project Title: Development of an H2O2-Inactivated Dengue Virus Vaccine

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Progress: We have optimized virus growth and purification parameters and have almost completed cGMP production of the Master and Working virus banks.

Funding Sources: NIH 5R01AI098723

Percent P51 Dollars: 0%

Project Title: Development of a Safe and Effective Vaccine Against West Nile Virus

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

Project Description: The goal of this proposal is to optimize a WNV vaccine and produce clinical-grade vaccine under cGMP conditions for later Phase I clinical trials.

Project Progress: We have completed cGMP vaccine manufacturing and successfully submitted an IND to the FDA with approval to move forward into Phase I clinical trials. The first-in-human trials are expected to begin in February, 2015.

Funding Sources: NIH 5U01AI082196

Percent P51 Dollars: 0%

Project Title: Development of a Yellow Fever Vaccine for Vulnerable Populations

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: In this Phase II proposal, we provide strong preliminary data from our Phase I application demonstrating the antigenicity, immunogenicity, and protective efficacy of a proprietary new vaccine platform that can be used to develop a safer and highly effective Yellow Fever Vaccine.

Project Progress: We have completed optimization of an improved yellow fever vaccine that shows high immunogenicity in mice. Production of cGMP vaccine suitable for Phase I clinical trials is planned for July, 2015.

Funding Sources: NIAID R44 AI079898, Private Source

Percent P51 Dollars: 0%

Project Title: Impact of immune senescence on herpes zoster in a nonhuman primate model

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of California - Riverside

Project Description: The goals of this project are to gain a better understanding of the immune response to VZV thereby identifying key aspects of the immune response that prevent virus reactivation and the onset of herpes zoster. This subcontract will continue the nonhuman primate work at ONPRC.

Project Progress: Animals have been infected with virus and blood/tissue samples have been harvested for further study.

Funding Sources: NIH 5R01AG037042

Percent P51 Dollars: 0%

Project Title: Mechanisms of Orthopoxvirus Host Control and Viral Immune Evasion

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

Project Description: The goal of this proposal is to determine the mechanisms underlying immune evasion strategies of orthopoxviruses.

Project Progress: We recently published a paper with Excluded by Requester Excluded by Requester et al. PLoS Pathog. 2014) demonstrating that the B22R protein of monkeypox and smallpox is responsible for inhibiting antiviral CD4+ and CD8+ T cell responses.

Funding Sources: NIH U19AI109948

Percent P51 Dollars: 0%

Project Title: Nicotine, Nicotinic Receptors and Lung Cancer

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The overwhelming majority of lung cancers are associated with smoking and most lung cancers express nicotinic acetylcholine receptors (nAChR) that are activated by the nicotine in cigarette smoke. The objective of this application is to characterize how the interaction of nicotine with nicotinic acetylcholine receptors (nAChR) expressed by lung cancers stimulates tumor growth with the ultimate objective of developing new therapeutic approaches to lung cancer by blocking this proliferative pathway. The nicotinic receptors are ligand-gated ion channels composed of 5 subunits, either a mixture of alpha and beta subunits or 5 of the same alpha subunit. Binding of a nicotinic agonist such as acetylcholine or nicotine opens the ion channel allowing entry of Na+ or Ca++ into the cell. While the nAChR are best known for their role as neurotransmitter receptors in the CNS, they are also widely expressed in non-neuronal cells. Our laboratory has been a leader in showing that essentially all lung cancers express nAChR and binding of nicotine to the nAChR stimulates lung cancer growth. The real world importance of nicotine as a stimulus for lung cancer growth has recently been confirmed by multiple genome-wide association studies linking polymorphisms in nicotinic receptors to increased risk of lung cancer even when corrected for numbers of cigarettes smoked. Strongest linkage by far has been with polymorphisms in the 15q25.1 nicotinic receptor gene cluster that encodes the alpha3, alpha5 and beta4 nAChR subunits. Critically, the exact role of these nAChR subunits in mediating the ability of nicotine to stimulate cancer growth is unknown. In addition, how the polymorphism of greatest interest, rs16969968 which changes the Asp at residue 398 (a5D398) of the 15 nAChR subunit to Asn (a5N398) affects lung cancer growth is totally unknown. It is also likely that besides the a5D398 to a5N398 mutation, other mutations occur in the 15q25.1 nAChR gene locus that affects lung cancer growth.

Project Progress: We have demonstrated that the alpha5398N mutation makes lung cancer cells less responsive to nicotine. This suggests that the increased lung cancer risk associated with the D398N polymorphism primarily reflects increased smoking and nicotine addiction. Tobacco smoke exposure studies with mice bearing the D398N polymorphism are presently in progress to determine the direct effects of the polymorphism on lung cancer development. New studies have shown potential for compounds that target multiple nAChR subunits at the same time to reduce lung cancer cell growth.

Funding Sources: NIH 5R01CA151601

Percent P51 Dollars: 0%

Project Title: Proprietary Info Novel targets of Proprietary Info injury

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: Inflammation is a major component in the pathogenesis of Proprietary Info Cell signaling pathways prominently involved in the inflammatory cascade are initiated through Proprietary Info Proprietary Info therapeutics Proprietary Info induced by systemic administration of Proprietary Info Proprietary Info Potential deleterious side effects preclude translation. We have found that additional Proprietary Info are also potent targets to induce Proprietary Info reprograms cell signaling during subsequent Proprietary Info and the resultant Proprietary Info Proprietary Info are well tolerated in humans offering rapid translation as Proprietary Info for patients at high risk (e.g. new Proprietary Info). Here we propose to characterize this novel Proprietary Info therapy and demonstrate the efficacy and Proprietary Info We will address the potential mechanisms that underlie Proprietary Info and whether these mechanisms act systemically and/or are located Proprietary Info as human treatments may optimally be directed Proprietary Info

Project Progress: Our work on the development of an apparatus to measure Proprietary Info Proprietary Info has progressed, with modifications made to Proprietary Info and to the feeder re ward system. The apparatus will used to measure the affect of Proprietary Info Proprietary Info

Funding Sources: NIH 5R01NS062381

Percent P51 Dollars: 0%

Project Title: Cognition in Rhesus Macaques in Relation to Age and Endocrine Status

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Description: In men and male rhesus macaques testosterone (T) and dehydroepiandrosterone (DHEA, an adrenal androgen precursor) show characteristic 24-hour patterns in the circulation, and both show significant age-related decreases. Although the exact physiological consequence of these hormonal changes is unclear, both T and DHEA are thought to act as intracrine substrates for estradiol (E2) synthesis in the brain. Therefore, it is plausible that their age-related decline negatively impacts brain function, either directly through androgen receptors and/or indirectly through estrogen receptors. Using the rhesus macaque as a translational animal model, we propose to test the hypothesis that age-related attenuation of circulating T and DHEA levels negatively impacts centrally-mediated physiological processes, including the circadian sleep-wake cycle and cognition. Moreover, we predict that physiological testosterone supplementation, designed to mimic the circulating 24-hour T pattern of young animals, will ameliorate these age-associated disorders.

Project Progress: We have established an androgen supplementation paradigm that accurately reproduces "youthful" circulating levels of 5α-DHT and 17β-estradiol in old males, both in terms of concentration and 24-hour pattern. Proprietary Info

Proprietary Info Our results also demonstrate a significant negative correlation between quality of sleep and cognitive performance, emphasizing the importance of maintaining healthy circadian rhythms in the elderly.

Funding Sources: NIH 5R01AG036670

Percent P51 Dollars: 0%

Project Title: Effects of Steroid Hormones on the Aging Brain

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Proprietary Info

Proprietary Info

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Modulation of Immune senescence by androgen treatment in aged male macaques

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of California, Riverside

Project Description: Aging results in a progressive decline in immune function, which leads to increased morbidity and mortality related to infections. In men, increasing age also results in significant perturbations in the levels of circulating androgens (testosterone and dehydroepiandrosterone (DHEA)), which has been linked to sarcopenia, osteoporosis, cardiovascular disease and diabetes. Since sex steroid levels modulate immune function, it is likely that the age-related decline in androgen levels will also affect immune senescence. To gain a better understanding of the pleiotropic effects of androgen supplementation in aged men we have developed a novel paradigm of androgen supplementation in which testosterone and DHEA are administered to mimic the natural circadian rhythm of these hormones. This approach can restore both testosterone and DHEA levels to "youthful" 24-hour rhythms in aged male rhesus macaques. The overall goal of this project is to use this innovative paradigm to test the hypothesis that *physiological* testosterone and DHEA supplementation, designed to mimic the circulating 24-hour pattern of young animals, will ameliorate major biomarkers of immune senescence and improve T cell responses to vaccination. Specifically, we will be assessing the impact of physiological androgen supplementation on the severity of immune senescence by examining: 1) the frequency of naïve and memory T and B cell subsets; 2) thymic output; 3) plasma levels of key inflammatory cytokines; and inflammatory cytokine production by 4) T cells and 5) innate immune cells. We will then characterize the impact of physiological androgen supplementation on the anti-viral immune response following vaccination with modified vaccinia ankara (MVA) as well as the seasonal influenza vaccine by measuring: 1) kinetics and magnitude of T and B cell proliferation; 2) frequency of responding Tcells; and 3) IgG antibody titer. Finally, we will examine the impact of androgen supplementation on the homeostasis of tissue resident lymphocytes by determining: 1) T and B cell subset distribution in bone marrow,lymph nodes, bronchoalveolar lavage, and gut biopsies; and 2) the cytokine milieu of these tissues.

Project Progress: During the second year of this exploratory study we collected serial blood samples from young, old and old-androgen-treated males to monitor white blood cell changes. In addition, we vaccinated the animals against MVA, as well as the seasonal influenza. Proprietary Info

Proprietary Info

Funding Sources: NIH 1R21AG043896

Percent P51 Dollars: 0%

Project Title: Pacific Northwest Regional Center of Excellence, Nonhuman Primate Core

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of Arizona

Project Description: The Nonhuman Primate (NHP) Core is a multicenter Core structured to provide the Pacific Northwest Regional Center of Excellence (PNWRCE) with resources for purpose-bred animals and unique facilities and specialized investigative and technical expertise for infectious disease research that is best conducted using NHPs. The Core's performance sites include the Oregon and Washington National Primate Research Centers (ONPRC, Beaverton, OR, and WaNPRC, Seattle, WA), and the Proprietary Info Private Source campus, Proprietary Info Nonhuman primates are unique, long-lived species that share many physiologic similarities with humans. These similarities include body composition, maturation, reproduction, metabolism and close genetic relatedness. Of NHPs available for research, Old World monkey species have the closest evolutionary relationship to humans and they are essential surrogates for biomedical research focused on major human diseases that lack suitable alternative animal models. The organization and function of the NHP immune system closely resembles that of humans and their contribution to understanding the complex interrelationships of the different components of the immune system in the defense against infectious agents is particularly notable. Nonhuman primates have long been recognized for their value as comparative models for human vaccine development, efficacy testing and safety evaluation, and for the investigation of fundamental questions in basic immunology. Many of these models have demonstrated merit for pathogenesis research and vaccine development to contain emerging and re-emerging infectious diseases, H5N1 and 1918 influenza (1-3), Ebola and Marburg viruses (4), monkey pox virus (5, 6), West Nile virus (7, 8), Junin virus (9), yellow fever virus and Dengue fever virus (10, 11). Their research value notwithstanding, NHPs are complex, higher order species that require specialized expertise, infrastructure and staff in a research setting.

Project Progress: The Center's nonhuman primate studies were completed during the prior reporting period. No nonhuman primate studies were conducted during the current reporting period.

Funding Sources: NIH U54AI081680

Percent P51 Dollars: 0%

Project Title: An Effector Memory T Cell-Inducing Subunit Vaccine against Malaria

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
U.S. Military Malaria Vaccine Program, Navy Component
Malaria Department, Naval Medical Research Center
U.S. Military Malaria Vaccine Development Branch, LPD, NIAID, NIH

Project Description: The ultimate goal of this project is to develop a sterilizing vaccine against malaria. The specific hypothesis tested in this proposal is that sterilizing immunity against malaria can be achieved by induction of a lasting effector memory T cell (TEM) response targeting the liver stage of Plasmodium parasites. Repeated immunizations with live or irradiated sporozoites are known to protect vaccinated individuals against malaria challenge. Recent evidence suggests that this protection correlated with the presence of frequent pluripotent TEM, suggesting that permanent sterilizing immunity against malaria requires the induction of high levels of long-lived TEM by vaccination. To test this hypothesis, we propose to use recombinant cytomegalovirus (CMV) as a vaccine vector because CMV is the prototypical virus inducing long-lived TEM that do not show signs of T cell exhaustion. This unique capability of CMV vectors was recently applied to induce long-lived TEM against simian immunodeficiency virus, resulting in protection against SIV-challenge that was by far superior to conventional heterologous prime/boost vaccines with respect to efficacy and duration. Since sterilizing protection against Plasmodium knowlesi parasites was only partial and short lived when heterologous prime/boost vaccines were used, we will examine whether CMV-derived vaccine vectors will similarly confer lasting and efficacious immunity against challenge with *Plasmodium knowlesi* (Pk) sporozoites. We propose to generate recombinant RhCMV expressing four Pk antigens previously used for heterologous prime boost vaccination: the circumsporozoite protein (CSP), the sporozoite surface protein 2 or thrombospondin-related adhesion protein (SSP2 or TRAP), the apical merozoite antigen-1 (AMA1) and the C-terminus of the merozoite surface protein 1 (MSP1c). We will inoculate animals with this panel of four recombinant RhCMV/Pk vectors and monitor the development of TEM in blood, lung and liver. To determine whether the RhCMV/Pk4 vaccine is protective we will challenge with *P. knowlesi* sporozoites. Upon completion of this exploratory project, we will thus know whether a TEM-inducing vaccine can improve the level and duration of sterilizing immunity induced by subunit vaccines against malaria parasites.

Project Progress: We immunized eight animals with four RhCMV vectors lacking the Rh187-Rh189 gene region and each expressing one of the four Pk antigens. We demonstrated that each of the animals developed T cell responses to each of the four Pk antigens. Animals were challenged with 100 live sporozoites and the development of blood parasitemia was recorded. Compared to the non-vaccinated, CMV-positive control cohort of eight animals the vaccinated group demonstrated a delay of blood parasitemia with one animal being sterile. We concluded that the vaccine reduced the pre-erythrocytic parasite burden of P. knowlesi by about 50% but had no effect once blood stages developed.

Funding Sources: NIH 1R21AI103498

Percent P51 Dollars: 0%

Project Title: Evaluation of Immunogenicity and Protection Conferred by CMV Vaccine Vectors against Plasmodium knowlesi Malaria in Rhesus Monkeys

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The long-term goal of the research (Cooperative Work) conducted under this contract is to develop vaccines to prevent malaria in deployed U.S. military forces, non-military travelers and residents of malaria endemic areas. The short-term goal is to understand whether recombinant cytomegalovirus (CMV) vectors encoding malaria proteins induce an immune response that is as protective as or more protective than our current best recombinant viral regimens, such as DNA/pox. Under MIDRP proposal F0351_13_NM, the Government plans to use the simian malaria *Plasmodium knowlesi* in the rhesus macaque (*Macaca mulatta*) as the model for comparing the level of protection afforded by CMV with that afforded historically by DNA/pox. NMRC's interest in the CMV vector is due to the high concentration of liver-resident CD8+ effector T cells induced by this vector. We believe that strong CD8+ T cell responses are required to kill developing malaria parasites in the liver, and that CMV may be superior to DNA/Ad in generating these cells.

Project Progress: We immunized eight animals with four RhCMV vectors each expressing one of the four Pk antigens (CSP, SSP2, AMA-1, MSP1). We demonstrated that each of the animals developed T cell responses to each of the four Pk antigens. Animals were challenged with 100 live sporozoites and the development of blood parasitemia was recorded. Compared to a non-vaccinated, CMV-positive control cohort of eight animals the vaccinated group demonstrated a delay of blood parasitemia. We conclude that the vaccine reduced the pre-erythrocytic parasite burden of P. knowlesi by about 50% but had no effect once blood stages developed.

Funding Sources: Naval Medical Logistics Command N62645-13-C-4021

Percent P51 Dollars: 0%

Project Title: Evasion of Antigen Presentation by Rhesus Cytomegalovirus

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Description: The ultimate goal of our research is to understand the balance between immune stimulation and immune evasion of cytomegalovirus (CMV) and to use this understanding for the development of new treatments and vaccines. One of the major challenges for CMV vaccine development is the fact that CMV establishes secondary persistent infections in CMV-immune individuals despite the presence of significant antibody and T cell responses. However, this unique ability also represents an opportunity for the design of CMV-based vaccine vectors that can be used repeatedly despite pre-existing immunity to the vector. We recently demonstrated that super-infection by CMV is enabled by the viral US2-11 glycoproteins - US2, US3, US6 and US11- all of which inhibit antigen presentation by major histocompatibility complex class I (MHC-I) to CD8+ T cells. These observations suggest that CMV lacking the US2-11 region can be used to monitor whether a CMV-specific CD8+ T cell response is "protective", i.e., able to control primary viremia as observed for sero-positive individuals. A goal of this proposal is therefore to define the CD8+ T cell response required for protection against US2-11-deleted virus and to correlate these results with protection against primary infection with wildtype virus. A further goal is to determine the contribution of each individual immunevasin encoded in the US2-11 region in promoting super-infection.

Project Progress: We demonstrated that Rh189, the RhCMV homologue of HCMV US11, inhibits the induction of canonical T cells, i.e., T cells immunodominant in SIV-infected animals or induced by other vector systems (Science, 2013). To determine whether HCMV US11 performs the same function we replaced Rh189 with US11 in RhCMV/SIVgag vectors and demonstrated expression of the HCMV protein. By taking advantage of our recent observation that HCMV is capable of inducing a T cell response to heterologous antigens we also generated an HCMV vector expressing the SIVgag, but lacking US11. Both of these vectors will be examined in MamuA01-positive animals for their ability to elicit T cell responses to canonical epitopes.

Excluded by Requester

Funding Sources: NIH 5R01AI059457

Percent P51 Dollars: 0%

Project Title: Immunological Characterization of a Novel HCMV Vaccine Platform

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester VGTI, OHSU

Project Description:

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

Project Progress: We inoculated two specific pathogen free male rhesus macaques with 10^6 PFU of BAC-derived VGTI-1. Immunological monitoring is ongoing.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Mechanisms of Orthopoxvirus Host Control and Viral Immune Evasion: Project 3: T Cell Control by Cowpoxvirus

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: The central goals of this project are to characterize novel and unique molecular mechanisms by which Cowpox virus (CPXV) inhibits T cell stimulation and the relevance of these evasion mechanisms for viral virulence and the development of anti-viral immunity. This work is expected to have implications for our understanding of the immune control of virulent orthopoxviruses (OPXV) and lead to the discovery of novel means to regulate unwanted T cell responses. In preliminary experiments we show that CPXV encodes two T cell evasion genes that are absent in VACV and operate independently of antigen presentation to directly inactivate T cells: CPXV14 prevents activation of naïve T cells, particularly CD8+ T cells, whereas CPXV219 inactivates effector and memory T cells (both CD4+ and CD8+ in human and CD4+ in mouse). Importantly, deletion of CPXV14 dramatically attenuates CPXV in mice, whereas deletion of MPXV197 (the monkeypox virus homologue of CPXV219) strongly reduces MPXV virulence in rhesus macaques. Based on these results we hypothesize that T cells are reduced in their capacity to control CPXV in vivo due to multilayered evasion strategies that include both inhibition of antigen presentation and direct inactivation of T cells. In Specific Aim 1, we will examine the virulence of CPXV lacking individual T cell inhibitory ORFs or combinations thereof in mice. Together with Project 1, we will also determine the impact of T cell evasion on the induction of poxvirus-specific T cell and antibody responses during infection. We anticipate that CPXV lacking T cell evasion genes will be attenuated due to increased T cell control, and such deletion mutants will induce increased T cell and antibody responses. In Specific Aim 2, we will test the hypothesis that CPXV219 engages an inhibitory receptor on T cells, a process that counteracts TCR-dependent signal transduction. We will determine at which point the TCR-dependent signal transduction cascade is blocked and identify the target on T cells. CPXV219 belongs to the B22R family of large transmembrane glycoproteins encoded by several OPXV, including VARV, but the function of this protein family is currently unknown. In Specific Aim 3, we will elucidate how CPXV14 as well as related SECRET-domain containing poxviral proteins prevent activation of naïve murine T cells by anti-CD3 and anti-CD28. Together with Project 2 we will examine the role of Fc-receptors or FcR-like proteins in T cell inactivation. We will identify the protein responsible for CPXV14 inhibition and we will further characterize the molecular mechanism by which human and mouse T cell activation is blocked.

Project Progress: We recently published that ORF197, the monkeypox homologue of CPXV219, profoundly impacts viral virulence in non-human primates (Excluded by Requester 2014). While wildtype MPXV was highly virulent in monkeys, as evident by prolonged fever, high levels of viremia, numerous skin lesions and 50% mortality, MPXV lacking MPXV197 caused only a brief fever episode and was severely deficient in dissemination as evident from the lack of cutaneous lesions and lack of mortality. These results strongly support our hypothesis that T cell evasion is critical for poxviral virulence. We are in the process of studying the impact of CPXV14 on viral virulence in mice using a newly derived CPXV14 mutant since the original mutant also carried a mutation in CPXV2017. We are also in the process of generating an independent CPXV14 mutant using the CPXV BAC. Preliminary data suggest that, compared to WT virus, CPXV14-deleted virus is attenuated in vivo.

Funding Sources: Washington University/NIH U19 AI109948-01

Percent P51 Dollars: 0%

Project Title: Safety and Immunogenicity of Single-Cycle HCMV in Non-Human Primates

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: The ultimate goal of this project is to design and evaluate the engineered safety features built into a vaccine against human cytomegalovirus (HCMV). HCMV pathogenesis is both the reason for developing an effective vaccine and a serious safety concern to be addressed in the design of CMV vectors. HCMV can cause serious disease complications in immunosuppressed individuals, particularly solid organ and bone marrow transplant recipients, and this virus is the leading infectious cause of congenital birth defects. Recently, single-cycle CMVs were shown to induce long-term immune responses comparable to wild-type (WT) CMV in mice (Excluded by Requester Virol. 2010; Excluded by Requester Plos Pathogens 2011) and monkeys (our unpublished observations). This suggests that a rationally designed single- cycle HCMV vaccine may be effective against disease caused by this virus. Particularly, this attenuated vaccine should prevent congenital infection and disease in transplant patients, without compromising the immunogenicity needed for protection. The rational design aspect of attenuation is in stark contrast to previous approaches that used traditional methods of tissue-culture adaptation. The resulting CMV-vaccine (strain Towne) was unable to generate the level of immune response observed in naturally infected individuals, and duration of the response was relatively short-lived. In contrast, preliminary data in rhesus macaques (RM) using rhesus CMV (RhCMV) demonstrates that spread-deficient and single- cycle RhCMV can induce long-term immunity.

This project takes advantage of our preliminary observation that clinical strains of HCMV expressing heterologous antigens (SIV) were capable of inducing a lasting T cell response in RM. Given the known species-specificity of CMV this result was quite unexpected. While HCMV-infection of RM will most likely not be a suitable model for HCMV pathogenesis, it will allow us to address some fundamental questions regarding the translatability of results obtained in the RhCMV model to HCMV. Specifically, we can address the question whether single-cycle HCMV is capable of inducing lasting T cell responses as observed for mouse and rhesus CMV and, if so, whether the T cell and antibody response induced by single- cycle viruses prevents super-infection by virus lacking MHC-I inhibitory genes.

Monitoring HCMV-infection of RM is facilitated by the insertion of immunological markers. In this project we will use antigens derived from HSV2. These vectors, generated as part of the HSV2 project funded by Takeda, will dovetail to provide in vivo data for these constructs.

Upon successful completion of this program we will establish whether single-cycle HCMV can recapitulate the immune response observed with WT HCMV, and clear the path to clinical testing of single-cycle HCMV vectors to prevent HCMV disease.

Project Progress: We inoculation two specific pathogen free male rhesus macaques with 10^6 PFU of single cycle VGTI-1 expressing a fusion protein of UL79 and the FKBP-degradation domain in which the open reading frame UL78 was replaced with a fragment of the herpes simplex virus 2 ICP4 gene. Immunological monitoring is ongoing.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Reducing Latent Viral Reservoirs in Infant Macaques

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: Cocktails of antiretroviral (ART) drugs have been successful in reducing viremia to undetectable levels in HIV+ adult subjects, but the drugs are unable to eliminate latent virus in certain cellular and tissue compartments. While ART is the standard of care for HIV+ mothers and their infants who are exposed to infection risk before, during, and after birth, the field has not discovered therapy that could reduce or eliminate established latent viral reservoirs. The objective of the proposed project is to adapt an established nonhuman primate model of persistent pathogenic SHIV infection in newborn rhesus macaques to study the effects of very early therapy using potent human neutralizing monoclonals (NmAbs). Newborn macaques infected orally with HIVSF162P3 develop widely dispersed and rapidly diverging viral quasispecies in blood and tissues. We have shown that newborn macaques passively treated with neutralizing IgG were protected from disease and death. Thus NAbs present during acute infection altered the dynamics of infection and reduced viral spread and size of the reservoir. The project will define the therapeutic role that potent NmAbs play in (i) controlling virus load,
(ii) affecting the size of the integrated viral reservoir, and (iii) influencing the development of effective adaptive immune responses.

Project Progress: We have tested a cocktail of two potent human NmAbs in the newborn model. At two different doses of antibodies administered subcutaneously at 24 hours after oral viral exposure, there is no evidence for viral replication in blood. The tissue virus quantification, still in progress, supports the data in the blood samples and suggests that the infection was aborted or fully controlled by this antibody treatment.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Epitope-Targeted Vaccines for HIV-1 Prevention

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

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

Project Progress: We have received a number of V1V2-specific human monoclonal antibodies from Excluded by Requester and have characterized these for neutralization against HIV-1 and SHIV isolates. We are discussing the possibility of performing passive transfer protection experiments prior to performing vaccine studies. These in vivo studies will be initiated early in 2015.

Funding Sources: rivate Source

Percent P51 Dollars: 0%

Project Title: Oral, Replicating Ad4-HIV Vaccine Development & Evaluation in NHP Challenge Model

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Request er | Privat eSource

Project Description: Development of a vaccine to prevent, or reduce the rate of, HIV infections remains a high priority despite recent setbacks in the field. The lessons from failed and successful experimental programs indicate the need to apply new approaches to HIV vaccine design with the goal of inducing immune responses that are the appropriate type, quality, magnitude and active in the appropriate sites in the body. A promising approach is the use of the Adenovirus serotype 4 (Ad4) as a vaccine delivery vehicle. The Ad4 virus is a component in the US Military adenovirus vaccine which was formulated for administration in an oral dosage form. Oral delivery should be advantageous for HIV vaccines because this route of administration is more likely to induce mucosal immune responses than parenteral injection and would target the gut mucosal tissues in particular. The Ad4 vaccine vector is replication-competent in humans which should drive the induction and expansion of immune responses that are different, in terms of magnitude and effector functions, than those induced by non- replicating vectors. In Y1, multiple Ad4 vectors will be engineered to express unique antigens including: 1) HIV-1 Env clade C protein for the purpose of inducing antibody responses broadly effective against a variety of HIV strains; 2) GBV-C E2 glycoprotein, which may induce antibodies that block HIV-1 cellular attachment; and 3) Gag protein, which may induce T cell responses which promote killing of HIV-1 virus infected cells. Since human adenoviruses such as Ad4 do not replicate in non-human animals, including NHPs, we will also construct analogous replicating Simian adenovirus (SAd7) vectors to allow a direct comparison of the efficacy of Ad4 (non-replicating vector in NHPs) with an analogous replicating vector, SAd7. All vectors will be assessed for immunogenicity in small animals (mice /rabbits) before proceeding to NHP studies in Y2. Once immunogenicity is confirmed in NHPs, we will evaluate their efficacy in an NHP R5 SHIV clade C challenge study. Both antibody (neutralizing and ADCVI) and T cell immune responses (IFN-) will be determined. Completion of this SBIR program will provide sufficient data to determine the utility of this Ad4 vector system for inducing effective antibody and T cell responses and potentially could yield an experimental vaccine suitable for clinical development.

Project Progress: Rhesus macaques immunized with the adenovirus vectors and recombinant proteins have generated strong T cell responses and antibodies. These animals will be immunized once more and challenged this year to determine the effectiveness of these vaccines in protection from infection by mucosal exposure.

Funding Sources Privat eSource

Percent P51 Dollars: 0%

Project Title: Passive Transfer Studies in Rhesus Macaques to Investigate the Efficacy of Protection of Anti-V2 HIV-1 mAb 697D

Core Scientists Associated with the Project:
Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester — Private Source

Project Description:
Traditionally, PBMC based 90% neutralization titers have been used for estimating *in vivo* protection in the macaque mucosal challenge model. While neutralization has been associated with antibodies shown to protect in this setting, there is evidence that yet, undefined mechanisms may lead to protection against infection. The immune correlates of the human HIV vaccine trail in Thailand (RV144) revealed a reduction in infection risk associated with IgG antibodies binding to scaffolded HIV1 V1V2, but avidity, ADCC, or neutralizing antibodies did not significantly predict HIV1 infection rate. In order to determine if a V2specific antibody can protect against SHIV repeated challenge in the absence of neutralizing capability, we will conduct a passive transfer experiment in twelve rhesus macaques. If protection efficacy is achieved, this study will set the stage for future studies to explore undetermined mechanisms that may contribute to protection. The mAb 697D is a valid candidate for testing the protective efficacy of V2 antibodies because it is highly crossreactive with many trains of HIV1 and reacts with gp70V1V2 scaffold which was the only significant inverse correlate of risk identified in RV144. To choose a challenge virus, we will test available SHIVs for neutralization *in vitro* by mAb 697D before starting the *in vivo* phase of the study. A primatized version of mAb 697D will be engineered and produced to reduce the risk of antihuman antibody responses in treated macaques. We will first examine the pharmacokinetics (PK) of the primatized mAb 697D in three macaques to determine the best interval for mAb dosing and to confirm the systemic transport of the antibody. Once the *in vivo* halflife of mAb 697D is established, we will begin the passive transfer study to evaluate the protection efficacy of mAb 697D compared to an isotype control antibody or untreated controls. A dose of 50 mg/kg of mAb 697D will be given subcutaneously before the first SHIV exposure and continuing at intervals to be determined from the PK study. Based on animal titration data of the SHIV stock chosen as the challenge virus, we will use a dilution of virus that is expected to infect all control animals within 46 inoculations delivered intrarectally (*i.r.*). Repeated *i.r.* exposures will be applied twice per week. Regular blood draws will monitor for plasma virus and passively transferred antibody concentrations. After a total of 12 challenges, we will assess whether mAb 697D provides protective benefits compared to controls.

Project Progress: We have received a number of V1V2-specific human monoclonal antibodies from Excluded by Requester and Excluded by [illegible] and have characterized these for neutralization against HIV-1 and SHIV isolates. The in vivo work is in the planning stages with the collaborators, and will be completed this year. We are in the process of producing and purifying approximately half a gram of the human mAb 830A for these experiments.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Programming HIV Immunity for Broadly Neutralizing Antibodies by Vaccination

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source
Oregon Health & Science University

Private Source
Oregon Health & Science University

Private Source

Project Description: This program project brings together a dynamic team of experienced HIV investigators who bring individual and collective strengths to design and test novel vaccines to elicit neutralizing antibodies (NAbs). The overall goal is to design novel vaccines based on env genes from HIV-infected subjects who develop broad NAbs (bNAbs) in an accelerated fashion. In Project 1, we will identify multiple HIV-1 infected, ART-naive subjects who developed both autologous and bNAbs within the first 2-3 years of infection and characterize the epitope-specificities of these bNAbs. With Project 3, we will define changes that accrue to the subjects' cloned quasispecies Envs from initial infection through broadening. We hypothesize that specific diversification of the quasispecies drives maturation of bNAbs in vivo, by presenting new epitopes in escape variants, or by focusing the response on more conserved epitopes. In Project 2, we will characterize the temporal development and maintenance of functional T-helper (Th) responses that allow B cells to respond to the changes in the Env proteins produced by the patient's quasispecies variants in Project 1. We hypothesize that the initial ability to generate bNAbs correlates with a relatively intact CD4+ Th response early in infection, ultimately lost with continued viremia. We will adapt a novel technology to sort Env-specific B cells from these subjects and characterize NAbs that neutralize diverse isolates, to refine our choice of Env immunogens. In Project 3, we will work with Project 1 to clone env gp160 variants to define the autologous NAbs and the pathways of env escape; vaccines will be based on these natural longitudinal env variants that arise during broadening. Variants will be used singly and in mixtures to "program" humoral immunity in vaccinated rabbits and macaques. We hypothesize that these vaccines will elicit broader NAbs than other vaccines to date.

Project Progress: Based on studies in rabbits, we have identified Envs to use as DNA and protein vaccines that are very effective at generating autologous NAbs and bNAbs in rhesus macaques. These data are linked to mapping data in human sera obtained by [redacted] laboratory and to human NmAbs cloned from these individuals in [redacted] laboratory. We plan to perform a vaccine challenge experiment in rhesus macaques to test the effectiveness of the induced antibodies in protection from SHIV challenge.

Excluded by Requester
Excluded by Requester

Funding Sources: NIH P01AI078064

Percent P51 Dollars: 0%

Project Title: Reducing Latent Viral Reservoirs in Infant Macaques

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: Recent successes in achieving a functional cure for HIV infection are redirecting the field to examine therapeutic regimens to eliminate latent virus reservoirs. Cocktails of antiretroviral (ART) drugs have been successful in reducing viremia to undetectable levels in HIV+ adult subjects that have access to the therapy. Yet, the drugs are unable to eliminate latent virus in certain cellular and tissue compartments. While ART is the standard of care for HIV+ mothers and their infants who are exposed to infection risk before, during, and after birth, the field has not addressed an extension of ART therapy that could abate virus expansion and eliminate established latent viral reservoirs. A proven nonhuman primate model for perinatal infection that examines new therapeutic regimens that can be instituted at or immediately following infection is needed to address whether it is possible to eradicate HIV. The objective of the proposed project is to adapt an established model of persistent pathogenic SHIV infection in newborn rhesus macaques to study the effects of very early therapies with or without ART. Understanding the full contribution of antibodies, including neutralizing antibodies (NAbs), in HIV-1 infection remains one of the highest research priorities. Passively transferred NAbs can provide sterilizing immunity in nonhuman primate models and when present early in infection can change the course of SIV or SHIV infection stabilizing the adaptive immune response to prevent viral divergence. Studies designed to define how well antibodies can affect the viral reservoir are the next steps in the field. The central hypothesis of this research proposal is that therapeutic treatment with potent neutralizing human monoclonal antibodies (NmAbs) will result in highly controlled or undetectable viral reservoirs in babies born to HIV-infected mothers. Newborn rhesus macaques when infected orally with SHIV-SF162P3 develop widely dispersed and rapidly diverging viral quasispecies in blood and tissues within the first few days to weeks of infection resulting in high and persistent viremia. However, in newborn macaques that receive passive treatment with neutralizing IgG, disease and death is prevented demonstrating that NAbs present during acute infection can alter the dynamics of infection and reduce viral spread and establishment of the reservoir. Once the timing and characterization of latent viral pools are characterized, the project will define the roles that NmAbs play in (i) controlling virus load, (ii) affecting the size of the integrated viral reservoir, and (iii) influencing the development of effective adaptive immune responses. The project will also examine whether NmAb cocktails that are effective when used alone can further augment the ability of ART resulting in more potent and durable reduction in latency. The contribution of the proposed research is expected to define the advantage of passively transferred neutralizing antibodies as therapeutics in a perinatal setting either alone or in concert with ART.

Project Progress: We have initiated these studies using a low dose cocktail of two powerful human NmAbs given subcutaneously 24 hours after oral virus exposure. This NmAb cocktail was very effective in preventing detectable infection, and we are currently testing whether CD8+ T cell depletion can help to show whether any latent virus is able to replicate. We will expand these studies in the coming year to test additional variables to optimize this treatment and to plan for combination drug plus antibody therapy.

Funding Sources: NIH R01HD080459

Percent P51 Dollars: 0%

Project Title: Targeting Neutralizing Epitopes in the MPER of HIV Env

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester | Private Source

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

Project Progress: Excluded by Requester laboratory is scheduled to perform in vivo and in vitro work in the second year of this grant. To date, we have participated in teleconferences with the PI and Co-investigators and have been involved in the planning for the work to start this year.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Immunogenicity of RhCMV Vectored Conserved SIV Vaccine

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: There are two major obstacles to an effective protective HIV vaccine based on stimulating CD8 T cell immunity. The first is the variability of the virus and the second is the poor quality of most vaccine-induced T cell responses. The first obstacle is being overcome by development of immunogenic vaccine constructs that focus the CD8 T cell responses only on the most conserved regions of the virus. The CHAVI-ID designed second generation HIVconsv mosaic vaccine should achieve this.

The second obstacle was problematic because no CD8 T cell-inducing vaccine was fully protective. Recently Excluded by Requester has shown that a recombinant CMV vectored vaccine could enable 50% of rhesus macaques to completely clear SIV after challenge with a homologous virus.

Here we propose a collaboration between the Excluded by Requester laboratories with Excluded by Requester who is part of the extended Excluded by Requester laboratory, funded through a supplement to CHAVI-ID, to combine these two technologies and test the immunogenicity of a rhesus CMV-vectored SIV conserved region immunogen in rhesus macaques. An SIV version of the conserved region vaccine construct has been made and will be inserted into the 68-1-RhCMV vaccine strain. Four SIV negative rhesus macaques will be immunized with this vaccine and the T cell responses compared to those in four SIV negative rhesus macaques that will be immunized with the same immunogen delivered by a combination of adenovirus prime and a pox virus boost (Chimpanzee adenovirus OX1 and MVA, respectively). The latter is a 'conventional' vaccine that is known to stimulate strong T cell responses in macaques. The immune responses stimulated by the two vaccines will be compared in detail as will the ability of the CD8 T cells to inhibit SIV replication in vitro.

The experiments will provide enough immunogenicity data to enable the investigators to decide whether to follow this preliminary study with a SIV challenge study and whether the CMV delivery approach should be combined with the conserved immunogen approach in humans to protect against HIV-1.

Project Progress: We are currently in the process of constructing the RhCMV vectors to be used in this study. Thus far, we have generated PCR products to SIVcons239 and SIVconsE660 gag/nef consensus region flanked by NheI and BamHI restriction sites. These products were then cloned into our pOri recombination plasmid. The vectors have been sequenced, confirming proper gene insertion and expression was confirmed by transfection into 293 cells and western blotting for the V5 tag. The plasmids are currently being used for BAC recombination and final virus construction.

Funding Sources: Duke University/NIH 5 UM1 AI100645

Percent P51 Dollars: 0%

Project Title: HIV Envelope-based Vaccines from Superinfection to Elicit Neutralizing Antibodies

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

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

Project Progress: We have completed the immunogenicity study for this project in rhesus macaques and are currently conducting analysis of the data. Twelve macaques, in two groups of six, were co-immunized with DNA and soluble protein over a study period of 25 weeks using Env sequences derived from a superinfected individual that had developed a broadly neutralizing antibody response during infection. Early results indicate that the Env vaccines induced HIV-1 neutralizing antibodies in macaques that will be characterized and evaluated for strength and potency against a panel of test viruses.

Funding Sources: NIH 1R21AI104392

Percent P51 Dollars: 0%

Project Title: Development of HIV-1 Vaccines Targeting Broadly Neutralizing Epitopes

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: The objective of this study is to develop HIV-1 vaccines targeting broadly neutralizing epitopes. Broadly neutralizing antibodies (bNAb) have been shown to be able to block infection in HIV-1 infection models; as such the development of such antibodies is believed to be a vital component of any HIV-1 vaccine strategy. These bNAbs target conserved regions of HIV-1 envelope (Env), which allow for their breadth of reactivity. The elicitation of antibodies targeting these conserved regions through vaccination, however, has proven to be difficult. Currently there are no vaccine constructs that are able to effectively elicit neutralizing antibodies to these broadly neutralizing epitopes. The first aim of this project is to develop E2-based vaccines targeting the broadly neutralizing epitopes of the HIV-1 envelope. To complete this aim the Env regions of MPER and V1V2 will be computationally modeled onto the surface of the E2 scaffold protein. This will be done to ensure that the proper conformation is presented on the surface of the vaccine particle. Once the modeling has been completed, wild-type SF162 MPER and V1V2 as well as E2 will be modified as required to match the model antigens. Completed Env-E2 constructs will be produced and purified from mammalian cells. The constructs will be tested by Western Blot, Native PAGE, competition assay, as well as by immunoprecipitation to ensure that the V1V2 and MPER regions are presented properly on the purified Env-E2 particles. Aim 2 of this project is to determine the immunogenicity and breadth of neutralizing antibodies generated following vaccination with Env-E2 constructs. To test this aim rabbits will be vaccinated with the Env-E2 vaccines delivering a total of 4 vaccinations given at 6 week intervals. The elicitation of antibody responses will be measured by ELISA to gp120, gp41, gp140, and the Env peptide set. Additionally, neutralization will be measured by TZM-bl neutralization assay to SF162, a panel of tier 1 and 2 pseudoviruses as well as HIV-2/HIV-1 (MPER and V1V2) chimera viruses. The overall evaluation of the elicited immune responses will determine the strength of antibody response generated by the vaccines as well as to determine the region(s) of Env targeted by these responses. If this project is successful it will greatly advance the field of HIV-1 vaccine development by providing a neutralizing antibody component to an overall HIV-1 vaccine strategy.

Project Progress: MPER has been computationally modeled onto the surface of the E2 particle. Work is currently underway to generate and clone a restricted MPER epitope.

Funding Sources: NIH F32AI106489

Percent P51 Dollars: 0%

Project Title: DARE: Delaney AIDS Research Enterprise to Find a Cure

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
University of California, San Francisco

Project Description: The failure to cure HIV infection is believed to result from low-level viral production/ replication, the presence of latent replication-competent provirus in resting CD4+ T cells and T cell dysfunction stemming from persistent immune activation. Current antiretroviral therapies (ART) cannot eradicate the reservoir of long-lived latently infected cells or reverse immune dysregulation. The goal of this project is to determine whether SIV-specific immune responses elicited by RhCMV/SIV vector vaccination results in progressive reduction in (or clearance of) SIV infection, including both viral production and cellular viral reservoirs, in rhesus macaques (RM) on ART over time, and/or result in significant protection against viral rebound after ART cessation.

Project Progress: We intravenously infected 18 RM with 2 focus forming units of SIVmac239. Starting at day 42 post-SIV challenge, ART was initiated consisting of a combination of Tenofovir (20mg/kg), Emtricitabine (50mg/kg) and Dolutegravir (2.5mg/kg) administered subcutaneously on a daily basis. At 34 weeks post-challenge, RMs were randomized into 2 groups and received two rounds of RhCMV/SIV vectors (gag, rev/nef/tat, env, pol-1 [5' of pol] and pol-2 [3' half of pol]) (n=12) or identical doses of RhCMV/empty vectors (n=6). Approximately 1 year post-RhCMV/SIV vector vaccination, we plan to discontinue therapy and determine the rate and extent of viral recrudescence in each group, and any immunologic correlates of viral control.

Funding Sources: NIH U19AI096109

Percent P51 Dollars: 0%

Project Title: Impact of Proprietary Info on SIV Persistence in Antiretroviral-Treated SIV-Infected Macaques

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Private Source

Project Description: The primary objective of this Administrative Supplement is to characterize the effects of Proprietary Info on mononuclear cell depletion and recovery in blood and tissue, and to determine whether results in reduction in (or clearance of) long-lived latently infected T-cells in SIV-infected nonhuman primates on suppressive antiretroviral therapy.

Project Progress: The study has been delayed due to slow contract negotiations between OHSU and the pharmaceutical companies that will be supplying the reagents for the study. We have just recently obtained agreements with Proprietary Info and Proprietary Info W are still working on obtaining a material transfer agreement (MTA) Proprietary Info Healthcare for use of their drug Proprietary Info The study will begin as soon as the necessary MTAs are in place.

Funding Sources: University of California, San Francisco/NIH 5U19 AI096109

Percent P51 Dollars: 0%

Project Title: An Investigative Intravenous Pharmacodynamic Study in the Rhesus Monkey to Evaluate Various OX40 Agonists

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Oregon Health & Science University

Project Description: OX40 (CD134) is a member of the tumor necrosis factor (TNF) receptor family of molecules expressed primarily on activated CD4+ and CD8+ T cells. The ligand for OX40 (OX40L, CD252) belongs to the TNF superfamily, and is expressed on professional antigen-presenting cells (APC) such as mature dendritic cells, activated B cells and macrophages. The interaction between OX40 and OX40L provides an important co-stimulatory signal to activated T cells, leading to the expansion and survival of antigen-specific activated T cells. Therefore, it has been an attractive target to modulate immune responses, particularly for tumor immune therapy. The primary goal of this study is to evaluate proliferation of peripheral blood T cells (immunostained for intracellular ki-67) by flow cytometry following dosing with various OX40 agonists that MedImmune manufactured. The secondary goals of this study are to evaluate the pharmacokinetics of the various OX40 agonists and to explore additional biomarkers of pharmacodynamic (PD) activity.

MEDI6383 is a human OX40 ligand fusion protein currently in clinical development for the treatment of advanced solid malignancies. In vitro, this OX40 agonist binds and activates the human OX40 receptor to potently induce activation and proliferation of OX40-expressing human T cells. Given that MEDI6383 binds and signals through non-human primate OX40 with similar potency as human OX40, we hypothesized that the fusion protein would mediate T cell activation in vivo in a non-human primate model.

Project Progress: Peripheral CD4 and CD8 memory T cell activation and proliferation were observed after administration of MEDI6383, and differed quantitatively and qualitatively from that following treatment with the mouse anti-human OX40 monoclonal antibody. Likewise, MEDI6383 also induced the proliferation of peripheral B cells, suggesting an effect on T cell-to-B cell crosstalk in vivo. Other pharmacodynamic changes were also observed with OX40 agonism.

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: Consortium for AIDS Vaccine Research in Nonhuman Primates-- Project 2: CMV Vectors and Early Control of Mucosal SIV Challenge / Core F1: Nonhuman Primate Core

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

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

Project Description: We have demonstrated that CMV/SIV vectors can 1) re-infect CMV+ rhesus macaques (RM), 2) during re-infection, elicit potent and persistent SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory" (TEM) bias, and 3) completely protect ~50% of vaccinated RM from progressive infection after limiting dose rectal challenge with the highly pathogenic SIVmac239 virus. The protection manifested in these RM is distinct from previous vaccines in its abruptness and extent, with protected RM exhibiting a viral burst in plasma of varying size upon initial infection, followed by immediate control to undetectable levels. Although occasional viral blips in plasma are observed in protected RM, these decline with time, and after 1 year, protection is unaffected by CD8+ or CD4+ cell depletion, and extensive tissue analysis with ultrasensitive nested PCR has shown only rare detection of ~ single copy SIV nucleic acid and no viable SIV. Protection correlates with the total SIV-specific CD8+ TEM generated during the vaccine phase, and occurs without an anamnestic response. These data indicate a novel pattern of protection consistent with very early control, likely taking place at the site of viral entry and/or early sites of viral replication and amplification, and involving tissue-resident CD8+ TEM. Thus, CMV vectors and the "TEM" vaccine concept offer a new and powerful approach to HIV/AIDS vaccine development. In this project, our major goals are to delineate the mechanisms responsible for this unique protection, and determine the quantitative and/or qualitative determinants of protection vs. non-protection. First (S.A. 1), in collaboration with Project 1, we will use a serial necropsy approach to define the spatiotemporal progression of SIV infection after mucosal challenge of unvaccinated RM, both the trajectory of viral infection from the portal of entry to systemic infection, and the development of the anti-SIV immune response. Then (S.A. 2), with this baseline established, we will determine when and where the high frequency, tissue-based SIV-specific T cell responses elicited by RhCMV/SIV vectors intercept infection after mucosal challenge, delineate the function of these cells at this intercept, and determine the functional requirements for stringent viral control -- in comparison to responses elicited by replication-deficient adenovirus and poxvirus vectors (Project 1) and live attenuated SIV vaccines (Project 3). Finally (S.A. 3), we will determine the extent of latent and/or active infection in short-term vs. long-term RhCMV/SIV vector protected RM and the activity of SIV-specific T cells in these RM, so as to determine the mechanism of long-term aviremic control, and to explore the possibility of eventual functional clearance of the infection.

Project Progress: The major progress of this project is the demonstration that monkeys protected from progressive SIV infection by RhCMV/SIV vectors are in fact initially infected with SIV after challenge, that this initial infection spreads to distant sites via both lymphatic and hematogenous routes, but that, over time, the infection is progressive cleared such that by 18 months post challenge, the animals are free of SIV infection by multiple stringent criteria. Current efforts to determine the correlates of this protection have indicated that MHC SIV-specific E-restricted CD8+ T cell response frequencies are slightly higher in the tissues of protected animals vs. non-protected monkeys in the first few weeks post infection, but despite this, CD8+ cell depletion in the first 2-3 of protection does not abrogate protection. Our current plan is to initiate CD8+ T cell depletion prior to challenge to resolve this issue.

Funding Sources: NIH U19AI095985

Percent P51 Dollars: 0%

Project Title: DARE: Delaney AIDS Research Enterprise to Find a Cure

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

University of California, San Francisco
Oregon Health & Science University
University of California, San Francisco
Oregon Health & Science University

Private Source

Project Description: The failure to cure HIV infection is believed to result from low-level viral production/replication, the presence of latent replication-competent provirus in resting CD4+ T cells and T-cell dysfunction stemming from persistent immune activation. Current antiretroviral therapies (ART) cannot eradicate the reservoir of long-lived latently infected cells or reverse immune dysregulation. The goal of this project is to determine whether SIV-specific immune responses elicited by RhCMV/SIV vector vaccination results in progressive reduction in (or clearance of) SIV infection, including both viral production and cellular viral reservoirs, in rhesus macaques (RM) on ART over time, and/or result in significant protection against viral rebound after ART cessation.

Project Progress: This project is currently supporting a single monkey experiment designed to test the ability of strain 68-1 RhCMV/SIV to reduce the (fully formed) SIV reservoir of, and/or control SIV reactivation in SIV+ monkeys on optimally suppressive combination antiretroviral therapy (cART) that was initiated 42 days after the onset of SIV infection. Of the 18 day 42 cART-treated monkeys available for this study, 12 and 6 were randomized to be therapeutically vaccinated with either SIV insert containing or control insert containing RhCMV vectors, respectively. Both sets of monkeys have received 2 doses of their respective vectors, and the animals are currently being followed for immune response and reservoir size until cART cessation (anticipated in August, 2015), at which time they will be assessed for post cART viral control.

Funding Sources: NIH U19AI096109

Percent P51 Dollars: 0%

Project Title: Development of a CMV Vector-Based Therapeutic HIV/AIDS Vaccine

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: Our work in the rhesus macaque (RM)-SIV model of AIDS has shown that in the prophylactic vaccine setting, the high-frequency, SIV-specific, effector memory T cell responses generated and indefinitely maintained by persistent CMV/SIV vectors can completely control and subsequently, as assessed by multiple stringent criteria, clear a highly pathogenic SIV infection – the first demonstration of an immunologically mediated functional (and perhaps complete) cure of an AIDS-causing lentivirus infection. In addition, several other features of the CMV vector platform make it uniquely suited for a therapeutic HIV/AIDS vaccine, including the findings that: 1) CMV vector immunogenicity is unaffected by prior immunity to either CMV or the SIV inserts within the recombinant CMV vaccine, and 2) the CD8+ T cell responses elicited by CMV vectors recognize unconventional SIV epitopes (epitopes not targeted by natural responses elicited by SIV itself) and, therefore, the efficacy of these responses is almost certainly not affected by prior immune escape from responses to natural infection. These remarkable findings provide a strong rationale to evaluate the CMV vector platform in a therapeutic vaccine designed to cure previously established, ART-suppressed, AIDS-causing virus infections. In this regard, the purpose of this proposal is to conduct a proof-of-concept trial in the RM-SIV model to determine the ability of this novel vaccine to functionally cure or eradicate SIV infection in the setting of a previously established, ART-suppressed SIV infection. The finding of CMV vector efficacy in this experiment – defined as the demonstration of a statistically significant reduction in SIV reservoirs during ART, and/or a reduction in the frequency, extent, or timing of viral rebound after ART cessation in the vaccinated vs. control groups – would provide a strong impetus for clinical assessment of the CMV vector therapeutic vaccine concept in ART-suppressed HIV+ patients using the clinical CMV vectors being developed in our currently funded CAVD grant.

Project Progress: The project is currently following 33 monkeys that were infected with SIVmac239 and placed on combination anti-retroviral therapy (cART) between day 4 and day 9 post-infection. All monkeys manifested detectable plasma viremia in the first 3 weeks post-infection, but have since been largely aviremic (pvl <30 SIV RNA copies/ml) in subsequent follow-up. 17 and 16 monkeys were vaccinated with RhCMV/SIV vectors (gag; rev/nef/tat; pol; and env) or RhCMV/control vectors, respectively, at 3 and 6 months post infection, and both immune responses and SIV reservoirs will be monitored through August, 2015, at which time cART will discontinued and the animals will be monitored for viral rebound.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Development of an Effector-Memory T Cell AIDS Vaccine

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester	University of California, Davis
	Private Source
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Frederick National Laboratory for Cancer Research
	Oregon Health & Science University
	Private Source
	Oregon Health & Science University
	University of California, Davis

Project Description: The T cell memory elicited by conventional vaccines (memory responses that, upon pathogen encounter, require effector expansion, differentiation and migration to mediate anti-viral activity) has proved to be of limited effectiveness in HIV/SIV infection. This poor efficacy is likely due to a 'kinetic mismatch' between viral replication and the time necessary to produce and mobilize anti-viral effectors from such vaccine-elicited responses, allowing the systemically distributed and rapidly replicating virus to escape stringent immune control. An alternative approach is to develop a vaccine that elicits tissue-based effector memory T cell responses that can intercept the infection in the first hours and days of infection, when it's most vulnerable to immune control. Work from our group has shown that RhCMV/SIV vectors can elicit potent, long-lasting SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory" (TEM) bias, and completely protect 50% of vaccinated RM from progressive SIV infection after limiting dose, intra-rectal challenge with the highly pathogenic SIVmac239 virus. Protection correlates with peak total SIV-specific CD8+ T cell responses in blood during the vaccine phase, which likely reflects the degree to which these cells are seeded into effector tissues. Taken together, these data indicate a novel pattern of protection consistent with very early control, likely occurring at the site of viral entry or early sites of viral replication and amplification, and mediated by tissue-resident CD8+ TEM. The goal of this HIVRAD is twofold: first, to understand the immunologic basis of this unique protection so as to develop second-generation strategies to increase efficacy towards 100%, and second, to develop vectors that retain optimal efficacy, but have less or no capacity to cause vector-related disease.

Project Progress: The project has made highly significant progress on many fronts in the past year, most particularly in our ground-breaking demonstration that primate CMV has evolved mechanisms to control the epitope targeting of CD8+ T cell responses that are elicited by CMV infection. Indeed, we now have the ability to genetically modify CMV vectors so as to elicit CD8+ T cells with strikingly different epitope recognition patterns, making CMV the first vaccine platform with "programmable" CD8+ T cell immunodominance hierarchies. The major advance of the last year was the finding that the unique unconventional SIV-specific CD8+ T cell responses elicited by strain 68-1 (UL128/UL130-deleted) RhCMV vectors are not – in contrast to all other vaccines – restricted by polymorphic MHC Ia molecules, but rather are approximately two-thirds restricted by MHC II molecules and one-third restricted by MHC E molecules, the latter a group of non-polymorphorhic MHC Ib molecules that are primarily involved in NK cell recognition. The finding that MHC E can restricted a broad CD8+ T cell responses is paradigm-breaking and blurs the distinction between innate and adaptive immunity. In addition, we have made a truly single-cycle RhCMV/SIV vector (FKBP-UL79) that is fully immunogenic in rhesus macaques. Finally, we have confirmed that a tropism-modified RhCMV vector, designed to be unable to replicate in CNS cells (neurons and glial cells) due to growth restriction in cells

expressing the mi124 microRNA, is also fully immunogenic in rhesus macaques, and in initial experiments, does not cause CNS damage after fetal inoculation.

Funding Sources: NIH 5P01AI094417

Percent P51 Dollars: 0%

Project Title: Development and In Vivo Characterization of Safety-Enhanced RhCMV/SIV Vectors

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

University of California, Davis
University of California, Davis
University of California, Davis

Project Description: We have demonstrated that CMV/SIV vectors can 1) re-infect CMV+ rhesus macaques (RM), 2) during re-infection, elicit potent and persistent SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory" (TEM) bias, and 3) completely protect ~50% of vaccinated RM from progressive infection after limiting dose rectal challenge with the highly pathogenic SIVmac239 virus. The protection manifested in these RM is distinct from previous vaccines in its abruptness and extent, with protected RM exhibiting a viral burst in plasma of varying size upon initial infection, followed by immediate control to undetectable levels. Although occasional viral blips in plasma are observed in protected RM, these decline with time, and after 1 year, protection is unaffected by CD8+ or CD4+ cell depletion, and extensive tissue analysis with ultrasensitive nested PCR has shown only rare detection of ~ single copy SIV nucleic acid and no viable SIV. Protection correlates with the total SIV-specific CD8+ TEM generated during the vaccine phase, and occurs without an anamnestic response. These data indicate a novel pattern of protection consistent with very early control, likely taking place at the site of viral entry and/or early sites of viral replication and amplification, and involving tissue-resident CD8+ TEM. Thus, CMV vectors and the "TEM" vaccine concept offer a powerful new approach to HIV/AIDS vaccine development. However, fully replicative CMV vectors are unlikely to be advanced to human use due to the pathogenic potential of CMV. A central goal is therefore to develop CMV vectors that maintain immunogenicity and efficacy, but are safe to use in humans.

Project Progress: In year 5 of this project, we will focus on the development, validation and *in vivo* analysis of RhCMV and HCMV vectors that combine the FKBP-UL79 attenuation modification with either pp71 deletion (RhCMV and HCMV) or FKBP targeting of pp71 (HCMV only, since we know this approach is effective for HCMV, but not for RhCMV). In addition we will complete an on-going challenge study designed to compare 1) the efficacy of these 68-1.2 vectors (which elicit conventionally restricted CD8+ T cell responses) to that of the original strain 68-1 (UL128/U130-deleted) RhCMV vectors (which elicit unconventionally targeted CD8+ T cell responses restricted by MHC II and MHC E, rather than polymorphic MHC Ia), and 2) the efficacy of vaccination with either strain 68-1 or strain 68-1.2 RhCMV/SIV vectors to that of vaccination with both 68-1 and 68-1.2 vectors (which elicit both conventional and unconventional CD8+ T cell responses of astonishing breadth). The vaccine phase of this experiment will end in late Spring to early Summer, 2015 (depending on the time needed to deconvolute all responses to the individual epitope level and determine the restricting MHC (MHC 1 vs. II vs. E) for each epitope-specific response) such that repeated, limiting dose SIVmac239 challenge will initiate in Summer, 2015, with initial efficacy determination by Fall, 2015, and final efficacy assessment completed by the end of the grant period.

Funding Sources: NIH R01AI095113

Percent P51 Dollars: 0%

Project Title: Development of Attenuated CMV Vectors for an HIV/AIDS Vaccine

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: The overall goal of this project is the development of an HCMV vector-based HIV/AIDS vaccine (comprised of one or more HIV insert-expressing HCMV vectors) that is optimized for safety, efficacy and manufacturability. The fundamental concept is to retain the natural unique immunogenicity of CMV while making the CMV vectors safe enough for use as a prophylactic vaccine. CMV vectors are designed to be persistent at low level so as to provide the "just right" amount of antigen stimulation that elicits and maintains the effector memory T cell responses responsible for protection – not "too little" stimulation that would result in reversion of the responses to a resting (central) memory phenotype, and not "too much" stimulation that would result in response exhaustion (or result in adverse effects due to excess viral replication). While a wildtype (WT) CMV vector would (like natural CMV infection) achieve this balance in immune competent individuals, such a CMV vector would also retain the potential of natural CMV for excess (pathogenic) viral replication in situations of immune compromise. Since any vector intended for use as a prophylactic vaccine must be safe in the entire general population, a critical goal in CMV vector development is therefore the design of "attenuated" vectors that persist at the level required for an effective effector memory T cell vaccine, but are restricted in their ability to replicate and/or spread at levels associated with disease, even in otherwise vulnerable subjects. In the past 5 years, we have explored CMV biology in the rhesus monkey and have come up with a primary attenuation strategy – genetic deletion of UL82 (a gene that encodes the tegument protein pp71) ¬– that we believe when applied to HCMV will result in manufacturable HCMV/HIV vectors that will achieve this balance after human vaccination. We have also developed additional genetic modifications that enhance safety, and potentially efficacy, but before these additional features can be evaluated, we must first validate the primary attenuation strategy in human beings.

Thus, our vaccine development process will occur in 2 steps. In the first step, we will construct and manufacture (using existing GMP-qualified cell lines) a prototype pp71-deficient HCMV/HIVgag vector for a first-in-man phase 1 clinical trial of an attenuated HCMV vector. This prototype vector will not be sufficiently optimized for further development, but will constitute the first crossover of our CMV vector platform from monkeys to humans. This trial is intended to address the following critical development issues: 1) confirmation of the safety of pp71-deficient HCMV vector design in humans, 2) confirmation that HCMV-seropositive humans can be super-infected with HCMV-based vectors, 3) determination of the relationship between pp71-deficient HCMV vector dose and immunogenicity, and 4) evaluation of the quantity, quality (effector memory differentiation and function) and durability of the vector-elicited HIVgag-specific T cell responses.

The second step, which will occur in parallel with step 1, is the development, validation and production of a 2nd generation vector (or vector set) that is optimized for safety (this vector design will include genetic changes in addition to pp71 deletion that will serve as secondary attenuation), efficacy (this vector design will have 1 or more vectors with multiple HIV inserts encoding Gag, Pol, and Nef that will be sequence-optimized for cross-reactivity against global M group HIVs and will have optimized CD8+ T cell epitope programming – either conventional or unconventional CD8+ T cell epitopes, as dictated by the presence or absence of UL128-131 genes, or potentially, comprise a vector set with both vector types), and manufacture (will have a custom developed GMP-qualified pp71-complementing cell line for efficient manufacture of fully complemented vector). In addition, we will, in parallel, perform stringent safety and stability analysis in the rhesus macaque model to confirm that the 2nd generation attenuation strategies are stable over the long term (e.g., does not revert to WT, even under "stressed" conditions), completely prevent transmission from person to person or mother to

fetus, and protect against any possibility of the vector causing direct or indirect disease (the former from lytic infection, the latter from chronic active infection with excess local or systemic immune activation).

Project Progress: This project has just started and we currently initiating work on all the above mentioned aims.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Development of Safety- and Efficacy-Enhanced CMV Vector for an HIV/AIDS Vaccine

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: Worldwide there were an estimated 2.6 million new HIV infections in 2009 (UNAIDS report, 2010), and although this number reflects a decline from the peak incidence in 1999, it is generally agreed that an effective prophylactic vaccine is the only practical means by which the HIV/AIDS epidemic can be definitively controlled. To date, HIV/AIDS vaccines designed to harness cellular immunity to control HIV infection have been largely unsuccessful, due, in our opinion, to the ability of systemic HIV infections to evade T cell immunity, and the failure of conventional T cell vaccine approaches to manifest anti-viral effector activity immediately after mucosal infection (prior to systemic spread), when the virus is most vulnerable. We have now designed and validated a novel vaccine approach that surmounts this hurdle. Using the rhesus macaque (RM)-SIV model of AIDS, we have demonstrated that persistent vectors based on the ubiquitous β-herpesvirus cytomegalovirus (CMV) elicit and indefinitely maintain high frequency, tissue-resident effector memory T cell (TEM) responses that can intercept and stringently control a highly pathogenic, AIDS-causing SIV very early in infection and maintain this control (or perhaps even clear infection) over the long term. In addition, we have shown that Rhesus (Rh) CMV vectors: 1) can be used repeatedly in RhCMV+ RM without inhibition of immunogenicity by pre-existing immunity; 2) elicit T cell responses that manifest unusually broad epitope targeting; and 3) can be modified to have an enormous exogenous sequence-carrying capacity (>15kb), all characteristics that offer distinct advantages over alternative vaccine approaches. Thus, CMV vectors and the "TEM" responses they elicit offer a powerful new approach to HIV/AIDS vaccine development. However, fully replicative (e.g., wildtype) human CMV (HCMV) vectors are unlikely to be advanced to broad human use due to the pathogenic potential of HCMV in immune-compromised subjects. A central goal is therefore the development of HCMV vectors that maintain immunogenicity and efficacy, but are safe enough for widespread clinical use. Fortunately, our studies have also demonstrated that a highly attenuated, spread-deficient RhCMV/SIV vector lacking the tegument protein pp71 (Δpp71) is robustly immunogenic in RM (equal to, or greater than, wildtype vectors), offering a clear development path for clinical translation of the unique protection associated with CMV vectors. In the work proposed here, we will use the rhesus model to develop a safe and effective RhCMV/SIV vector design, the essential features of which can then be incorporated into an HCMV/HIV vector design suitable for human use.

Project Progress: The overall goal of this project is to develop an optimized spread-deficient CMV vector for use as an effector-memory T cell-targeted HIV/AIDS vaccine. The project has 4 components: 1) assessment of the ability of the prototype (pp71-deleted) spread-deficient RhCMV/SIV vector design to protect rhesus macaques (RM) against homologous and heterologous challenge with highly pathogenic SIV, 2) to use the RM model to optimize design of multi-component RhCMV/SIV vectors using endogenous promoters for expression of multiple SIV inserts, 3) to construct and validate HCMV/HIV homologues of the optimized RhCMV/SIV vector designs and select candidate vectors for phase 1 clinical testing, and 4) to develop a product development plan (PDP) for the manufacture, regulatory approval, and phase 1 testing of optimized HCMV/HIV vector(s). With regard to component 1, we have constructed RhCMV/SIV vectors with both SIVmac239 and SIVE660 inserts and have vaccinated RM cohorts with these vectors, and are in the process of challenging these vaccinated RM vs. controls (importantly, even at this stage, we have seen typical protection with these attenuated vectors). With regard to component 2, we have demonstrated immunogenicity of pp71-deleted RhCMV vectors in which the pp71 sequence is replaced with SIV inserts (with the pp71 promoter driving expression of the SIV insert). We have identified 4 other neutral sites in which SIV inserts can replace the CMV gene with no compromise of vector function, and have constructed and validated multicomponent vectors. With regard to component 3, we have constructed a wildtype (wt) HCMV BAC from the clinical strain TR to

serve as the starting point for our HCMV/HIV vector, as well as a prototype HCMV/HIVgag-pp71 replacement vector. With respect to component 4, we have determined that the manufacture of a pp71-deleted HCMV vector would be complicated by the requirement for a GMP-validated pp71-complementing cell line, and have therefore moved forward 2 other vector designs with comparable attenuation that can be manufactured using a pre-existing validated cell line without complementation.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Efficacy of Oral CMV/SIV Vectors

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Frederick National Laboratory for Cancer Research

Private Source

Oregon Health & Science University

Oregon Health & Science University

Private Source

Oregon Health & Science University

Project Description: Two large scale nonhuman primate (NHP) efficacy studies have convincingly demonstrated that CMV/SIV vectors can 1) re-infect CMV-seropositive rhesus macaques (RM), 2) during re-infection, elicit potent and persistent SIV-specific CD4+ and CD8+ T cell responses with a strong "effector memory bias", and 3) protect ~50% of vaccinated RM from progressive SIV infection after limiting dose rectal challenge with the highly pathogenic, CCR5-tropic SIVmac239 virus. The protection manifested in these RM is distinct from previous vaccines in its abruptness and extent, with protected RM manifesting a viral burst in plasma of varying size upon initial infection, followed by immediate control to undetectable levels. Protection correlates with the extent of total SIV-specific CD8+ T cells generation during the vaccine phase, and is stable in the vast majority of protected RM for at least 6 months. These data indicate a novel pattern of protection consistent with very early control, likely taking place in the site of viral entry and/or early sites of viral replication and amplification, and mediated by tissue-resident TEM.

Project Progress: Extensive evaluation of the administration of RhCMV/SIV vector via oral vs. subcutaneous inoculation reveals mostly identical immunogenicity, but with the oral route providing slightly higher SIV-specific T cell responses in the small and large intestine. Whether this increased T cell response magnitude in the gut translates to higher efficacy is currently being assessed in a study in which animals given the same vectors either orally (n=15) or subcutaneously (n=15) are challenged with limiting dose SIVmac239 via the intra-rectal route. We are currently in the vaccine phase of this experiment with challenge to be initiated mid-year, 2015.

Funding Sources: NIH 5R01DE021291

Percent P51 Dollars: 0%

Project Title: Induction of Broad Functional Class II Restricted CD8+ T Cell Responses: Translation from NHP to Humans (MHC II- and MHC E-restricted CD8+ T Cells and Control of HIV)

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: Worldwide there were an estimated 2.7 million new HIV infections in 2010 (UNAIDS report, 2011), and although this number reflects a 21% decline from the peak incidence in 1997, it is generally agreed that an effective prophylactic vaccine is the only practical means by which the HIV/AIDS epidemic can be definitively controlled. However, the unique evolutionary adaptations of HIV have stymied the development of such a vaccine for nearly 30 years. HIV and its nonhuman primate counterpart, SIV, manifest 1) massive replication, high mutation rates, genetic malleability and functional plasticity leading to rapid evolution, 2) specific genetic mechanisms to thwart innate and adaptive immune mechanisms, 3) envelope adaptations to avoid antibody (Ab) neutralization, 4) genetic integration and establishment of latency, and 5) in AIDS-susceptible species (humans, Asian macaques), dysregulated immune function, all of which conspire to provide for efficient evasion of host anti-viral immunity and persistent infection. Indeed, once a spreading HIV/SIV infection is systemically established, complete viral clearance by immune mechanisms has long been considered unachievable, and stringent, long-term control of a fully pathogenic HIV or SIV is rare, limited to individuals with particular genetic polymorphisms that either handicap the virus, or provide for an unusually effective immune response. However, there is increasing evidence that the initial viral bridgehead in the first few days after mucosal exposure, made, typically, by one or two viral species, is much more vulnerable. At this stage, immunity would only need to act on a much smaller, less diverse and more localized viral population, and if anti-viral immune responses could suppress the viral reproductive ratio (R0) to <1, the infection may be subject to complete control and even elimination. Unfortunately, few vaccines tested to date have been able to exploit this early putative vulnerability. Ab-targeted vaccines have been stymied by the difficulty in identifying immunogens and delivery vehicles capable of eliciting and maintaining highly effective anti-viral Abs, either broadly neutralizing Abs, or Abs capable of interfering with early infection by other mechanisms. Moreover, none of the T cell-targeted vaccine strategies investigated to date has been able to meet this “early intervention” requirement.

In the past decade, Excluded by Requester research group has designed a novel vaccine approach that effectively addresses these biologic hurdles. In a series of publications (1-3), these investigators have demonstrated that persistent vaccine vectors based on the ubiquitous herpesvirus cytomegalovirus (CMV) elicit and indefinitely maintain systemic high-frequency, circulating and tissue-resident effector memory T cell (TEM) responses that can intercept and stringently control a highly pathogenic, AIDS-causing SIV very early, if not immediately, after exposure. Moreover, these responses not only maintain this control over the long term, but over weeks to months, actually clear the infection to the degree that protected monkeys are not distinguishable from non-SIV-exposed animals by state-of-the-art analysis at necropsy. Although the early viral “intercept” and continuous immune surveillance afforded by these TEM-type responses were almost certainly required for this remarkable efficacy, during the course of these studies it was discovered that TEM differentiation was not the only unique feature of the CMV vector-elicited immune responses associated with this protection. The fibroblast-adapted CMV vectors responsible for the efficacy described above were also found to generate an unprecedented array of SIV epitope-specific CD8+ T cell responses (3-fold the breadth of conventional responses) that were restricted, not by classical polymorphic MHC class I (MHC I) proteins, but rather by MHC class II (MHC II; two-thirds of responses) and non-classical MHC E (one-third of responses) proteins (4). Even more remarkable was the finding that in contrast to conventional CD8+ T cell responses, many of the unconventional viral epitopes targeted by these responses were common to most or even all monkeys, despite the fact that these monkeys were out-bred and quite genetically heterogeneous. These highly unusual CD8+ T cell responses were found to be due to deletion of 2 genes, UL128 and UL130, in the fibroblast-adapted CMV vector compared to wildtype CMV, and repair of these 2 genes completely reversed the recognition properties of vector-elicited CD8+ T cells back to classical MHC I restriction and conventional epitope breadth (4).

Thus, CMV vaccine vectors can be genetically programed to generate distinct types of CD8+ T cell responses based on the number and nature of the epitopes recognized and the host MHC molecules that present these epitopes. Since the ability of CD8+ T cells to mediate anti-viral effector function critically depends on the nature (and often, breadth) of viral antigen presentation of the surface of virally infected cells, this response programming is likely to have major influence on vaccine efficacy. Indeed, given that HIV and SIV have evolved to evade conventional CD8+ T cell responses, it's possible that the unconventionally targeted CD8+ T cell responses elicited by the UL128/UL130-deleted CMV vectors account for their demonstrated efficacy against SIV challenge. Moreover, it is possible that the magnitude and distribution of these unconventional responses or a component of these responses might explain why some vaccinated monkeys are completely protected and others show no protection at all. In this regard, it is also noteworthy that since the discovery of these responses in UL128/UL130-deleted CMV vector-vaccinated monkeys, careful and specific scrutiny of CD8+ T cell responses in humans and monkeys with spontaneous (e.g., not vaccine-related) HIV or SIV control has led to the identification of minor, but unequivocal, MHC II-restricted, HIV- or SIV-specific CD8+ T cell populations. This finding raises the question of whether these spontaneous (e.g., non-CMV vector-elicited) unconventional CD8+ T cell responses might have contributed to the viral control in these subjects. If unconventional CD8+ T cells do have enhanced anti-HIV/SIV efficacy, the mechanisms responsible for this efficacy and the mechanisms responsible for the generation of these response become important issues for HIV vaccine development, both to inform the clinical development of CMV vectors and to develop alternative methods to generate these responses if CMV vector development encounters regulatory or manufacturing obstacles, or if CMV vector efficacy can be enhanced by a non-CMV vector priming component. In response to this imperative, and colleagues at Oregon Health & Science University (OHSU) have – in this proposal - joined forces with of the of and of to collaboratively determine 1) the mechanisms responsible for generation of unconventionally targeted CD8+ T cell responses, 2) the functional implications of unconventional epitope recognition by CD8+ T cells, and most importantly, 3) whether unconventionally targeted SIV- or HIV-specific CD8+ T cells manifest enhanced in vivo viral control compared to conventionally targeted CD8+ T cell responses.

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Private Source
Private Source
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Private Source
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Private Source

Project Progress: This project has just started and we currently initiating work on all the above mentioned aims.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: OHSU/AERAS Project 2: Vector Production and Efficacy Experiment #2

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: The Bacille Calmette-Guérin (BCG) vaccine, created in 1921, is the only existing vaccine against tuberculosis (TB). Unfortunately, it is only partially effective. It provides some protection against severe forms of pediatric TB, but is unreliable against adult pulmonary TB, which accounts for most of the disease burden worldwide. Although BCG is the most widely administered vaccine in the world, there have never been as many world-wide cases of TB. There is therefore an urgent need for a modern, safe and effective vaccine that would prevent all forms of TB. Our previous studies with recombinant RhCMV encoding exogenous antigen inserts have demonstrated the ability of these vectors to elicit and maintain high frequency insert-specific, effector-differentiated CD4+ and CD8+ T cells in both lymphoid tissues and extra-lymphoid effector sites (including, notably, the lung). To explore the possibility that the CMV vector platform would provide anti-TB immune responses with superior efficacy, we entered collaboration with the Private Source in 2011 to use the rhesus macaque model of TB to perform an efficacy trial comparing BCG vaccination, vaccination with RhCMV vectors expressing 9 TB antigens (85A/85B/Rv3407/Rv1733c/Rv2626c/Rpf A/Rpf C/Rpf D/ESAT6), or a combination of the 2 vaccines (BCG prime; BCG boost). As shown in the figure below, we have completed this initial study and have not only demonstrated superior efficacy of RhCMV/TB vectors over BCG, but have shown that the addition of a BCG prime to RhCMV/TB vaccination partially abrogate the latter's protection. Based on these promising results, we are continuing our collaboration with Private Source to perform a second study designed to confirm the efficacy of the original RhCMV/TB vector set, as well as to potentially optimize efficacy by also investigating a different RhCMV backbone (which we know gives a qualitatively different immune response) and a different TB insert design.

Project Progress: The first assessment of RhCMV/TB vaccines has been completed. Based on the statistically significant 73% efficacy observed in the first study (superior to the gold standard BCG vaccine), we have embarked on a second study designed to confirm efficacy of the original mix of strain 68.1 RhCMV vectors expressing 9 TB antigens (85A/85B/Rv3407/Rv1733c/Rv2626c/Rpf A/Rpf C/Rpf D/ESAT6) and to compare the efficacy of these vectors to 1) strain 68-1.2 RhCMV vectors (UL128/UL130-repaired) expressing the same inserts, and 2) a single strain 68-1 RhCMV vector expressing a single insert encoding a 85A + Rv3407 + Rv2626c + Rpf A + Rpf D + ESAT6 fusion protein (n = 9 per group). All 27 monkeys in the vaccine groups have been vaccinated and boosted at this time and we anticipate challenging these animals and an n = 9 unvaccinated control group in the 3rd quarter of 2015.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Role of Memory T Cell Dynamics in SIV Infection

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Frederick National Laboratory for Cancer Research
Oregon Health & Science University

Project Description: HIV and its rhesus macaque (RM) counterpart SIV share a pattern of infection and a constellation of immunologic and pathobiologic features such that the vast majority of susceptible (untreated) people or RM infected with these agents experience unremitting infection and progressive immune deficiency. In work funded by this grant, we pioneered analysis of the *in vivo* immunobiology of naïve vs. memory (TN vs. TM) and central vs. effector memory (TCM vs. TEM) T cells in the RM model (including their homeostatic and functional regulation) and demonstrated the direct relevance of this physiology to SIV pathogenesis and immunity. In particular, we demonstrated that the mechanisms that maintain CD4+ TCM homeostasis and regulate CD4+ TCM differentiation into CD4+ TEM determine the development of immunodeficiency (AIDS) in SIV-infected RM. More recently, we have: 1) shown that IL-7 and IL-15 are critical regulators of CD4+ TCM homeostasis in RM, 2) developed a TN-deficient RM model and used this model to show that CD4+ TN are dispensable for both CD4+ TCM stability and CD4+ TEM production in SIV-infected RM, and 3) developed a method for long-term *in vivo* IL-15 blockade in RM (a "rhesusized" anti-IL-15 mAb) and used this method to show the importance of IL-15 in TEM homeostasis and that complete NK depletion (a second consequence of IL-15 blockade) has little impact on virologic control and disease progression in SIV-infected RM. In the extension of this work, we will use the CD4+ and CD8+ TN depletion models and *in vivo* manipulation of IL-15 and IL-7 to define the fundamental mechanisms underlying: 1) SIV persistence and replication set points (immune evasion vs. immune control), 2) deterioration of CD4+ T cell-mediated and overall immunity leading to AIDS, and 3) the establishment and maintenance of SIV reservoirs and immune reconstitution following pharmacologic control of viral replication (using ART regimens capable of long-term suppression of SIV in RM to <30 RNA copies/mL of plasma and improved methods for monitoring residual viral RNA and DNA in tissues). Identification of these mechanisms will be a crucial step in the development of novel therapeutic approaches aimed at enhancing immune control of HIV replication, "disconnecting" HIV replication from disease progression, and/or augmenting immune recovery and reservoir clearance during anti-retroviral therapy.

Project Progress: The current focus of this project is two-fold: 1) the determination of mechanisms by which SIV can maintain persistent replication characterization in the face of highly effective immunity, and 2) the elucidation of the immunobiology of SIV reservoirs after the administration of effective anti-retroviral therapy (ART), including the ability of cellular immunity to influence spontaneous and induced viral reactivation and to limit viral dissemination after ART cessation. A major accomplishment in the last year was the elucidation that B cell follicles constitute a sanctuary against highly effective SIV-specific CD8+ T cell responses, allowing persistent SIV replication in elite controller monkeys, and that these follicles are the major site of spontaneous SIV reactivation in SIV+ monkeys on highly effective ART. We have also continued to optimize the monkey model for ART-mediated viral control and reservoir analysis, showing that placing monkeys on ART 12 days after SIVmac infection provides for a stable and measureable SIVmac reservoir, yet allows for complete viral control in the vast majority of monkeys (which is problematic when ART initiation is delayed into plateau phase of infection, because in this situation, up to a third of monkeys will not have sustained viral control – plasma viral load below 30 copy eq/ml). We expect this model will allow for more efficient analysis of SIV reservoirs as it greatly reduces the waste involved in ART treatment failures.

Funding Sources: NIH R37AI054292

Percent P51 Dollars: 0%

Project Title: Inducing donor-specific tolerance through clonal deletion

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of California, Riverside

Project Description: Each year there are approximately 16,000 kidney transplants performed in the U.S. The outcomes of transplantation are dependent upon the continuous use of immunosuppressive drugs, which can increase susceptibility to infections and cancers as well as nephrotoxicity. There is therefore an urgent need to discover novel approaches to induce donor specific tolerance, thus eliminating the need for long-term immunosuppression. Our long-term goal is to induce donor-specific tolerance in a rhesus monkey model of kidney transplantation using a novel approach to specifically eliminate allospecific lymphocytes. The working hypothesis of this proposal is that sensitizing a recipient using a donor-specific lymphocyte transfusion (DST) will induce the activation of alloreactive lymphocytes that can subsequently be depleted using agents targeting activation markers. We will first identify the dose of PBMC needed to induce effective optimization of the recipient. We will use an adaptive study design starting with 1 x 10^8 cells followed by dose escalation or de-escalation by a factor of 10. The development of the alloresponse will be monitored by measuring the generation of donor-specific T cells and alloantibodies by the recipient. We will then optimize the timing of administration of Brentuximab vedotin, an FDA approved drug that targets activated T and B cells, which upregulate CD30. We will deliver this agent day -1, the peak, and 1 week after the peak of T/B cell activation. The success of this approach will be evaluated by repeating the DST 3 weeks after the last Brentuximab vedotin administration.

Project Progress: We were able to demonstrate that transferring non-syngeneic PBMC resulted in an allo-reactive T cell response as evidenced by increased expression of Ki67 in naïve and central memory CD4 and CD8 T cells. Interestingly, no B cell proliferation was observed. We also determined that re-challenge resulted in increased proliferation of CD8 T cells primarily. Importantly, we were able to detect increased expression of CD30 and CD70 on both CD4 and CD8 T cells. The company decided that they did not want to pursue phase 2 of this study so the in vivo CD30 administration portion was not carried out and this project is now closed.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: 32nd Annual Symposium on NHP Models for AIDS

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: This conference grant (R13) application request funds to partially cover the cost of planning, organizing, publicizing and hosting the 32nd Annual Symposium on Nonhuman Primate Models for AIDS. The Symposium will be hosted by the Oregon National Primate Research Center (ONPRC), Oregon Health & Science University (OHSU), and will be held November 11-14, 2014, at Proprietary in Portland, OR. This meeting has become the premier forum for the presentation and exchange of the most recent advances in AIDS research utilizing animal models. It is anticipated that approximately 250 scientists from around the world will attend this meeting. The latest findings in primate pathogenesis, immunology, virology, vaccines, therapeutics, genomics, and curative approaches will be presented. Four consecutive half-day and two quarter-day scientific sessions will be held, each devoted to a different discipline. Each session will have an invited Chair, who will give a 30- minute presentation to open the first half of the session, and a co-Chair, who will moderate the session and entertain questions. A Scientific Program Committee consisting of sixteen members representing a broad spectrum of institutions will review abstracts and assign oral or poster presentation for each of the scientific sessions. Criteria for selection will include relevance of he topic to the theme of the meeting and the originality and quality of the information contained in the abstract. Those individuals giving formal presentations will be asked to submit their presentations in manuscript form for publication in the Journal of Medical Primatology. In addition, there will also be poster sessions for those meritorious presentations that cannot be accommodated in one of the five platform sessions. The conference will include an opening day welcome reception, a second day poster session reception and a banquet on the third day of the symposium. To further the educational mission of the meeting, an Outreach Session, primarily aimed at high school science teachers and general community members, will be held. This event will be hosted with the assistance of the Proprietary Info and the OHSU Proprietary Info which is dedicated to promoting public understanding of the implications and applications of the process of biomedical research. We are confident that the knowledge gained from this meeting will shed light on how HIV and SIV cause disease and how to develop vaccines to prevent infection and therapies to control and eventually cure HIV infection.

Project Progress: The 32nd Annual Symposium on Nonhuman Primate Models for AIDS occurred November 11-14, 2014, at Proprietary Info in Portland, OR. The Symposium attracted 229 scientists from all over the world, including Japan, France, Germany, and Italy.

Funding Sources: NIH R13OD010788

Percent P51 Dollars: 0%

Project Title: A Novel APOBEC-Based Vaccine Approach for HIV

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: This project will test the hypothesis that inducing high-frequency T cells against APOBEC3 proteins will protect animals from SIV replication. We will produce two rhesus CMV vectors, each encoding a separate Vif-sensitive APOBEC3 protein, and vaccinate macaques. We will subsequently challenge vaccinated and control animals with low-dose mucosal SIV and measure protection from SIV replication.

Project Progress: We have initiated construction of APOBEC-expressing CMV vaccine vectors and anticipate vaccination to commence by the end of this year. We are also currently testing the ability of APOBEC-specific CD8+ T cells to recognize and eliminate SIV+ cells.

Funding Sources: George Washington University/NIH R33 AI93179

Percent P51 Dollars: 0%

Project Title: CNIRH: UCSF-GM Center for AIDS Research: Defining and Eliminating the Macrophage Reservoir

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: The cellular source of HIV that persists during highly active antiretroviral therapy (HAART) remains unclear. Infection of mononuclear phagocytes is a key feature of lentiviruses such as HIV and SIV, yet the contribution of these cells to viral persistence is poorly understood and controversial. Here, we hypothesize that macrophages act as viral sanctuaries during HAART and set forth a research plan to directly test this hypothesis using a novel macrophage depletion technique. Thus, the goal of the proposed research is to determine if macrophages are responsible for continued viral replication during HAART and viral rebound following HAART cessation. This will be compared to the CD4 lymphocyte reservoir via antibody-mediated CD4 T cell depletion.

Project Progress: We have inoculated 12 macaques with SIVmac251 and initiated cART at day 9 post infection. Following full cART-mediated suppression of SIV replication we have depleted either CD4+ T cells or macrophages and are currently measuring the impact on the latent reservoir size.

Funding Sources: Creative and Novel Ideas in HIV Research (CNIHR)/NIH P30AI027763

Percent P51 Dollars: 0%

Project Title: Defining Non-classical, CMV-induced CD8 T Cell Responses

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: With 34 million people currently living with HIV worldwide, developing a prophylactic HIV vaccine remains a top global health priority. A CMV-based vaccine approach recently provided striking protection from pathogenic SIV replication with ~50% of rhesus macaques protected. In these protected animals, we have observed CMV-induced, SIV-specific CD8+ T cell responses that are phenotypically and functionally distinct from CD8+ T cells engendered by any other vaccine regimen, including natural infection, studied to date. The magnitude of these CMV-induced CD8+ T cell responses correlates with the profound protection from SIV replication and, strikingly, may not be restricted by MHC-I. However, rhesus macaques exhibit remarkably complex MHC genetics, thereby obfuscating the study of these protective, CMV-induced CD8+ T cell responses. In contrast, Mauritian cynomolgus macaques (MCM), descendants from a population bottleneck event, exhibit simplified MHC genetics with only seven completely described MHC haplotypes. Therefore, MCM are the ideal model to study the genetics of CMV-induced protective immunity. To this end, we will use MCM to define the restricting MHC molecule for the CMV-induced CD8+ T cell responses.

Project Progress: We have determined that the commonly used rhesus CMV vector, strain 68-1, cannot infect MCM to induce T cell responses. We created a panel of CMV vectors based on 68-1 with various viral ORFs repaired. These studies definitely identify UL36 as necessary and sufficient for infection of MCM.

Funding Sources: NIH R21AI108401

Percent P51 Dollars: 0%

Project Title: Endogenous Retrovirus-specific Antibodies to Block AIDS Virus Infection

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of California – San Francisco

Project Description: An antibody-based vaccine that blocks transmission remains the Holy Grail for an HIV vaccine. Unfortunately, such a vaccine has proven elusive, due in part to the heavy glycosylation and extreme variability of the HIV Env glycoprotein. Circulating HIV-1 strains can differ from each other by up to 35% in the Env protein and this enormous sequence diversity is a major stumbling block to the development of a conventional HIV vaccine. Novel vaccine targets are therefore urgently needed. While the cancer research field has recognized the utility of endogenous retrovirus (ERV)-specific immune responses for cancer treatment, this approach has not been applied to HIV vaccine development. Here, we propose a novel antibody-based vaccine approach that circumvents the obstacle of HIV Env's sequence diversity and heavy glycosylation by targeting a surrogate marker of HIV-1 infection, the ERV Env protein. Based on our preliminary data in both SIV-infected macaques and HIV-infected patients, we hypothesize that ERV-specific antibodies represent an alternate, stable target to block transmission of AIDS viruses.

Project Progress: Despite the presence of the ERV-K Env ORF in rhesus macaques, SIV infection fails to activate this ERV. Therefore, we utilized the humanized BLT mouse model to determine if a non-neutralizing, ADCC-inducing antibody targeting ERV-K Env on the surface of HIV-1-infected human cells can mediate protection against infection.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Graft versus Host Immunity in SIV Clearance following Stem Cell Transplantation

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description:
Three patients remain HIV free in the absence of cART following leukemia-related, MHC-matched, allogenic hematopoietic stem cell transplantation (HSCT). The mechanisms underlying this functional cure are not known, but may depend on graft-versus-host disease in the transplant recipients. Non-human primates are the best model of HIV infection, but no studies have directly assessed the role of graft-versus-host disease in the clearance of the HIV reservoir following MHC-matched, allogenic HSCT. Mauritian cynomolgus macaques (MCM) have extremely simplified genetics, allowing for the identification of fully MHC-matched animals. We intend to define the contribution of graft-versus-host disease to HIV clearance following HSCT using this novel, MHC-matched non-human primate model. In specific aim 1, we will infect 4 MCM with SIV and 4 weeks later administer cART until virus is undetectable in plasma. These animals will then receive MHC-matched HSCT, graft-versus host disease will be measured, and 12 weeks later cART will be lifted. We will monitor animals for an additional 16 weeks to measure SIV rebound in the plasma and tissues. Overall, this study will build a new model of MHC-matched, allogenic HSCT in non-human primates and use this model to assess the role of graft-versus-host disease in HIV clearance following HSCT.

Project Progress: We have performed three stem cell transplants in genetically identical MCM and determined the optimal conditioning regimen and peri-transplant care. We are currently monitoring for donor chimerism and plan to initiate the first SIV+ HSCT transplants using sex-matched MCM in the coming year.

Funding Sources: NIH R21 AI112433

Percent P51 Dollars: 0%

Project Title: Targeting HIV Reservoirs via Y Chromosome-specific Graft versus Host Immunity

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: With 34 million people currently living with HIV, stopping the HIV epidemic remains imperative. Combination antiretroviral therapy (cART) limits viral replication, but is not curative. Thus, there is an urgent need to design a functional cure via elimination of the viral reservoir. There are now 3 HIV patients who remain HIV free in the absence of cART following leukemia-related, MHC-matched, allogenic hematopoietic stem cell transplantation (HSCT). The mechanisms underlying this functional cure are not known, but may depend on graft-versus-host immunity in the transplant recipients. Non-human primates are the best model of HIV infection, but the majority of studies focus on autologous or MHC-mismatched allogenic HSCT due to the complexity of non-human primate MHC. Thus, no studies have directly assessed the role of graft-versus-host immunity in the clearance of the HIV reservoir following MHC-matched, allogenic HSCT. We intend to define the contribution of graft-versus-host immunity to HIV clearance following HSCT using a novel, Mauritian cynomolgus macaque (MCM) model. MCM have extremely simplified genetics due to a recent bottleneck approximately 500 years ago. Therefore, we are able to readily identify fully MHC-matched animals, a situation akin to the MHC-matching most often performed in human HSCT. In specific aim 1, we will establish a safe and effective nonmyeolablative regimen in SIV-infected MCMs. In specific aim 2, we will perform MHC-matched HSCT, measure graft-versus host immunity, and correlate it to SIV rebound in the plasma and tissues. Overall, this study will build a new model of MHC-matched, allogenic HSCT in non-human primates and use this model to assess the role of graft-versus-host immunity in HIV clearance following HSCT.

Project Progress: We have performed three stem cell transplants in genetically identical MCM and determined the optimal conditioning regimen and peri-transplant care. We are currently monitoring for donor chimerism and plan to initiate the first SIV+ HSCT transplants using sex-mismatched MCM in the coming year.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: UCSF-GVI Center for AIDS Research: Targeting Tim-3 for Elimination of HIV Reservoirs

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: This project will test the hypothesis that directly targeting the Tim-3:Gal-9 pathway can destroy latently HIV-infected CD4+ T cells. We will administer the most efficacious Tim-3:Gal-9 reagent to HAART-suppressed, SIV-infected macaques to demonstrate proof-of-principle that targeting this pathway is a viable approach to clearing the HIV latent reservoir.
Project Progress: We characterized the role of Tim-3 in the nonhuman primate of SIV infection. We have now generated Tim-3 specific blocking antibodies and are testing them for in vitro activity.

Funding Sources: University of Hawaii/UCSF/NIH 5P30 AI027763

Percent P51 Dollars: 0%

Project Title: An Unconventional, Effector Memory T Cell Vaccine for Influenza

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The world may be facing an impending crisis and immediate threat from an uncontrolled influenza outbreak. An influenza pandemic has greater potential to cause large numbers of deaths/illnesses over a shorter time period than virtually any other natural health threat. Antibody-mediated influenza vaccines are extremely strain- specific due to highly variable hemagglutinin (HA) and neuraminidase (NA) antigens. Moreover, influenza vaccines are not effective in the elderly population that is most at risk for developing lethal infection. For this reason, there is an urgent need to develop vaccines that control multiple strains over many years including in the elderly. The clearest means of preventing or minimizing the global catastrophe that will result from widespread infection of a susceptible human population with a new influenza pandemic strain is prophylactic vaccination aimed at inducing broadly reactive, universal immune responses against a range of viral isolates and subtypes. The goal of this project is to demonstrate that effector memory T cell (TEM) induced by CMV- vectors carrying conserved flu antigens will protect against deadly forms of influenza virus. To this end we will design new Rhesus CMV vaccine vectors expressing conserved influenza internal proteins and test the ability of the novel T cells induced by these vaccines to protect against highly pathogenic avian influenza. Successful completion of these studies would lay the foundations for a novel approach to develop a universal influenza vaccine.

Project Progress: Three replication-deficient rhesus CMV vaccine vectors have been constructed (expressing influenza M, NP, or PB1). Animals will be vaccinated in the coming year and immunogenicity in peripheral blood and in the lung will be monitored.

Funding Sources: NIH R21AI112837

Percent P51 Dollars: 0%

Project Title: Antibody-Based Therapy of Chikungunya Virus

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Abstract: Chikungunya virus (CHKV) is a mosquito-transmitted alphavirus that causes explosive epidemics of a severe febrile illness characterized by debilitating polyarthalgia in humans. CHKV caused an estimated 1.3 million new cases in India alone in 2006, and has the potential to spread globally because of the distribution and abundance of its mosquito vectors, Aedes aegypti and Aedes albopictus. During recent outbreaks more severe forms of CHKV were observed, including encephalopathy and hemorrhagic fever, suggesting the emergence of more virulent strains. Closer to the US, in 2013-14 CHIKV has infected hundreds of thousands of people on multiple island nations of the Caribbean. Currently, no specific treatment or vaccine is available. Given its global burden, the increased travel into CHKV-endemic areas, and the worldwide spread of its mosquito vector, there is a pressing need for the development of therapeutic agents against CHKV. Therefore, in order to reduce the impact of this virus and the devastating polyarthralgia that it causes, we must develop new therapies and vaccines to treat persistent CHIKV infections. We will continue to determine the efficacy of anti-CHIKV immunotherapeutics. For the purposes of this application [redacted] lab will provide management and execution of all aspects of CHIKV studies. His lab has considerable experience with all facets of the proposed studies, including viral infections, processing of samples for viral load and dissemination, and characterization of the host immune response to the virus.

Excluded by Requester

Project Progress: There is no progress in this project yet as experiments are expected to begin March, 2015.

Funding Sources: Subcontract with Private Source

Percent P51 Dollars: 0%

Project Title: Induction of Robust T Cell Response to RRV-LANA

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Kaposi's sarcoma is the leading cancer observed in individuals with AIDS. In vivo models that can recapitulate most/all aspects of Kaposi's sarcoma-associated herpesvirus (KSHV) infection and disease are absolutely required to develop and test new vaccines to prevent the increase in KSHV infection and disease. Currently, the rhesus macaque (RM) model of KSHV-like disease fulfills most of these aspects, as animals experimentally infected with the simian immunodeficiency virus (SIV) and rhesus macaque rhadinovirus (RRV) develop B cell lymphoproliferative diseases (LPD) similar to AIDS patients co-infected with KSHV. Importantly, RM exhibit similar immunological responses to RRV infection, as humans infected with KSHV. Specifically, RM infected with RRV possess low CD4+ and CD8+ T cell responses to the virus, which could be one host factor that allows the virus to maintain a persistent infection. In this application, we intend to test the properties of the newly developed rhesus cytomegalovirus (RhCMV) vaccine vector system to stimulate a robust T cell response in RM that can recognize RRV latency-associated nuclear antigen (LANA). Once the immune responses to RRV LANA are characterized in vaccinated animals, the animals will be challenged with RRV and monitored for virus infection and persistence. The long-term objectives of this study aim to evaluate the ability of RhCMV vectors to induce a strong T cell response to RRV-LANA and whether this T cell immunity is capable of clearing RRV infection and persistence in a relevant model of KSHV infection.

Project Progress: We have found that the eight RM vaccinated with vectors encoding the RRV antigens (LANA, vFLIP and vcyclin) developed CD4+ and CD8+ T cell responses to the viral antigens, with the most abundant CD4+ and CD8+ T cell responses directed against LANA, followed by FLIP. RM vaccinated with the control RhCMV vector encoding SIV-gag did not develop CD4+ or CD8+ T cell responses to the RRV antigens. These data demonstrate that robust T cell responses to RRV antigens can be generated from RhCMV vectors. The next phase, which includes boosting and challenge, will be conducted in the coming year.

Funding Sources: NIH R21CA183608

Percent P51 Dollars: 0%

Project Title: Rhesus HHV-8 Homologue in AIDS-Related Malignancies

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: Viruses cause an array of disease manifestations ranging from acute respiratory disease, intestinal diarrhea, hemorrhagic fevers, hepatitis, cancer, and chronic autoimmune disease and, in some instances, death. One virus that was recently identified to be associated with cancer in humans in 1995 is human herpesvirus 8 (HHV8)/Kaposi's sarcoma-associated herpesvirus (KSHV). An accumulation of scientific evidence now substantiates HHV8 as the etiological agent responsible for classical and acquired immunodeficiency disease syndrome (AIDS)-related Kaposi's sarcoma (KS), as well as other lymphoproliferative disorders (LPDs) in immunocompetent and human immunodeficiency virus (HIV)-infected humans. Despite all of this scientific evidence it is difficult to fully understand how the virus causes disease without the ability to follow a natural infection. As such, alternative in vivo models that are readily accessible and can recapitulate HHV8 infection and associated disease are absolutely needed to identify viral determinants of pathogenesis and how these specific determinants, either viral open reading frames (ORFs) or other viral-encoded macromolecules are involved in HHV8-mediated pathogenesis. Here, we propose to utilize a closely related and relevant virus that can manifest similar biological outcomes in its natural host. The genome of the virus, referred to as rhesus rhadinovirus (RRV) has been characterized and shown to be essentially colinear and encodes most of the viral ORFs thought to be associated with pathogenesis. More importantly, in vivo studies show that RRV infection in its natural host recapitulates many, if not most of the properties of HHV8, including persistence and LPDs. The long term goals of the proposed research project are to better understand how HHV8 interacts with its host, utilizing RRV and experimental infection its natural host.

Project Progress: This grant was successfully renewed in 2014. We published the phenotype of the vCD200 nonsense virus (vCD200ns) and found very interesting results suggesting this virus exhibits higher viral loads. Disease potential is similar to wild-type virus, as both were found to be associated with a RRV+ lymphoma. As such, we conclude that vCD200 is an important viral gene that is not essential for growth or disease, but is likely to be involved in the regulation of the host immune response to the virus.

Funding Sources: NIH R01CA075922

Percent P51 Dollars: 0%

Project Title: Postmenopausal Monkey Resource

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester	Oregon Health & Science University
	University of California - Riverside
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Project Description: The Women's Health Initiative trial (WHI) has turned women's health at menopause into a minefield. The combined hormone arm (Prempro) was ended prematurely due to increased incidence of breast cancer, arteriosclerosis, stroke and cognitive decline. The WHI trial generated considerable controversy in the field because it was interpreted as an indictment of post-menopausal hormone replacement, when in fact, it did not study hormone replacement, which would have required use of the natural hormones, estradiol (E) and progesterone. WHI administered synthetic hormones a decade or more after menopause, raising the questions of whether bioidentical hormones are better and whether there is an optimal time frame for hormone therapy. Follow up studies, which have used natural hormones, have shown that indeed, they need to be administered at perimenopause, but the endpoints were limited to one or two systems. We hypothesize that estradiol (E) replacement will be beneficial when started immediately after ovariectomy/hysterectomy (Ovx), but delayed treatment will have no beneficial, or even adverse, effects on many of the systems under study. We propose to establish a postmenopausal monkey resource with aged Ovx rhesus monkeys on a Western Style Diet (WSD) and treated with placebo, immediate-E or delayed-E replacement. We will obtain longitudinal assessments of social behavior, activity, temperature, cognitive function, brain structure, immune function, fat accumulation, glucose metabolism and bone density. We will obtain postmortem assessments of coronary arteries, breast tissue, fat insulin sensitivity, and determine the cellular and molecular function of multiple neural systems.

Project Progress: We have already detected significant effects of ovariectomy with placebo or delayed E on glucose and insulin metabolism, as well as fat distribution. Proprietary Info

Proprietary Info

Funding Sources: NIH 5R24OD011895

Percent P51 Dollars: 0%

Project Title: Role of Serotonin in Mediating Stress-Induced Fertility

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester University of Pittsburgh

Project Description: The overall goal of this grant is to continue our studies to determine the mechanisms by which common life stresses (i.e., dieting, moderate exercise and psychological stress) impair activity of the reproductive axis and fertility. Female cynomolgus monkeys, which like women have 28-day menstrual cycles throughout the year, show individual differences in responsiveness to stress, with stress-sensitive animals rapidly developing stress-induced reproductive dysfunction, and stress-resilient animals maintaining normal menstrual cyclicity throughout stress exposure. The stress used for these studies is patterned after that documented in women with Functional Hypothalamic Amenorrhea (FHA; a clinical condition which accounts for as much as 30% of female infertility) in which monkeys are exposed to a mild psychological stress (moving to a new room) and a moderate metabolic stress (a 20% decrease in calorie intake and moderate running for an hour a day, five days a week). Monkeys that continue to ovulate for two stress cycles are classified as Highly Stress Resilient (HSR); monkeys that ovulate in the first stress cycle but not the second are classified as Medium Stress Resilient (MSR) and monkeys that do not ovulate in either stress cycle are classified as Stress Sensitive (SS).

Project Progress: Significant progress was made on the subcontract of this grant to ONPRC. The effect of stress on HSR and SS animals showed a significant increase in norepinephrine (NE) with little effect on serotonin. Moreover, stress increased KISS1 gene expression in both HSR and SS animals. We hypothesize that stress-induced NE can block the negative feedback effect of estradiol (E) on KISS1 gene expression. The competitive renewal application for this grant will be submitted for the February 5, 2015 deadline.

Funding Sources: NIH 5R01HD062618

Percent P51 Dollars: 0%

Project Title: Steroid Regulation of Serotonin in Male Macaques

Core Scientists Associated with Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The serotonin system governs many higher order neural functions that control the interaction and perception of an individual with their internal and external environment. As such, dysfunction of the serotonin system has been implicated in a wide variety of psychopathologies. It has been reasoned that androgens act on the serotonin system to reduce serotonin and thereby increase aggression. However, knowledge of the steroid receptor profile in serotonin neurons of male human and nonhuman primates is lacking and little is known of the actions of androgens on gene expression in serotonin neurons.

Project Progress: We have evidence that the dogma surrounding serotonin and aggression was wrong due to misguided interpretations of different compartments of the serotonin system. We discovered that androgens elevated serotonin related gene expression in a manner that would increase serotonin neurotransmission. In addition, we discovered estradiol (E) from aromatase metabolism of T was necessary for serotonin axonal transport. We found that androgens increased yawning, which we believe is an affiliative behavior and not a mild aggressive behavior. Serotonin neurons in male NHPs do not contain androgen receptors (AR). Rather ARs were located in neighboring neurons. However, serotonin neurons in male NHPs did contain ERα and ERβ. The competitive renewal for this application is due in which we will test our hypothesis regarding yawning and further examine locus ceruleus and hypothalamic neurotransmitters and peptides involved in aggressive behavior. In addition, we will identify the phenotype of the neurons that contain AR in the dorsal raphe.

Funding Sources: NIH 5R01MH086542

Percent P51 Dollars: 0%

Project Title: Effects of CG and VEGF on the Vasculature of the Primate Ovary and Uterus

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester

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

Project Description: Studies are proposed to examine the role of a critical local factor, vascular endothelial growth factor (VEGF) in the response to chorionic gonadotropin (CG) during controlled ovulation cycles (COS) in rhesus macaques, an excellent non-human primate model of women's reproductive health. The experiments proposed in this R21 application should discern between the VEGF-dependent and independent actions of CG resulting in early and late onset symptoms of ovarian hyperstimulation syndrome (OHSS). The contribution of CG-induced VEGF to induce the marked ovarian/systemic hyperpermeability associated with onset of OHSS has not been directly investigated in primates. Women with polycystic ovarian syndrome (PCOS~ approximately 5-10% of women in the USA) are at high risk for developing OHSS during COS for infertility treatments~ avoidance of OHSS during COS is a major concern for infertility specialists. To date, investigations into the relationship between vascular structure/function of reproductive tissues and actions of local angiogenic factors have been indirect or static in nature involving single observations after tissue removal. The PI has applied sensitive, minimally invasive techniques enabling repeated measurements of vascular structure-function in the ovaries and uterus of nonhuman primates. Contrast enhanced-Ultrasound (CE-US) and Dynamic Contrast Enhanced- Magnetic Resonance Imaging (DCE-MRI) protocols allow direct quantification of blood flow/volume and tissue permeability of reproductive tissues. Notably, it is possible to simultaneously apply the proposed novel imaging approaches to the uterus, as well as the ovary, to discern the VEGF-dependent versus-independent effects of CG on vascular dynamics in primates. In addition to quantifying the effects of VEGF neutralization on vascular function of reproductive tissues, effects on other angiogenic factors (angiopoietins, ANGPTs) will be quantified as possible therapeutic interventions for OHSS. The results of these experiments will guide future studies investigating novel molecules affecting both ovarian and uterine/systemic vascular function by both imaging and molecular methods. These techniques can be used to identify and evaluate specific therapeutic interventions for women at risk for OHSS and infertility.

Project Progress: Since the start of funding in July 2014, all protocols for DCE-MRI were verified and normal cycle control DCE-MRI and CE-US scanning sessions will be complete as of the middle of February 2015. Validation COS cycles determined that free VEGF is readily measured in follicular fluid aspirated at time of oocyte collection, but is undetectable in serum at any time. Therefore, subsequent ongoing protocols include administration of a VEGF neutralizing antibody Avastin both before ovulatory hCG bolus or five days after to evaluate the effects of VEGF neutralization on systemic permeability and reproductive tract vascular flow during COS. The preliminary data from these control and COS cycles will contribute to Pending Support

Pending Support

Funding Sources: NIH 1R21HD078819-01A1

Percent P51 Dollars: 0%

Project Title: Elucidating Clinically-Relevant Mechanisms of Aneuploidy Generation and Resolution in IVF Embryos

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: The loss and gain of whole chromosomes, or aneuploidy, occurs in a staggering 50-80% of human embryos at the cleavage-stage, is frequently mitotic in origin, and a major factor contributing to nominal *in vitro* fertilization (IVF) success and live birth rates. By combining karyotypic reconstruction of all cells in cleaving human embryos with dynamic assessment of cell cycle parameters predictive of successful embryo development, we recently demonstrated that chromosomally normal (euploid) embryos could be largely distinguished from aneuploid embryos by the 4-cell stage. The major goals of the current study is to use a multi-disciplinary approach that integrates non-invasive time-lapse imaging, novel gene silencing technologies and single cell epigenetic/transcriptional analyses to determine the potential mechanism(s) by which chromosomal abnormalities are generated during early rhesus embryogenesis. Collectively, we expect that the findings from this study will provide for significant translational applications to human IVF, including the potential to improve success rates for infertile couples.

Project Progress: Using a recently obtained time-lapse imaging system, we determined that rhesus pre-implantation embryos exhibit similar cell cycle parameter kinetics during the first three mitotic divisions as human embryos, but with Proprietary Info and are currently evaluating if developmental timing differences can be used to distinguish chromosomally normal and abnormal embryos. Using PRIMe-Seq, a program developed at ONPRC that utilizes a more complete genome build (*MacaM*) than the older publicly available iteration, 250 primers for specific rhesus genes were designed and tested in single embryos and cells. A distinct expression pattern between euploid and aneuploid embryos was established that is being used to identify additional candidate genes for further functional testing. We have also injected fertilized oocytes with control morpholinos to determine the concentration at which normal rhesus embryonic development proceeds for subsequent targeted gene silencing.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Elucidating Clinically-Relevant Mechanisms of Aneuploidy Generation and Resolution in IVF Embryos

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description:

Since the introduction of human *in vitro* fertilization (IVF) over 35 years ago, one of the major challenges has been to identify the embryo(s) most suitable for transfer and likely to result in a normal term pregnancy. Despite significant efforts to improve embryo selection techniques, the average live birth rate is still only ~30% per IVF cycle and one of the primary contributors to IVF failure is thought to be whole chromosomal abnormalities (aneuploidy) that arise during pre-implantation development. Recently, we demonstrated that a process called cellular fragmentation contributes to the increased incidence of aneuploidy at the cleavage-stage via containment of missing chromosomes within micronuclei or fragments. We also determined that unbalanced partial chromosomal losses and gains are detected in fragmented aneuploid embryos, but not euploid embryos, to suggest a relationship between sub-chromosomal instability and aneuploidy in the human embryo. Using a combination of live cell imaging and comprehensive chromosomal assessment, this study aims to elucidate the molecular basis of increased embryonic sub-chromosomal and whole chromosomal instability and its effects on primate pre-implantation development. Ultimately, the findings from this work will enhance our understanding of normal human embryogenesis and potentially improve IVF success whilst avoiding the adverse pregnancy outcomes associated with multiple embryo transfer.

Project Progress:

By closely examining the nuclear structure of cleavage-stage rhesus macaque embryos, we have determined that they exhibit a high frequency of multi- and micro-nucleation similar to what is observed in human embryos at this stage of development. Proprietary Info

Proprietary Info

Funding Sources: Proprietary Info

Percent P51 Dollars: 0%

Project Title: Mechanisms of Aneuploidy Generation and Correction in Pre-Implantation Embryos

Core Scientists Associated with the Project:
Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Project Description: Aneuploidy, or chromosomal abnormalities, is incredibly common at the cleavage-stage of pre-implantation in certain mammalian species. The mechanism by which this occurs and whether there are corrective means to overcome aneuploidy generation is unknown and the focus of the proposed studies. Our
Proprietary Info
Proprietary Info
Given the ethical limitations of human embryo research, we will utilize closely related nonhuman primate embryos to model human pre-implantation development. Humans and the rhesus macaque have similar frequencies of aneuploidy at the cleavage-stage, Proprietary Info and Proprietary Info in their DNA. Using a combination of time-lapse image, chromosomal and gene expression analysis, we will determine whether there are significant differences in Proprietary Info cellular behavior and chromosome dynamics between euploid and aneuploid primate embryos (Aim I). We will also test the function of rhesus Proprieta ry Info (Aim II) and if the addition of aneuploidy-selective compounds can assist in overcoming aneuploidy generation at this stage of development (Aim III). This work will greatly contribute to our knowledge of normal human embryogenesis as well as assist in the diagnosis and treatment of human reproductive failure.

Project Progress: Although whole genome amplification (WGA) and DNA labeling for Array-Comparative Genomic Hybridization (A-CGH) for aneuploidy detection has taken a considerable amount of time to troubleshoot, we are continuing to work with the manufacturer to adapt their microarray protocol for ploidy assessment in single rhesus cells as well as attempt a non-PCR-based technique called multiple displacement amplification (MDA) for WGA. We have designed and tested approximately 250 rhesus macaque primer sets to different gene families, including but not limited to, Proprietary Info
Proprietary Info
In evaluating Propriet ary Info specific antibodies for the assessment of gene silencing efficiency, we have observed a unique pattern of expression during rhesus pre-implantation development. Proprietary Info
Proprietary Info
Proprietary Info
Lastly, the addition of the aneuploidy-selective compounds to embryo culture media significantly improved blastocyst formation rates to suggest that it may also circumvent aneuploidy generation since aneuploid embryos often arrest prior to the blastocyst stage.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Primate Model of Mid-Gestation Ureaplasma in Utero Infection: Prevention of Neurologic Sequelae

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

University of Washington
Oregon Health & Science University
University of Nebraska Medical Center
Oregon Health & Science University
University of Alabama at Birmingham

Project Description: The objectives of this proposal are to assess the therapeutic effect of antenatal maternal antibiotic therapy in preventing or mollifying cerebral white matter damage in the neonate (as a consequence of prolonged U.parvum intra-amniotic infection, IAI) and to correlate neurobehavioral outcomes with neuropathologic findings of neonatal brain injury. Our hypothesis is that treatment of U.parvum IAI with a specific macrolide antibiotic, azithromycin (AZI) will mitigate fetal origins of cerebral white matter injury and decrease the severity of perinatal neurological impairment. We will utilize non-human primate model of IAI, with inoculation of U.parvum (serovar 1) at 105 days gestation. Our new approach will mimic the indolent nature of Ureaplasma spp. infections during human pregnancies by prolonging fetal exposure to these microorganisms and the resultant inflammatory milieu, with the potential for intensified brain injury. Fetal cardiovascular hemodynamic and regional circulatory changes in response to U.parvum IAI, and maternal therapy, will be monitored by Doppler ultrasonography and linked with magnetic resonance imaging (MRI) of the fetal brain during critical periods of development. Neurodevelopmental outcomes such as dysfunctional neuromuscular dexterity, neurobehavioral and cognitive abnormalities will be correlated with neuropathologic findings of perinatal white matter inflammation. A number of mechanistic endpoints will be ascertained that will aid in our understanding of the causal links among Ureaplasma infections, fetal inflammatory responses, and hemodynamic adaptations which portend cerebral white matter damage and neurological disabilities.

Project Progress: We have made considerable progress in our ability to ensure the survival of very immature and sick neonates with the provision of extensive respiratory support, assisted ventilation and nutritional support via central access. We have shown that infants exposed to *U. parvum* IAI require a higher level of clinical intervention compared to control and AZI-treated infants. Furthermore, cognitive and behavioral development in those infants whose mothers received antibiotic therapy is not compromised, suggesting the safety of antenatal antibiotic therapy and improved neonatal health.

Funding Sources: NIH 5R01HD069610

Percent P51 Dollars: 0%

Project Title: Extending the Interval of Action and Effectiveness of the Emergency Contraceptive Ulipristal Acetate

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Emergency contraception (EC) provides an option for women at risk for unintended pregnancy, including those that had intercourse without using any contraceptive method, those noting failure of their primary contraceptive method, and victims of sexual assault. The use of EC has risen steadily over the past decade, such that 10% of sexually active women reported using it at least once per year. Ulipristal acetate (UPA; ella™), a progesterone receptor antagonist that functions by inhibiting follicle rupture and release of a fertilizable egg, has emerged as an effective EC that prevents pregnancy even when taken up to five days after intercourse. At present, however, there is a significant gap in our understanding of why EC effectiveness drops dramatically when administered during or after the midcycle ovulatory luteinizing hormone (LH) surge. Our preliminary evidence indicates that the midcycle LH surge induces the expression of an enzyme within the ovulatory follicle that likely degrades UPA, possibly preventing it from inhibiting ovulation as well oocyte fertilization and embryo implantation. Thus, the molecular/biochemical studies included in this proposal will address the mechanism through which UPA efficacy diminishes post-LH surge, which in turn may lead to strategies whereby its contraceptive potential could be extended through the periovulatory interval into the period of implantation.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Identification of Intrafollicular Determinants Predictive of Oocyte & Embryo Developmental Potential

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The development of in vitro fertilization four decades ago has provided millions of infertile couples the opportunity to have children. Despite such remarkable advances in our understanding of reproductive physiology and its application toward the treatment of infertility, limitations in efficiency persist as measured by a low live birth rate. The success rate, approximately 35% for women under 37, has only marginally increased since in vitro fertilization appeared in the clinic. A major factor that limits its success is the use of subjective criteria for choosing which oocytes will be fertilized and which embryos that develop will be transferred back to the recipient. Thus, determining the molecular and cellular characteristics that define oocytes with the greatest potential to form embryos capable of yielding a healthy baby is of paramount importance. We hypothesize that in-depth metabolomic analysis of the follicular environment via collection of follicular fluid and the media obtained from embryo cultures shortly after fertilization, as well as non-invasive real-time imaging, will allow us to identify markers of optimal oocyte competency and embryonic developmental potential. Analysis of the follicular fluid and embryonic culture media metabolome will be accomplished through the use of state-of-the-art mass spectroscopy platforms, whereas real-time assessment of cell division parameters and embryo fragmentation will be assessed by recently developed, innovative live cell imaging techniques. These studies will be performed using a clinically relevant and experimentally tractable nonhuman primate model, the rhesus macaque. It is anticipated that the data obtained from these studies will identify molecular markers and cellular parameters that differentiate between oocytes with high versus low developmental potential, thereby limiting the unnecessary fertilization of oocytes unlikely to develop, implant into the uterus, and result in a normal term pregnancy.

Project Progress: This project was funded recently, within the previous 6 weeks. Thus, progress to date includes purchasing reagents and project planning.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Leukemia Inhibitory Factor As a Mediator of Primate Ovulation & Oocyte Maturation

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The processes occurring within the primate follicle resulting in the release of a mature ovum (ovulation) that fertilizes and undergoes subsequent embryonic development are incompletely defined. Systematic characterization of such events are necessary for advancing infertility treatments and developing novel, non-hormonal forms of contraception. In this regard, a genomic study conducted by the P.I. identified most, if not all, the genes whose expression increases through the rhesus macaque periovulatory interval following an ovulatory stimulus. Such mRNAs are likely involved in activities necessary for follicle rupture, which include the formation of a hyaluronan-rich extracellular matrix between cumulus cells and the loss of their cell-cell contacts (cumulus-oocyte expansion; C-OE), as well as the cytoplasmic and nuclear maturation of the oocyte required for subsequent fertilization and embryonic development. From the resultant database and additional studies, it was discovered that leukemia inhibitory factor (LIF) mRNA and protein increased in the follicle from undetectable levels before an ovulatory stimulus (human chorionic gonadotropin; hCG; 0 h controls) to peak values prior to (12 h post-hCG) and following ovulation (36 h post-hCG). Furthermore, mRNAs encoding downstream signaling components responsible for LIF action (glycoprotein 130, or gp130; janus kinase 1, or JAK1; signal transducer and activator of transcription 3, or STAT3) were highest in unruptured rhesus macaque follicles 12 h after hCG administration and those that had ovulated 36 h post-hCG. The mRNAs encoding both cell surface LIF binding proteins (LIF receptor, or LIFR; gp130) were further localized to isolated oocytes and granulosa cells.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: NIH 5R21HD072528

Percent P51 Dollars: 0%

Project Title: Somatostatin receptor antagonist effects on follicle development

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health & Science University

Project Description: The majority of evidence collected to date supports the idea that women are born with a finite number of eggs/oocytes that declines with age. The vast majority of this reserve is in the form of the primordial follicle, which is comprised of an oocyte surrounded by a single flattened layer of granulosa cells. When primordial follicles leave this quiescent state, the granulosa cells enlarge and begin to divide, while the oocyte increases in diameter. During each menstrual cycle, multiple primordial follicles undergo this irreversible transformation and begin further development and maturation once they enter such a growth phase. Shortly thereafter, one of the multiple follicles becomes dominant and is destined to ovulate, whereas the subordinate follicles are lost through the process of atresia. Current infertility treatments rely on the use of exogenous gonadotropins to stimulate the survival and development of numerous growing follicles, which then can be collected for fertilization and transfer back to the recipient. This strategy depends on sufficient numbers of growing post-primordial follicles that are responsive to exogenous FSH and LH since primordial follicles are insensitive to the growth-promoting activities of these hormones. Therefore, the rate-limiting step in current infertility treatments is the number of primordial follicles that transition into an activated or hormone responsive state. In some women, the numbers of primordial follicles that enter the growing pool are very few and result in failed infertility treatment cycles. In the mouse, a somatostatin receptor (SSTR) antagonist has been shown to promote activation of primordial follicles as well as subsequent follicle development, resulting in increased numbers of oocytes retrieved following ovarian stimulation. The current project will test if a similar effect can be observed in a nonhuman primate model.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: Center for development of non-surgical permanent contraception; primate testing contraceptive leads

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University

Project Description: Our long term goal is to develop a low-cost, nonsurgical approach to permanent female contraception in alignment with the Gates Global Program to improve human health by preventing unintended pregnancy. Although new methods of permanent female contraception (e.g. Essure) have been developed privately, these involve expensive technology and a high level of surgical training, and are not practical technologies to utilize in low resource settings. Our hypothesis is that increased funding for research in permanent contraception would yield one or more approaches that could be studied for feasibility and that a preferred option could then be developed for initial human clinical trials. To support this goal and further investigate our hypothesis, we proposed establishing an Oregon Center for Permanent Contraception Research (OPERM) at the Oregon National Primate Research Center (ONPRC) of the Oregon Health & Science University (OHSU). This project provides funding for planning of a center proposal that will include infrastructure improvements, animal resources, scientific support and research funds over a 5-year period of funding.

Project Progress: A scientific advisory board was established, and in May 2014 an Experts' Meeting on Nonsurgical Permanent Contraception was held. Research ideas were solicited, and a comprehensive application for the center was submitted. In November 2014, the new Oregon Permanent Contraception Research Center (OPERM) was established with a 3-year $5 million award from the Private Source

Private Source

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Development of a Center for Research in Permanent Contraception

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: Our long term goal is to develop a low-cost, nonsurgical approach to permanent female contraception in alignment with the Private Source to improve human health by preventing unintended pregnancy. Although new methods of permanent female contraception (e.g. Essure) have been developed privately, these involve expensive technology and a high level of surgical training, and are not practical technologies to utilize in low resource settings. Our hypothesis is that increased funding for research in permanent contraception would yield one or more approaches that could be studied for feasibility and that a preferred option could then be developed for initial human clinical trials. To support this goal and further investigate our hypothesis, we proposed establishing an Oregon Center for Permanent Contraception Research (OPERM) at the Oregon National Primate Research Center (ONPRC) of the Oregon Health & Science University (OHSU). This project provides funding for planning of a center proposal that will include infrastructure improvements, animal resources, scientific support and research funds over a 5-year period of funding.

Project Progress:

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Development of a Center for Research in Permanent Contraception

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: Our long term goal is to develop a low-cost, nonsurgical approach to permanent female contraception in alignment with the Gates Global Program to improve human health by preventing unintended pregnancy. Although new methods of permanent female contraception (e.g. Essure) have been developed privately, these involve expensive technology and a high level of surgical training, and are not practical technologies to utilize in low resource settings. Our hypothesis is that increased funding for research in permanent contraception would yield one or more approaches that could be studied for feasibility and that a preferred option could then be developed for initial human clinical trials. To support this goal and further investigate our hypothesis, we proposed establishing an Oregon Center for Permanent Contraception Research (OPERM) at the Oregon National Primate Research Center (ONPRC) of the Oregon Health & Science University (OHSU). This project provides funding for planning of a center proposal that will include infrastructure improvements, animal resources, scientific support and research funds over a 5-year period of funding.

Project Progress:

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Polidocanol Foam for Permanent Female Contraception

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: Our goal is to develop a low-cost, medical approach to permanent female contraception. Our prototype agent is polidocanol administered as foam. Building upon results from our Phase 1 Grand Challenges grant that demonstrated that polidocanol foam (PF) can block the fallopian tubes of rhesus macaques without causing adverse non-target effects, we proposed a series of experiments to optimize the technique with the goal of high (>99%) efficacy with a single treatment. We also proposed studying the use of doxycycline as an adjunctive sclerosing agent, and to assess efficacy as a function of menstrual cycle stage and contraceptive hormonal treatment. The best approach will be tested in a contraception experiment in baboons. Other objectives include studying perceptions of a new nonsurgical approach to permanent contraception in India, and the development of a delivery and verification system that could be used in human studies.

Project Progress: Studies in the baboon demonstrated that a single treatment approach with 5% PF could cause tubal obstruction. In 2014, evaluation of single treatment approaches to PF was completed and a contraception study initiated at the Southwest National Primate Center using the baboon model and the study is in progress.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Altered Nuclear Transfer

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester	Private Source

Project Description: The goal of this project is to generate important new insights concerning epigenetic factors in oocytes governing reprogramming following SCNT and formation and maintenance of the first two lineages in mammalian embryos, the ICM and trophectoderm (TE). Our main hypothesis is that experimental modulation of expression levels for key transcription factors in oocytes will prevent formation of the TE while enhancing the production of the ICM lineage and hence ESCs. These alterations should preclude the formation of an embryo while promoting and enhancing donor nucleus reprogramming required for the formation of a single lineage from which pluripotent ESCs can be established. We propose an iterative scheme, where the murine system will permit initial, rapid and cost-effective evaluation of potential candidate molecules. The most promising approaches will then be tested in the nonhuman primate system.

Project Progress: We demonstrate that, in contrast to *Oct4* role in the maintenance of pluripotency, maternal *Oct4* (oocyte) is not crucial for either the establishment of totipotency in embryos, or the induction of pluripotency in somatic cells using oocytes. However, we defined candidate reprogramming factors in mouse oocytes and 2-cell embryos and implicated *Bmi1, Hsf1, Brg1* and *Apobec1* as critical factors required for reprogramming.

Funding Sources: NIH R01HD059946

Percent P51 Dollars: 0%

Project Title: Histocompatible Primate Embryonic Stem Cells

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: The goal of this project is to generate important new insights concerning reprogramming of primate somatic cells to the pluripotent state employing somatic cell nuclear transfer (SCNT) and direct reprogramming approaches and to conduct comparative pluripotency assessments using expression profiling, genetic and epigenetic analysis and in vitro and in vivo differentiation assays. Our main hypothesis is that primate pluripotent cells experimentally derived using these two alternative approaches are equivalent to each other and to embryonic stem cells (ESCs) isolated from fertilized embryos. Another goal of this application is to evaluate, for the first time, the potential of monkey ESCs derived from fertilized or SCNT embryos and induced pluripotent (iPS) cells to generate chimeras upon injection into developing embryos.

Project Progress: We have shown that in addition to oocytes, cytoplasm of 2-cell mouse embryos also supports efficient reprogramming of transplanted somatic cell nuclei to pluripotent and totipotent stages. The cell cycle synchronization between the donor nucleus and recipient cytoplasm is the most critical parameter determining success. This discovery could aid efforts to generate autologous human ES cells for regenerative applications, as donated or discarded embryos are more accessible than unfertilized MII oocytes.

Funding Sources: NIH 5R01HD057121

Percent P51 Dollars: 0%

Project Title: Mitochondrial Gene Therapy

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Mutations in mitochondrial (mt)DNA are associated with a wide range of human diseases including premature aging, myopathies, neurodegenerative diseases, diabetes, cancer and infertility. In light of the fact that many of these disorders are dependent on the heteroplasmic state of the mtDNA and associated threshold effects, it is difficult to provide accurate genetic counseling based on preimplantation or prenatal genetic diagnoses. At present, there are no cures for mitochondrial disorders and available treatments only improve symptoms and slow disease progression. The main goal of this proposal is to generate important new insights concerning feasibility, efficacy and safety of novel reproductive options designed to minimize the occurrence of mtDNA- defects in a clinically relevant nonhuman primate model. Our main hypothesis is that mtDNA can be efficiently replaced by a novel approach, i.e., spindle transfer (ST) in mature metaphase II (MII) oocytes without interfering with subsequent nucleo-mtDNA compatibility and developmental competence. Our preliminary studies demonstrate the feasibility and efficacy of this approach in a nonhuman primate model. We hypothesize that reconstructed oocytes produced after spindle transfer will be nearly homoplasmic, capable of supporting normal fertilization and competent for full term development.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: NIH 5R01HD063276

Percent P51 Dollars: 0%

Project Title: Evaluation of a new Intra-Uterine System (IUS) in cynomolgus macaques

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Our goal is to develop a new intrauterine system (IUS) for the purpose of contraception in women. Unintended pregnancies and their consequences on health are widely recognized as serious public health issues worldwide. Contraception can greatly decrease unwanted and unplanned pregnancies and is thereby a major benefit to women's health. Many contraceptive methods have the disadvantage of having low efficacy, requiring very high user compliance, or being non-reversible. Intrauterine contraceptives are reversible and show very high contraceptive efficacy because they combine a very effective mechanism of action and no risk for use-related failures. Hormone -releasing IUS are exceptional contraceptives, but use of hormone releasing IUS is not acceptable to many women. Non-medicated IUDs, like the Lippes Loop or copper-releasing IUDs, have the drawback of increased menstrual periods, menstrual blood loss and increased irregular bleeding. Prostaglandins are key regulators of uterine physiology including menses and are involved in uterine pathology. Inhibitors of prostaglandin synthesis (COX inhibitors: e.g. indomethacin) are effective in reducing menstrual blood loss associated with IUD use. Therefore, we propose that administration of these drugs via IUS may provide the greatest protection against unwanted uterine bleeding in IUS users. Moreover, the amount of drug needed to block bleeding locally, within the uterus, is expected to be too low to exert unwanted systemic effects. Our plan is to create a new intrauterine contraceptive system for women that have no influence on the natural menstrual cycle or menstrual bleeding. The proposed IUS under development in nonhuman primates would maintain normal reproductive hormone profiles, menstrual bleeding patterns, and minimize irregular or breakthrough bleeding.

Project Progress: Medicated and non-medicated IUS have been created for evaluation in our NHP menstruation animal model.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: A macaque model for endometriosis induced pelvic pain and infertility

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Nonhuman primates (NHPs) constitute the most suitable animals for preclinical studies on endometriosis. We demonstrated that endometriosis can be created by inoculating menstrual endometrium in artificially-cycled hormone treated rhesus macaques. In Specific Aim 1 we propose to refine and validate a protocol for creating endometriosis in naturally cycling macaques. In Specific Aim 2, we will document the growth of induced endometriotic lesions and assess the effects of lesion abundance and size on the presentation of pain in the animals. Based on our pilot data, we designed a pain and discomfort scoring system, which will be combined with activity monitoring, to quantify discomfort in animals with induced disease and guide the prescription of pain relief for the animals. Like women, NHPs with endometriosis are expected to display reduced fertility compared to endometriosis-free subjects. In Specific Aim 3, we will assess the effect of the induced lesions on fertility. This research will provide a definitive assesment of techniques required to create endometriosis in the macaque for future studies, and characterize the progression of the disease with specific emphasis on assessment of pain and infertility in this useful NHP model.

Project Progress: Animals with induced endometriosis were fitted with activity monitors and scored for pain and discomfort associated with the induced disease. Animals with disease were monitored for a year and 50% showed evidence of discomfort. Control animals were pain free. Endometriotic and eutopic endometrium have been collected for analysis for mediators of inflammation.

Funding Sources: NIH 1R21OD012377

Percent P51 Dollars: 0%

Project Title: A modified macaque model for endometriosis: Inoculation of menstrual endometrium

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Project Description: Endometriosis is the presence of endometrium-like tissue outside of the uterine cavity. In previous studies we created an animal model for endometriosis by surgically transplanting endometrium to peritoneal sites in rhesus macaques. This method, however, required that the animals undergo hysterotomy, a major invasive abdominal surgery. Our goal in this study was to create a less invasive method of creating ectopic endometrium in macaques. We hypothesized that seeding of menstrual endometrium by laparoscopy would be less invasive and a superior approach compared to surgical transplantation because it closely resembles the reported pathogenesis of the disease. However, the "inoculation" method for creating ectopic endometrium had not been reliably developed in macaques. Therefore, this study had two aims. Aim 1 was to develop an endometrial seeding technique for use with rhesus macaques. Aim 2 was to analyze ectopic endometrium created in Aim 1 by histological and immunocytochemical methods.

Project Progress: Naturally cycling and artificially cycled macaques were compared as models for induced endometriosis. Seeding of menstrual debris was equally effective in artificially and naturally cycling animals. Immunohistochemistry revealed that he induced lesions contained endometrium like glands and stroma morphologically identical to naturally occurring endometriosis in the macaque.

Funding Sources: Oregon Health & Science University

Percent P51 Dollars: 0%

Project Title: Progestin Releasing Intra-Uterine Systems (IUS) and Vaginal Rings

Core Scientists Associated with the Project:
Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:
Excluded by Requester | Private Source

Project Description: Our broad goal is to develop new methods of contraception. Levonorgestrel (LNG) is a progestin used as a contraceptive in the Mirena IUS (intrauterine system). Contraception with LNG often results in uterine breakthrough bleeding, an undesirable outcome. The goal of this study is develop new progestin-releasing IUS and vaginal rings that cause less uterine bleeding as side effects. The new devices will be loaded with either Proprietary Info (a new progestin) or a combination of LNG plus indomethacin. LNG is a 9-nortestosterone derived progestin with long serological half-life (~36 hours) and a significant affinity (58% relative to testosterone) for the androgen receptor (AR). Proprietary Info has a short half-life (<30 minutes) and no known affinity for AR. We hypothesize that the androgenic effects combined with prolonged exposures could mediate events associated with bleeding. It has also been reported that breakthrough bleeding is associated with endometrial inflammation, and our preliminary data indicate that blockade of prostaglandin E2 signaling can reduce total menstrual blood loss. Intrauterine administration of an anti-inflammatory drug (indomethacin; an NSAID) could improve bleeding profile without affecting progestogenic actions of the progestin on the reproductive tract. The study has two specific aims. In Aim 1, we will assess IUS and vaginal administration of LNG and Proprietary Info In Specific Aim 2, we will investigate a combination progestin plus indomethacin-releasing IUS. .

Project Progress: Treatment with a combination IUS that released LNG and indomethacin produces fewer unwanted bleeding days compared to IUS that released LNG alone. LNG releasing IVR, were found to be contraceptive, whereas Proprietary Info releasing IVR failed to provide contraceptive protection.

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Contraception by Blockade of Periovulatory Events in Primates

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

University of Minnesota
Oregon Health & Science University
Oregon Health & Science University
University of South Florida
Oregon Health & Science University
Oregon Health & Science University

Project Description: The Oregon National Primate Research Center (ONPRC), Oregon Health & Science University (OHSU) continues a U54 Contraceptive Development Research Center that targets the discovery and development of novel contraceptive agents that prevent one or more periovulatory events in adult, female primates during the menstrual cycle. Three research projects and one animal core will utilize Old World (macaque) monkeys to generate new information and proof-of-concept regarding potential modalities for preventing oocyte fertilization, and hence fertility, in women. Project I, "Control of Oocyte Maturation" will address the hypothesis that novel follicle (granulosa) cell- and oocyte-derived proteins control nuclear and cytoplasmic maturation of the oocyte, and can be exploited to prevent timely egg maturation. Project II, "Control of Follicle Rupture and Cumulus-Oocyte Activities" will test whether specific antagonists of select granulosa- or oocyte-derived proteins disrupt cumulus-oocyte expansion or ovulation, and hence egg. Project III, "Control of Gamete Transport and Fertilization" will investigate reversible and nonreversible methods to locally prevent sperm and oocyte transport in the reproductive tract, and hence fertilization and fertility in female macaques. Based on progress in the prior grant interval and continued basic discovery and elucidation of drug action, promising agents will be tested in the Nonhuman Primate Contraceptive Core for contraceptive efficacy, reversibility and side effects. Collaborations with colleagues at the University of Minnesota and Private Source will facilitate drug discovery, nonhuman primate testing, and ultimately early (Phase I) clinical trials.

Private Source

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: NIH 5U54HD055744

Percent P51 Dollars: 0%

Project Title: Hyperandrogenemia, Diet and Female Reproductive Health

Core Scientists Associated with the Project:

Excluded by Requester

Other Affiliate Scientists with Institutional Affiliation:

Excluded by Requester	Oregon Health & Science University
	University of Pittsburgh
	University of California at Los Angeles
	University of California at Los Angeles
	University of California at Los Angeles
	Oregon Health & Science University
	Oregon Health & Science University
	University of California at Los Angeles
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University
	Oregon Health & Science University

Project Description: The Oregon National Primate Research Center (ONPRC) at the Oregon Health & Science University (OHSU) was awarded a Specialized Cooperative Center in Reproduction and Infertility Research (U54 SCCPIR), now categorized as a National Center for Translational Research in Reproduction and Infertility (P50 NCTRI), that addresses the effects of hyperandrogenemia and obesity on female reproductive health. An interdisciplinary, translational program is designed to discern between the effects of excess androgen exposure and metabolic changes due to a typical Western-style diet (WSD, high fat and fructose content) on: (1) the hypothalamus-pituitary-ovary-reproductive tract axis, as well as adipose tissue; (2) the impact on fertility; and (3) if the treatment effects are reversible. The NCTRI includes a nonhuman primate (NHP) Core that maintains four treatment groups of young, female rhesus monkeys (controls, testosterone or T-treated, WSD-treated, and T + WSD) for four years culminating in a fertility trial. In year 05, the reversibility of T and WSD actions will be examined. Three research projects (Project I: Metabolic and Neuroendocrine Responses to Androgen and Diet; Project II: Ovarian and Uterine Responses to Androgen and Diet; Project III: Effects of Androgen and Diet on Adipose Function) utilize the NHP Core monkeys. Project IV, Androgen Excess in Adipogenic Dysfunction in PCOS Women, studies a specific population of lean women with polycystic ovarian syndrome (PCOS). The NCTRI also includes Administrative and Outreach Cores.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: NIH 1U54HD071836

Percent P51 Dollars: 0%

Project Title: Progesterone Receptor and Action in the Primate Ovary

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester — Oregon Health & Science University

Project Description: The goal of this research is to understand the mechanisms whereby luteinizing hormone (LH) either directly, or indirectly via locally synthesized steroids, regulates the structure-function of the peri-ovulatory follicle or corpus luteum (CL) in primates during the menstrual cycle. Recent evidence suggests that specific genomic progesterone receptor isoforms (PGR-A and -B) regulate different activities in target tissue; and the discovery of nongenomic PGR membrane components (PGRMC1 and 2) adds another dimension to possible P actions in the ovary. Likewise, the PI's evidence that LH and P regulate expression of one estrogen receptor isoform (ER2) reintroduces the concept of local E action in the primate CL. Finally, recent whole genome analyses of the dynamics of the transcriptome in the macaque ovary provide the basis for manipulative studies to unravel the cellular and molecular events, prominently in immune cell-mediated processes, that are LH-dependent and steroid (P or E)-dependent in the primate ovulatory follicle or CL.

Project Progress: Injection of RNAi to the genomic PR into the preovulatory follicle prevented the rise in serum progesterone levels, expression of PR protein in follicle cells and blocked follicle rupture plus oocyte release. Thus, progesterone signaling through the genomic PR is required for ovulation and hence fertility in primates. Also, neutrophils/macrophages, but not natural killer cells, isolated from the corpus luteum near the end of the menstrual cycle secreted numerous cytokines, particularly MCP-1 and MDC. These cytokines form immune cells may be critical for regression of the corpus luteum, and hence initiation of the next, potentially fertile, menstrual cycle. This information is relevant to improving or controlling fertility in women.

Funding Sources: NIH 5R01HD020869

Percent P51 Dollars: 0%

Project Title: Activin A Expression and Function during Primate Follicular Development

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester Oregon Health and Science University

Project Description: Activin A, a member of the TGFβ family of paracrine factors, plays a major role during follicular development. Previous data suggest that activin A effects in the ovary may vary as function of stage of follicular development. Thus, studies are proposed to understand the dynamic expression of activin A in the primate ovary, as well as the role and function of actvin A in controlling ovarian follicular development and oocyte maturation in vitro. The Specific Aims include (1) evaluate the role of activin A in regulating primate follicle growth and steroidogenic potential; (2) examine the direct actions of activin A on primate follicle survival/growth, steroidogenic potential, and oocyte maturation in vitro; and (3) investigate activin A-regulated expression of genes that are related to follicular development and oocyte quality in antral follicles, as well as test the potential of activin A to serve as a biomarker to predict follicular development and oocyte competence during in vitro follicle maturation.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources Private Source

Percent P51 Dollars: 0%

Project Title: Oregon BIRCWH: Scholars in Women's Health Research Across the Lifespan

Core Scientists Associated with the Project:

Excluded by Requester

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health & Science University
Oregon Health & Science University

Project Description: Our overarching goal is to create a stimulating and nurturing environment for junior faculty to develop into leading interdisciplinary research scientists in women's health; we plan to maintain four scholars/year. Over the last two grant cycles, the Oregon BIRCWH has trained a diverse cadre of researchers who advanced basic, biomedical, behavioral, and translational research in women's health across the lifespan. OHSU provides a resource-rich environment whose culture promotes interdisciplinary team science. The Oregon BIRCWH has been successful with scholars receiving approximately $40 million dollars in research funding, publishing over 200 publications, and assuming national leadership positions. The BIRCWH is the only K12 career development program at OHSU specifically dedicated to career development in women's health research. The institution is deeply committed to the BIRCWH, providing each scholar up to 50 hours of statistical support, tuition free education through the Human Investigations Program, and direct financial contributions to support their research. We will continue the existing best practices that have made our program highly successful.

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: NIH 5K12HD043488

Percent P51 Dollars: 0%

Project Title: Efficacy and Pharmacokinetics of Proprietary Info to Male Rhesus Macaques

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health and Science University

Private Source

Project Description: World Health Organization statistics show that 122 million planned pregnancies occur worldwide per year. Yet, in spite of the availability of many different female contraceptive methods and of condoms, an additional 87 million pregnancies were unintended (representing 42% of all pregnancies), and 46 million pregnancies were terminated by abortion. In the U.S., the unintended pregnancy rate is 49% of all births, and about half of these are terminated by abortion. Surprisingly, in 50% of unintended pregnancies, women reported using a contraceptive. Thus, the development of novel, reversible, oral male contraceptive agents has been identified as a major advance needed to address this worldwide reproductive health issue by the National Institutes of Health, Institute of Medicine, and World Health Organization. In order to move any new male contraceptive agent into human clinical trials, efficacy and safety must be demonstrated in at least two non-primate species and in nonhuman primates. Proprietary Info

Proprietary Info

Project Progress: Proprietary Info

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

Project Title: Studies of Cryopreservation of Ovarian Function from Anti-Cancer Therapy (PIS)

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Oregon Health and Science University
Oregon Health and Science University

Project Description (one paragraph): The 5-year survival rate for adolescents and young women of reproductive ages is 82%. Cancer treatments can deplete follicles in the ovary leading to premature ovarian failure and infertility. Ovarian tissue cryopreservation is the only option for fertility preservation in prepubertal cancer patients or those who require immediate cancer therapy. The goal is to transplant the tissue back to the patient once she desires fertility. A rhesus monkey model was recently developed wherein ovarian cortical tissue (fresh or cryopreserved) is transplanted heterotopically (i.e. subcutaneously in the arm or abdomen) and then excised to identify the status of follicles developing within the transplants. Because the ovarian cortical tissue needs time to re-establish a blood supply, it is important to know how many follicles survive. Studies in mice and nohuman primates revealed that ovarian follicles and oocytes are protected from radiation damage by intra-ovarian administration of the anti-apoptotic factors sphingosine-1-phosphate (S1P), or its agonist, FTY720. Therefore, FTY720 treatment of cortical tissue prior to transplantation may prevent follicular apoptosis. The cleaved form of caspase-3 (cysteinyl aspartate-specific protease) initiates programmed cell death (apoptosis) and would be evident in dying follicles. While important for primordial follicle survival and growth in rodents, little is known about c-kit in the primate ovary. The presence of c-kit would indicate surviving follicles. To identify the status of follicles in transplanted ovarian tissue, the localization of cleaved caspase-3 and c-kit was determined in the ovarian cortex within one week after transplantation, and in the presence or absence of FTY720.

Project Progress: More ($P<0.05$) follicles were observed on day 4 than 7 regardless of treatment. Cleaved caspase-3 was not localized to preantral follicles of the ovarian cortex, suggesting that mechanisms other than apoptosis (i.e., autophagy, DNA damage, and/or necrosis) cause follicle loss post-transplantation. FTY720 did not maintain the cohort of preantral follicles after transplantation, and did not appear to directly or indirectly (via vasculature or stromal integrity) protect follicles against apoptosis. C-kit localization in preantral follicles after transplantation suggests this is an indicator of healthy follicles. In contrast to rodents where oocyte c-kit is only localized to oocytes, c-kit in preantral follicles was observed in both oocytes and granulosa cells. Preserving follicles post-transplantation may require agents other than FTY720, such as those that stimulate angiogenesis. Further improvement in transplantation of ovarian cortex for fertility preservation in cancer survivors is warranted.

Funding Sources: Private Source

Percent P51 Dollars: 0%

G. 1 (SpecialReportingRequirements.pdf)

Project Title: Proprietary Info aneuploidy-reduction pill in older women

Core Scientists Associated with the Project:

Affiliate or Visiting Scientists with Institutional Affiliation:

Excluded by Requester

Private Source

Oregon Health and Science University

Project Description: Maternal age-related oocyte (egg) aneuploidy is the main cause of congenital birth defects. Although impressive progress has been made in understanding how aneuploidies arise in oocytes, little is known about providing medical interventions to reduce them. The goal of our study is to develop a pill that could reduce aneuploidy in older women desiring to become mothers. We demonstrated that chemically-induced deficiency of the enzyme, ornithine decarboxylase (ODC), during ovulation increases oocyte aneuploidies in young mice. Older mice exhibit aging-related ODC deficiency and high incidence of oocyte aneuploidies, which can be rescued by peri-ovulatory oral supplementation with putrescine (a direct product of ODC)[Proprietary Info]

Proprietary Info

Project Progress Proprietary Info

Proprietary Info

Funding Sources: Private Source

Percent P51 Dollars: 0%

3. INFRASTRUCTURE IMPROVEMENTS

Replacement-drinking water lines for all corrals	44,000
New electrical service for Colony Building	97,000
Rebuild chiller #2	69,000
Replacement-2 water heaters, ASB 3 Building	22,000
DCM -80 Freezer, SPF lab	18,000
Autoclave - Research Building	39,000
Renovation for autoclave - Research building	3,777
Roof repair - Research Building	3,850
Supply and exhaust airflow reductions - ASB2	4,000
(50) Squeeze-back and perch additions, 4.5 sqft cages	6,250
(50) Squeeze-back and perch additions	6,250
(12) SS water supply lines	,428
(2) Mobile vertical tunnels	6,500
Concrete pads and drains for Corral 2 feed area	7,545
Heating for Feed Area 7	7,000
-80C freezer for Serology	4,400
Sub-total Expense	**500,000**

4. PUBLICATIONS

Publications Reported for this Reporting Period

NIH Public Access Compliance	Citation
PMC Journal In Process	Excluded by Requester Direct actions of androgens on the survival, growth and secretion of steroids and anti-Müllerian hormone by individual macaque follicles during three-dimensional culture. Hum Reprod. 2015 Mar;30(3):664-74. PubMed PMID: 25567619.
In process at NIHMS	Excluded by Requester et al. Nicotinic receptors in non-human primates: Analysis of genetic and functional conservation with humans. Neuropharmacology. 2015 Feb 7;PubMed PMID: 25661700; NIHMSID: NIHMS661887. [Epub ahead of print]
In process at NIHMS	Excluded by Requester et al. 3D structure tensor analysis of light microscopy data for validating diffusion MRI. Neuroimage. 2015 Feb 7;PubMed PMID: 25665963; NIHMSID: NIHMS662062. [Epub ahead of print]
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Composite Application Budget Summary

Categories	Budget Period
Salary, Wages and Fringe Benefits	7,646,486
Equipment	500,000
Travel	49,582
Participant/Trainee Support Costs	0
Other Direct Costs (excluding Consortium)	1,767,031
Consortium Costs	0
Direct Costs	9,963,099
Indirect Costs	2,649,670
Total Direct and Indirect Costs	12,612,769

Component Budget Summary

Components	Categories	Budget Period
8016-001 (Admin Core)	Salary, Wages and Fringe Benefits	194,642
	Equipment	0
	Travel	6,400
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	9,923
	Consortium Costs	0
	Direct Costs	210,965
	Indirect Costs	59,070
TOTALS	Total Direct and Indirect Costs	270,035
6123-001 (Core)	Salary, Wages and Fringe Benefits	49,169
	Equipment	0
	Travel	675
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	31,608
	Consortium Costs	0
	Direct Costs	81,452
	Indirect Costs	22,807
TOTALS	Total Direct and Indirect Costs	104,259
6122-002 (Core)	Salary, Wages and Fringe Benefits	61,234
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	25,704
	Consortium Costs	0
	Direct Costs	86,938
	Indirect Costs	24,343
TOTALS	Total Direct and Indirect Costs	111,281
6121-003 (Core)	Salary, Wages and Fringe Benefits	61,148
	Equipment	0
	Travel	237
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	21,922
	Consortium Costs	0
	Direct Costs	83,307
	Indirect Costs	23,326
TOTALS	Total Direct and Indirect Costs	106,633
6120-004 (Core)	Salary, Wages and Fringe Benefits	99,930
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	138,987
	Consortium Costs	0
	Direct Costs	238,917
	Indirect Costs	66,897
TOTALS	Total Direct and Indirect Costs	305,814

6127-005 (Core)	Salary, Wages and Fringe Benefits	291,755
	Equipment	0
	Travel	3,880
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	61,485
	Consortium Costs	0
	Direct Costs	357,120
	Indirect Costs	99,994
TOTALS	Total Direct and Indirect Costs	457,114
6126-006 (Core)	Salary, Wages and Fringe Benefits	112,185
	Equipment	0
	Travel	500
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	10,960
	Consortium Costs	0
	Direct Costs	123,645
	Indirect Costs	34,621
TOTALS	Total Direct and Indirect Costs	158,266
6125-007 (Core)	Salary, Wages and Fringe Benefits	188,535
	Equipment	0
	Travel	525
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	56,091
	Consortium Costs	0

	Direct Costs	245,151
	Indirect Costs	68,642
TOTALS	Total Direct and Indirect Costs	313,793
6124-008 (Core)	Salary, Wages and Fringe Benefits	115,023
	Equipment	0
	Travel	1,260
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	56,625
	Consortium Costs	0
	Direct Costs	172,908
	Indirect Costs	48,414
TOTALS	Total Direct and Indirect Costs	221,322
6115-009 (Core)	Salary, Wages and Fringe Benefits	744,491
	Equipment	0
	Travel	2,400
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	43,712
	Consortium Costs	0
	Direct Costs	790,603
	Indirect Costs	221,369
TOTALS	Total Direct and Indirect Costs	1,011,972
6114-010 (Core)	Salary, Wages and Fringe Benefits	271,395
	Equipment	0
	Travel	1,500

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	10,864
	Consortium Costs	0
	Direct Costs	283,759
	Indirect Costs	79,453
TOTALS	Total Direct and Indirect Costs	363,212
6113-011 (Core)	Salary, Wages and Fringe Benefits	186,561
	Equipment	0
	Travel	750
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	44,334
	Consortium Costs	0
	Direct Costs	231,645
	Indirect Costs	64,861
TOTALS	Total Direct and Indirect Costs	296,506
6112-012 (Core)	Salary, Wages and Fringe Benefits	543,836
	Equipment	0
	Travel	3,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	142,024
	Consortium Costs	0
	Direct Costs	688,860
	Indirect Costs	192,881
TOTALS	Total Direct and Indirect Costs	881,741

6119-013 (Core)	Salary, Wages and Fringe Benefits	13,122
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	49,046
	Consortium Costs	0
	Direct Costs	62,168
	Indirect Costs	17,407
TOTALS	Total Direct and Indirect Costs	79,575
6118-014 (Core)	Salary, Wages and Fringe Benefits	149,577
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	25,500
	Consortium Costs	0
	Direct Costs	175,077
	Indirect Costs	49,022
TOTALS	Total Direct and Indirect Costs	224,099
6117-015 (Core)	Salary, Wages and Fringe Benefits	173,220
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	221,152
	Consortium Costs	0

	Direct Costs	396,372
	Indirect Costs	110,984
TOTALS	Total Direct and Indirect Costs	507,356
6116-016 (Core)	Salary, Wages and Fringe Benefits	99,863
	Equipment	0
	Travel	880
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	32,680
	Consortium Costs	0
	Direct Costs	133,423
	Indirect Costs	37,358
TOTALS	Total Direct and Indirect Costs	170,781
6111-017 (Core)	Salary, Wages and Fringe Benefits	2,071,287
	Equipment	0
	Travel	5,100
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	196,627
	Consortium Costs	0
	Direct Costs	2,273,014
	Indirect Costs	636,444
TOTALS	Total Direct and Indirect Costs	2,909,458
6104-018 (Core)	Salary, Wages and Fringe Benefits	92,915
	Equipment	0
	Travel	450

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	26,056
	Consortium Costs	0
	Direct Costs	119,421
	Indirect Costs	33,438
TOTALS	Total Direct and Indirect Costs	152,859
6105-019 (Core)	Salary, Wages and Fringe Benefits	12,191
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	16,538
	Consortium Costs	0
	Direct Costs	28,729
	Indirect Costs	8,044
TOTALS	Total Direct and Indirect Costs	36,773
6106-020 (Core)	Salary, Wages and Fringe Benefits	21,839
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	705
	Consortium Costs	0
	Direct Costs	22,544
	Indirect Costs	6,312
TOTALS	Total Direct and Indirect Costs	28,856

6107-021 (Core)	Salary, Wages and Fringe Benefits	226,126
	Equipment	0
	Travel	7,280
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	40,387
	Consortium Costs	0
	Direct Costs	273,793
	Indirect Costs	76,662
TOTALS	Total Direct and Indirect Costs	350,455
6102-022 (Core)	Salary, Wages and Fringe Benefits	191,148
	Equipment	0
	Travel	1,395
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	40,188
	Consortium Costs	0
	Direct Costs	232,731
	Indirect Costs	65,165
TOTALS	Total Direct and Indirect Costs	297,896
6103-023 (Core)	Salary, Wages and Fringe Benefits	195,818
	Equipment	0
	Travel	1,050
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	208,972
	Consortium Costs	0

	Direct Costs	405,840
	Indirect Costs	113,635
TOTALS	Total Direct and Indirect Costs	519,475
6136-001 (Other)	Salary, Wages and Fringe Benefits	122,959
	Equipment	0
	Travel	10,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	48,000
	Consortium Costs	0
	Direct Costs	180,959
	Indirect Costs	50,669
TOTALS	Total Direct and Indirect Costs	231,628
6134-002 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	500,000
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	500,000
	Indirect Costs	0
TOTALS	Total Direct and Indirect Costs	500,000
6135-003 (Other)	Salary, Wages and Fringe Benefits	18,412
	Equipment	0
	Travel	300

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	825
	Consortium Costs	0
	Direct Costs	19,537
	Indirect Costs	5,470
TOTALS	Total Direct and Indirect Costs	25,007
6133-004 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	200,000
	Consortium Costs	0
	Direct Costs	200,000
	Indirect Costs	56,000
TOTALS	Total Direct and Indirect Costs	256,000
6130-001 (Project)	Salary, Wages and Fringe Benefits	313,049
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	1,068
	Consortium Costs	0
	Direct Costs	314,117
	Indirect Costs	87,953
TOTALS	Total Direct and Indirect Costs	402,070

6131-002 (Project)	Salary, Wages and Fringe Benefits	61,144
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	600
	Consortium Costs	0
	Direct Costs	61,744
	Indirect Costs	17,288
TOTALS	Total Direct and Indirect Costs	79,032
6128-003 (Project)	Salary, Wages and Fringe Benefits	522,134
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	750
	Consortium Costs	0
	Direct Costs	522,884
	Indirect Costs	146,408
TOTALS	Total Direct and Indirect Costs	669,292
6129-004 (Project)	Salary, Wages and Fringe Benefits	441,778
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	698
	Consortium Costs	0

	Direct Costs	442,476
	Indirect Costs	123,893
TOTALS	Total Direct and Indirect Costs	566,369
6132-005 (Project)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	3,000
	Consortium Costs	0
	Direct Costs	3,000
	Indirect Costs	840
TOTALS	Total Direct and Indirect Costs	3,840
TOTALS		**12,612,769**

Categories Budget Summary

Categories	Components	Budget Period
R&R Budget - Senior/Key Person Funds Requested	8016-001 (Admin Core)	91,063
	6123-001 (Core)	45,007
	6122-002 (Core)	49,512
	6121-003 (Core)	15,480
	6120-004 (Core)	15,479
	6127-005 (Core)	23,677
	6126-006 (Core)	16,530
	6125-007 (Core)	59,404
	6124-008 (Core)	9,398
	6115-009 (Core)	69,921
	6114-010 (Core)	47,590
	6113-011 (Core)	43,365
	6112-012 (Core)	96,334
	6119-013 (Core)	7,685
	6118-014 (Core)	0
	6117-015 (Core)	98,671
	6116-016 (Core)	15,477
	6111-017 (Core)	65,753
	6104-018 (Core)	22,226
	6105-019 (Core)	0
	6106-020 (Core)	0

	6107-021 (Core)	103,543
	6102-022 (Core)	35,543
	6103-023 (Core)	16,340
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	58,198
	6131-002 (Project)	23,481
	6128-003 (Project)	35,029
	6129-004 (Project)	58,581
	6132-005 (Project)	0
TOTALS		1,123,287
R&R Budget - Other Personnel Funds Requested	8016-001 (Admin Core)	103,579
	6123-001 (Core)	4,162
	6122-002 (Core)	11,722
	6121-003 (Core)	45,668
	6120-004 (Core)	84,451
	6127-005 (Core)	268,078
	6126-006 (Core)	95,655
	6125-007 (Core)	129,131
	6124-008 (Core)	105,625
	6115-009 (Core)	674,570
	6114-010 (Core)	223,805

	6113-011 (Core)	143,196
	6112-012 (Core)	447,502
	6119-013 (Core)	5,437
	6118-014 (Core)	149,577
	6117-015 (Core)	74,549
	6116-016 (Core)	84,386
	6111-017 (Core)	2,005,534
	6104-018 (Core)	70,689
	6105-019 (Core)	12,191
	6106-020 (Core)	21,839
	6107-021 (Core)	122,583
	6102-022 (Core)	155,605
	6103-023 (Core)	179,478
	6136-001 (Other)	122,959
	6134-002 (Other)	0
	6135-003 (Other)	18,412
	6133-004 (Other)	0
	6130-001 (Project)	254,851
	6131-002 (Project)	37,663
	6128-003 (Project)	487,105
	6129-004 (Project)	383,197
	6132-005 (Project)	0
TOTALS		6,523,199

R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	8016-001 (Admin Core)	194,642
	6123-001 (Core)	49,169
	6122-002 (Core)	61,234
	6121-003 (Core)	61,148
	6120-004 (Core)	99,930
	6127-005 (Core)	291,755
	6126-006 (Core)	112,185
	6125-007 (Core)	188,535
	6124-008 (Core)	115,023
	6115-009 (Core)	744,491
	6114-010 (Core)	271,395
	6113-011 (Core)	186,561
	6112-012 (Core)	543,836
	6119-013 (Core)	13,122
	6118-014 (Core)	149,577
	6117-015 (Core)	173,220
	6116-016 (Core)	99,863
	6111-017 (Core)	2,071,287
	6104-018 (Core)	92,915
	6105-019 (Core)	12,191
	6106-020 (Core)	21,839
	6107-021 (Core)	226,126
	6102-022 (Core)	191,148

	6103-023 (Core)	195,818
	6136-001 (Other)	122,959
	6134-002 (Other)	0
	6135-003 (Other)	18,412
	6133-004 (Other)	0
	6130-001 (Project)	313,049
	6131-002 (Project)	61,144
	6128-003 (Project)	522,134
	6129-004 (Project)	441,778
	6132-005 (Project)	0
TOTALS		7,646,486
R&R Budget - Section C. Total Equipment	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0

	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	500,000
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		500,000
R&R Budget - Domestic Travel	8016-001 (Admin Core)	6,400
	6123-001 (Core)	675
	6122-002 (Core)	0

	6121-003 (Core)	237
	6120-004 (Core)	0
	6127-005 (Core)	3,880
	6126-006 (Core)	500
	6125-007 (Core)	525
	6124-008 (Core)	1,260
	6115-009 (Core)	2,400
	6114-010 (Core)	1,500
	6113-011 (Core)	750
	6112-012 (Core)	3,000
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	2,000
	6116-016 (Core)	880
	6111-017 (Core)	5,100
	6104-018 (Core)	450
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	7,280
	6102-022 (Core)	1,395
	6103-023 (Core)	1,050
	6136-001 (Other)	10,000
	6134-002 (Other)	0
	6135-003 (Other)	300

	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		49,582
R&R Budget - Foreign Travel	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0

	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Section D. Total Travel	8016-001 (Admin Core)	6,400
	6123-001 (Core)	675
	6122-002 (Core)	0
	6121-003 (Core)	237
	6120-004 (Core)	0
	6127-005 (Core)	3,880
	6126-006 (Core)	500

	6125-007 (Core)	525
	6124-008 (Core)	1,260
	6115-009 (Core)	2,400
	6114-010 (Core)	1,500
	6113-011 (Core)	750
	6112-012 (Core)	3,000
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	2,000
	6116-016 (Core)	880
	6111-017 (Core)	5,100
	6104-018 (Core)	450
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	7,280
	6102-022 (Core)	1,395
	6103-023 (Core)	1,050
	6136-001 (Other)	10,000
	6134-002 (Other)	0
	6135-003 (Other)	300
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0

	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		49,582
R&R Budget - Tuition/Fees/Health Insurance	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0

	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Stipends	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0

	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Trainee Travel	8016-001 (Admin Core)	0

	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0

	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Subsistence	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0

	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Other Participants/Trainee Support Costs	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0

	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0

	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Section E. Total Participants/Trainee Support Costs	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0

	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Materials and Supplies	8016-001 (Admin Core)	1,450
	6123-001 (Core)	2,925
	6122-002 (Core)	3,750
	6121-003 (Core)	15,622
	6120-004 (Core)	76,490
	6127-005 (Core)	23,864
	6126-006 (Core)	2,750
	6125-007 (Core)	50,809
	6124-008 (Core)	20,400

	6115-009 (Core)	26,476
	6114-010 (Core)	7,244
	6113-011 (Core)	39,563
	6112-012 (Core)	74,790
	6119-013 (Core)	17,500
	6118-014 (Core)	500
	6117-015 (Core)	5,600
	6116-016 (Core)	27,520
	6111-017 (Core)	117,755
	6104-018 (Core)	2,509
	6105-019 (Core)	113
	6106-020 (Core)	675
	6107-021 (Core)	11,500
	6102-022 (Core)	23,186
	6103-023 (Core)	26,100
	6136-001 (Other)	24,000
	6134-002 (Other)	0
	6135-003 (Other)	450
	6133-004 (Other)	0
	6130-001 (Project)	355
	6131-002 (Project)	225
	6128-003 (Project)	375
	6129-004 (Project)	270
	6132-005 (Project)	0

TOTALS		604,766
R&R Budget - Publication Costs	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0

	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Consultant Services	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0

	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	525
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		525
R&R Budget - ADP/Computer Services	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0

	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0

	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Subawards/Consortium/Contractual Costs	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0

	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Equipment or Facility Rental User Fees	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0

	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0

	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Alterations and Renovations	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0

	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Other Direct Cost 1	8016-001 (Admin Core)	8,473
	6123-001 (Core)	28,683
	6122-002 (Core)	21,954
	6121-003 (Core)	6,300
	6120-004 (Core)	62,497
	6127-005 (Core)	37,621
	6126-006 (Core)	8,210
	6125-007 (Core)	5,282
	6124-008 (Core)	36,225
	6115-009 (Core)	17,236
	6114-010 (Core)	3,620

	6113-011 (Core)	4,771
	6112-012 (Core)	67,234
	6119-013 (Core)	31,546
	6118-014 (Core)	25,000
	6117-015 (Core)	215,552
	6116-016 (Core)	5,160
	6111-017 (Core)	78,872
	6104-018 (Core)	23,547
	6105-019 (Core)	16,425
	6106-020 (Core)	30
	6107-021 (Core)	28,887
	6102-022 (Core)	17,002
	6103-023 (Core)	182,347
	6136-001 (Other)	24,000
	6134-002 (Other)	0
	6135-003 (Other)	375
	6133-004 (Other)	200,000
	6130-001 (Project)	713
	6131-002 (Project)	375
	6128-003 (Project)	375
	6129-004 (Project)	428
	6132-005 (Project)	3,000
TOTALS		1,161,740
R&R Budget - Other Direct Cost 2	8016-001 (Admin Core)	0

	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0
	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0

	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Other Direct Cost 3	8016-001 (Admin Core)	0
	6123-001 (Core)	0
	6122-002 (Core)	0
	6121-003 (Core)	0
	6120-004 (Core)	0
	6127-005 (Core)	0
	6126-006 (Core)	0
	6125-007 (Core)	0
	6124-008 (Core)	0
	6115-009 (Core)	0
	6114-010 (Core)	0
	6113-011 (Core)	0
	6112-012 (Core)	0
	6119-013 (Core)	0
	6118-014 (Core)	0

	6117-015 (Core)	0
	6116-016 (Core)	0
	6111-017 (Core)	0
	6104-018 (Core)	0
	6105-019 (Core)	0
	6106-020 (Core)	0
	6107-021 (Core)	0
	6102-022 (Core)	0
	6103-023 (Core)	0
	6136-001 (Other)	0
	6134-002 (Other)	0
	6135-003 (Other)	0
	6133-004 (Other)	0
	6130-001 (Project)	0
	6131-002 (Project)	0
	6128-003 (Project)	0
	6129-004 (Project)	0
	6132-005 (Project)	0
TOTALS		0
R&R Budget - Section F. Total Other Direct Cost	8016-001 (Admin Core)	9,923
	6123-001 (Core)	31,608
	6122-002 (Core)	25,704
	6121-003 (Core)	21,922
	6120-004 (Core)	138,987

	6127-005 (Core)	61,485
	6126-006 (Core)	10,960
	6125-007 (Core)	56,091
	6124-008 (Core)	56,625
	6115-009 (Core)	43,712
	6114-010 (Core)	10,864
	6113-011 (Core)	44,334
	6112-012 (Core)	142,024
	6119-013 (Core)	49,046
	6118-014 (Core)	25,500
	6117-015 (Core)	221,152
	6116-016 (Core)	32,680
	6111-017 (Core)	196,627
	6104-018 (Core)	26,056
	6105-019 (Core)	16,538
	6106-020 (Core)	705
	6107-021 (Core)	40,387
	6102-022 (Core)	40,188
	6103-023 (Core)	208,972
	6136-001 (Other)	48,000
	6134-002 (Other)	0
	6135-003 (Other)	825
	6133-004 (Other)	200,000
	6130-001 (Project)	1,068

	6131-002 (Project)	600
	6128-003 (Project)	750
	6129-004 (Project)	698
	6132-005 (Project)	3,000
TOTALS		1,767,031
R&R Budget - Section G. Total Direct Cost (A thru F)	8016-001 (Admin Core)	210,965
	6123-001 (Core)	81,452
	6122-002 (Core)	86,938
	6121-003 (Core)	83,307
	6120-004 (Core)	238,917
	6127-005 (Core)	357,120
	6126-006 (Core)	123,645
	6125-007 (Core)	245,151
	6124-008 (Core)	172,908
	6115-009 (Core)	790,603
	6114-010 (Core)	283,759
	6113-011 (Core)	231,645
	6112-012 (Core)	688,860
	6119-013 (Core)	62,168
	6118-014 (Core)	175,077
	6117-015 (Core)	396,372
	6116-016 (Core)	133,423
	6111-017 (Core)	2,273,014
	6104-018 (Core)	119,421

	6105-019 (Core)	28,729
	6106-020 (Core)	22,544
	6107-021 (Core)	273,793
	6102-022 (Core)	232,731
	6103-023 (Core)	405,840
	6136-001 (Other)	180,959
	6134-002 (Other)	500,000
	6135-003 (Other)	19,537
	6133-004 (Other)	200,000
	6130-001 (Project)	314,117
	6131-002 (Project)	61,744
	6128-003 (Project)	522,884
	6129-004 (Project)	442,476
	6132-005 (Project)	3,000
TOTALS		9,963,099
R&R Budget - Section H. Indirect Costs	8016-001 (Admin Core)	59,070
	6123-001 (Core)	22,807
	6122-002 (Core)	24,343
	6121-003 (Core)	23,326
	6120-004 (Core)	66,897
	6127-005 (Core)	99,994
	6126-006 (Core)	34,621
	6125-007 (Core)	68,642
	6124-008 (Core)	48,414

	6115-009 (Core)	221,369
	6114-010 (Core)	79,453
	6113-011 (Core)	64,861
	6112-012 (Core)	192,881
	6119-013 (Core)	17,407
	6118-014 (Core)	49,022
	6117-015 (Core)	110,984
	6116-016 (Core)	37,358
	6111-017 (Core)	636,444
	6104-018 (Core)	33,438
	6105-019 (Core)	8,044
	6106-020 (Core)	6,312
	6107-021 (Core)	76,662
	6102-022 (Core)	65,165
	6103-023 (Core)	113,635
	6136-001 (Other)	50,669
	6134-002 (Other)	0
	6135-003 (Other)	5,470
	6133-004 (Other)	56,000
	6130-001 (Project)	87,953
	6131-002 (Project)	17,288
	6128-003 (Project)	146,408
	6129-004 (Project)	123,893
	6132-005 (Project)	840

TOTALS		2,649,670
R&R Budget - Section I. Total Direct and Indirect Costs (G +H)	8016-001 (Admin Core)	270,035
	6123-001 (Core)	104,259
	6122-002 (Core)	111,281
	6121-003 (Core)	106,633
	6120-004 (Core)	305,814
	6127-005 (Core)	457,114
	6126-006 (Core)	158,266
	6125-007 (Core)	313,793
	6124-008 (Core)	221,322
	6115-009 (Core)	1,011,972
	6114-010 (Core)	363,212
	6113-011 (Core)	296,506
	6112-012 (Core)	881,741
	6119-013 (Core)	79,575
	6118-014 (Core)	224,099
	6117-015 (Core)	507,356
	6116-016 (Core)	170,781
	6111-017 (Core)	2,909,458
	6104-018 (Core)	152,859
	6105-019 (Core)	36,773
	6106-020 (Core)	28,856
	6107-021 (Core)	350,455
	6102-022 (Core)	297,896

	6103-023 (Core)	519,475
	6136-001 (Other)	231,628
	6134-002 (Other)	500,000
	6135-003 (Other)	25,007
	6133-004 (Other)	256,000
	6130-001 (Project)	402,070
	6131-002 (Project)	79,032
	6128-003 (Project)	669,292
	6129-004 (Project)	566,369
	6132-005 (Project)	3,840
TOTALS		12,612,769

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?

Specific Aim 1. Provide leadership in setting scientific and strategic priorities by leading the strategic planning process and its integration across the Center. Efforts will continue to integrate the next five year plan of the Center with those of the OHSU's strategic planning and outcomes, linked through the Office of the Vice President for Research. Integrated leadership across the Center will be accomplished by scheduled and agenda-driven weekly meetings of the Director and Associate Directors, bimonthly meetings with the Division Chiefs, quarterly meetings with an expanded group of leaders, and regular monthly meetings of key committees to accomplish animal allocation, policy setting, and goals as noted in the Administrative Overview. Finally, the Director's office will continue to plan, coordinate, and sponsor scientific retreats and symposia in collaboration with the Division Chiefs and Interdisciplinary Research Program managers to identify shape opportunities for joint scientific ventures, joint recruitment, and new research initiatives.

Specific Aim 2. Promote and assure fair external and internal access to nonhuman primates and support cores for research. This aim is accomplished via the linked operations of the Research Advisory Committee (RAC), the Collaborative Research Unit (CRU), the Pilot Project Program, and the ONPRC animal allocation process and the Comparative Medicine Division, as well as through linkage with the NPRC Consortium. The CRU will continue to assure that all inquiries from external sources are directed to the appropriate internal collaborator for scientific leadership and expertise. Both the CRU and the Pilot Program have the goal of increased collaboration with outside investigators. The Associate Director for Research will continue to oversee the operation of the Research Support Cores, including procedures for access.

Specific Aim 3. Assure stable funding for the Center. This aim will be accomplished primarily via administration, oversight, and management of the submission of the P51 grant and its yearly progress reports. The office will continue to serve as the communication point for the National Scientific Advisory Board (NSAB) and arranges all meetings and reviews by this group for the purposes of advancing the P51 aims and goals. In addition, the Associate Director for Research will serve as the major liaison with the OHSU Foundation and the OHSU Office of Technology Transfer and Business Development, to align strategic funding initiatives and to promote and manage research interactions with industry and public-private partnerships.

Specific Aim 4. Provide effective communication within ONPRC and with OHSU, NIH, and the broader scientific and lay communities. The Office will continue to maintains minutes for all meetings on SharePoint, to publish the electronic newsletter, and to hold quarterly All-Campus meetings to inform employees of ongoing activities and initiatives. This Public Information Officer communicates scientific advances and administrative matters with the Office of Research Infrastructure Programs (ORIP) in DPCPSI at NIH. The Office will continue to work closely with OHSU's Strategic Communications office to publicize scientific breakthroughs. The Director will hold monthly meetings with the Vice President for Research and biannual meetings with the other NPRC Directors and senior staff and NIH staff. The Director's office oversees the ONPRC Outreach program, which is directed to scientists of all ages.

Specific Aim 5. Provide oversight and linkage to key regulatory functions that are integral to interactions with OHSU and state and local governments. The Director's Office will continue to provide a liaison with the Offices of Research Integrity, Research Safety, and Research Advocacy. The Office coordinates Emergency Response Planning in close collaboration with the Departments of Public Safety and Emergency Planning, working with local law enforcement and public safety groups. This office serves as the contact for the OHSU Government Relations office, which represents the ONPRC in state, local, and national meetings with elected officials.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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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?

We maintain the Center Website and are responsible for the electronic newsletter. Through our outreach program, we are invested in sharing our Center's activities and progress with our local communities and educators.

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

We will continue our regular activities and in addition, we will set the plan for the next year's Task Force activities and priorities. Specific new activities and initiatives will include recruitment of replacements for Division Chiefs and Core Directors as well as recruitment of new core scientists in areas such as general immunology and, in conjunction with the OHSU Knight Cardiovascular Institute, NHP cardiology research.

DIRECTORS OFFICE: ACCOMPLISHMENTS

1. **Provide leadership in setting scientific and strategic priorities by leading the strategic planning process and its integration across the Center**. Our office planned and executed the current formal strategic planning exercise, obtaining the services of an OHSU faculty business consultant. We provide leadership and staffing of the project manager for all of the Task Forces executing the strategic objectives, and we assure success through tracking and regular reporting. Via regular meetings of leadership, we have assured clear and regular communication of ongoing and new initiatives to all staff.

2. **Promote and assure fair external and internal access to nonhuman primates and support cores for research.** We have continued to streamline the process for requesting access to and subsequent assignment of animals for research projects. These procedures are being clarified for all involved groups, including the Animal Utilization Committee and the relevant staff in the Division of Comparative Medicine. In addition, new population modeling tools are being developed and incorporated into assignment discussions in order to make more strategic choices when animals are assigned, especially for long-term studies.

3. **Assure stable funding for the Center.** This office is responsible for overseeing all NIH correspondence related to the P51, G20s and CO6 grants. We continue to seek opportunities for investment in research projects from industry and non-profit foundations.

4. **Provide effective communication within ONPRC and with OHSU, NIH, and the broader scientific and lay communities**. There was a small refinement to Specific Aim 4, in that we moved oversight of the Center Library to the Director's Office. This has allowed more accurate, timely, and smoother reporting of publications as part of the P51 progress reports and reports to ORIP. We instituted regular meetings for employees after they have been here for 3-6 months to explain the Center organizational and leadership practices and processes. These meetings have improved understanding and communication and have enhanced community awareness.

5. **Provide oversight and linkage to key regulatory functions that are integral to interactions with OHSU and state and local governments.** We also changed Specific Aim 5, in that this unit is responsible for Incident Command response and materials on the West Campus as part of emergency planning with law enforcement and government entities. Excluded by Requester have met regularly with local, state, and national representatives to assure that these groups are informed of the progress of the Center in biomedical breakthroughs and as local employers.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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.		Joseph		Robertson		Principal Investigator	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.		Excluded by Requester				Director					73,320.00	17,743.00	91,063.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **91,063.00**

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	Division Staff	11.37			80,025.00	23,554.00	103,579.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**103,579.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**194,642.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	6,400.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**6,400.00**

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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	1,450.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	8,473.00
Total Other Direct Costs	**9,923.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**210,965.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	210,965.00	59,070.00
		Total Indirect Costs	**59,070.00**

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)	**270,035.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Business Services
Component Project Lead Information:
Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

BUSINESS SERVICES:
Business Services at the ONPRC provides services and resources to assist faculty and administration in the development and management of grants and other financial resources that fund the accomplishment of the strategic research mission of the ONPRC. The business functions are in accordance with OHSU policy and procedures, and NIH rules and regulations. The business service staff provides support for ONPRC ancillary proposals and awards. This includes from initial planning stages, to mid-project financial management and budget tracking, to close-out and final reporting of all non P51 projects. Business Services provides a single-point-of-contact for ONPRC staff to accomplish all business process tasks, accounts payable, requisitioning, fixed assets inventory, purchase orders and travel reimbursements. This facilitation of these processes helps free ONPRC staff to concentrate on their areas of expertise in research, support cores and other areas, and reduce the distraction that can result from the increased administrative burden in the conduct of research.

Through these functions, Business Services provide:
• Accountability and guidance in coordination with central University resources to internal and external funding guidelines, rules, and regulations, and budgetary and schedule commitments.
• Comprehensive support for all human resources and related systems processes at the university including hiring, on-boarding, union matters, labor distribution, etc.
• Provide single-point-of-contact efficiency for ONPRC staff in performing business processes such as ordering research supplies, obtaining purchase cards, submitting travel claims, processing internal billing charges, tracking fixed assets, submitting accounting adjustment forms, and many other business related processes.
• Budgetary development assistance for ancillary proposals and non-human primate costs.
• Consultation services for financial aspects of project planning.
• Education regarding university and federal systems; and requirements for the conduct of research projects with OHSU Research Grants and Contracts, Sponsored Projects Administration and Central Financial Services.
• Review and evaluation of financial progress and assistance in research project resource management.
• Research Award compliance and close-out in coordination with central University resources.
• Reporting and accounting expertise to provide information for individual projects as well as overall ONPRC financing and future projections.

Specific Aim 1: To provide appropriate levels of support and staffing to provide for the efficient, effective, and compliant conduct of the P51 award. This involved the facilitation of all business processes at the university in behalf of the core award and its budget managers from budget planning and submission to Federal Financial Report (FFR) calculation and providing assistance in progress report writing and submission.

Specific Aim 2: To provide excellent customer service to our ONPRC Divisions while maintaining productive relationships with OHSU Business and Grants Management Departments. Standard Operating procedures are being updated and created to clearly define roles and responsibilities. This will clarify and provide efficiencies in the day to day operations.

Specific Aim 3: Fully implement and utilize a radio-frequency identification (RFID) inventory system to track ONPRC fixed assets and include maintenance agreements and service dates on equipment. This will greatly reduce the time and effort involved in equipment inventory tracking and reduce the burden on lab personnel.

Specific Aim 4: Explore and implement a new system for budget development for the competing and non-competing P51 award. The current system is built on multiple Excel spreadsheets with extensive links. Alterations to the award require extensive manual changes throughout multiple spreadsheets which is error prone. The selection and implementation of a system better suited to the P51 award and the requirements of electronic submission will be necessary in the coming competitive period.

ADMINISTRATIVE SERVICES
The Associate Director for Administration is responsible for the overall infrastructure and financing of the ONPRC. He and his team provide comprehensive support for a safe, productive, and environmentally sound infrastructure to support the administrative and facility related needs of ONPRC research and NHP animal care staff. This includes the oversight and management of Center budgeting and financial planning and implementation, Business Services, Information Technology, Human Resources, Facilities, Construction, Campus Planning, and Library Services. The Associate Director and his team work with their University counterparts in participatory teamwork that facilitates the infrastructure support and financing of the ONPRC in areas such as grants management, design and construction, purchasing, logistics, budgeting, financial services, F&A rate proposal development and negotiation, security, emergency response, and library services. The ONPRC Administrative team also works with NIH, local governments, and utilities to provide comprehensive infrastructure support.

Through these functions and support team the Associate Director for Administration:
• Safeguards the resources of the ONPRC in association with OHSU central services.
• Ensures planning, management, and financing for the infrastructure resources that support NHP animal colonies and research.
• Ensures ONPRC services to facilitate the day to day business operation of the center in coordination with central university services.
• Ensures core and ancillary grant compliance in association with central Research Grant and Contracts.
• Ensure Information Systems resources appropriate to the NHP research mission.
• Ensures infrastructure construction and renovation projects are appropriately managed meeting the goals and aims of these projects and that their continued use is consistent with funding sources.

• Ensures compliance with local governments and regulatory agencies in relationship to the physical land and buildings.
• Ensures the security of the physical facilities.
• Ensures that appropriate, specialized NHP Library services are provided.
• Ensures financing and managerial support for sustainability related programs/projects.
• Provides essential support for emergency and Incident Command response.

Specific Aim 1: Ensure the continued provision of the effective and efficient operation of the ONPRC infrastructure resources, both physical and personnel resources, to provide an appropriate environment for the safe and effective conduct of animal care and research at the ONRPC.

Specific Aim 2: Work with the University to strengthen work and financing relationships and make timely and accurate resource requests to ensure that the additional expertise and funding necessary to support infrastructure development appropriate to the ONPRC NHP research endeavor are provided in a timely manner.

Specific Aim 3: Work with the University and local governments to establish a realistic and therefore fundable long-range master plan to provide a growth roadmap for the next ten years for the ONPRC.

Specific Aim 4: Increase engagement with other Administrative Directors in the NPRC consortium to continue work on defining and documenting best practices that can be used within the varied institutional environments throughout the NPRC system.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-BusinessServices_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

Standard operating procedures are being updated with clearly defined roles and responsibilities for the financial analysts as well as the administrative support in the divisions. The Business Services group participated in an internal university HR sponsored customer service training/coaching session. The group developed a “Customer Service Pledge” that will be incorporated into roles and responsibilities. The goal for the next reporting period is to finalize and implement the roles and responsibilities.

The university implemented a business intelligence software called Cognos to use for the university's budget, financial planning and forecasting. This budgeting platform has not been implemented with grant accounts, it has only been used with non-grant accounts at the university. We are working with the university's ITG Business Intelligence group to explore, design and test the feasibility of using the Cognos budgeting platform for the P51 award.

The Center is working with the university to develop a long-range infrastructure plan that will help guide institutional funding and priority for the center. In addition, planning will be starting with the City of Hillboro to update the master plan. In the next reporting period the goal is to complete the long range infrastructure plan. The master plan with the City of Hillsboro will be a multi-year project. This project will start in the next reporting period. Due to the lengthy timeline for this master plan, the long range plan developed for the university may be impacted and will need to be adjusted and updated accordingly.

BUSINESS SERVICES: ACCOMPLISHMENTS

In the P51 application, Business Services and Administrative Services appeared separately. These units have now been combined but the aims have remained nearly the same. One change that was made was to move the ONPRC Library under the management of the Director's Office, as well as the essential support for Incident Command Response.

The Center has a dedicated analyst that is responsible for P51 award. This position is responsible for P51 budget, financial reporting, submission of FFR and providing assistance with progress report. In addition, the cost accountant position specifically supports cost analysis and compliance for rate setting and recovery of costs, which provide program income to supplement the P51 award.

The center implemented a radio-frequency identification (RFID) inventory system for tracking and managing fixed assets at the center. This inventory tool has streamlined many manual functions associated with the equipment inventory function and provided the center with more reliable data. This system interfaces with the university's fixed asset system.

To make progress on ensuring continued efficient and effective operation infrastructure resources, both physical and personnel related, the center has accomplished the following: For personnel infrastructure resources, the center has established a formal reporting line between the center's HR manager and the host institution's Director for Research and Academics HR. This reporting line has been instrumental in bringing the center closer to the university's central HR unit, which has created additional opportunities for the center's HR manager to be included in more institutional wide activities that can have direct impact to the center. The center's HR manager is currently a member of the university's union bargaining team. This is extremely important to the center because the majority of our work force belongs to the union. For the physical operations infrastructure resources, regular meetings have been established with the university's Director of Facilities in order to integrate him into facilities operations and campus to ensure smooth transition for them provide the center with any back up support should the need arise. Historically there has not been a working relationship, or knowledge sharing, with the university's facilities group.

The center has established a process with the university's applicable units to submit a prioritized list of capital budget items in order request funding each year from the university to supplement the Improvements and Modernization funding from the P51.

The Administrative Directors/Chief Operating Officers have been meeting twice a year in person at the spring and fall Director's meetings. Starting in January 2015, regular monthly conference calls have been established for the group to share and discuss best practices as well as any other current issues that may arise that impact all the centers.

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Chief Operating Officer	Institutional Base Salary	EFFORT			26,906.00	8,637.00	35,543.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **35,543.00**

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						
13	Unit Staff	23.4			117,793.00	37,812.00	155,605.00
13	**Total Number Other Personnel**					**Total Other Personnel**	**155,605.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**191,148.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	1,395.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**1,395.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	23,186.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	17,002.00
Total Other Direct Costs	**40,188.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**232,731.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	232,731.00	65,165.00
		Total Indirect Costs	**65,165.00**

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)	**297,896.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Facilities
Component Project Lead Information:
Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

In support of the Associate Director for Administration, the Facilities and Property (F&P) Manager is responsible for the safe, efficient, sustainable and cost-effective management of ongoing operations, maintenance, upgrades, and security associated with the ONPRC campus buildings, grounds and infrastructure. On a daily basis, the F&P team works directly with the Division of Comparative Medicine (DCM) staff to assure that all animal housing and holding areas are in compliance with the applicable regulatory codes and standards for the proper care and use of laboratory animals. Additionally, the F&P staff provides support to all research laboratories and administrative areas to assure all of these spaces are kept clean, safe, and environmentally controlled, thereby allowing for a comfortable and productive work environment. With the relatively recent addition of a Sustainability Manager to the F&P, all operational approaches to maintaining the campus are being reviewed to incorporate the latest innovations in energy savings measures. The F&P Manager works closely with the University's Design and Construction department to plan, fund, design and construct major buildings on the campus in accordance with the rules for project management and financial accountability. As part of this responsibility, the F&P Manager also works directly with the City of Hillsboro and the city's regulatory agencies to assure that all construction and major renovations on the campus are in compliance with the ONPRC's Master Plan on file with the City of Hillsboro, and associated building codes and standards, including the proper care and treatment of storm water runoff, wetland maintenance, and protection of natural resources on the campus. As part of the campus security program, the F&P Manager works with the University's Public Safety Office and the local police and fire departments to assure that the campus is secure and safe at all times.

•Through these functions, the F&P Manager: Coordinates, with the F&P Operations Manager, to assure that all Heating, Ventilating and Air Conditioning (HVAC) equipment is operational and set to the proper temperature ranges at all times.
•Monitors and tracks necessary building repairs to assure the structural integrity and well-maintained appearance of all campus structures.
•Oversees the care and maintenance of all campus grounds, walkways, paths and roads to assure that the work performed to keep the property fully accessible and in good condition is being performed in a sustainable and cost effective manner.
•Ensures that future construction and tenant improvement projects and those working on those projects are fully versed in applicable standards, such as University, NIH, City (JHAs) and State standards.
•Coordinates with the ONPRC Business Office the University Central Financial Services and Design and Construction departments to assure proper funding exists for all new work on the campus
•Oversees campus security and programs for badging and key control access on campus.
•Coordinates with the Sustainability Manager to develop and implement best practices and energy management strategies for the campus

Specific Aim 1 – Ensure the continued safe, efficient, productive and sustainable operations at the ONPRC, complying will all local, state and federal regulations governing the administrative office spaces, research laboratories, and in particular, areas related to the care and welfare of the research animals.

Specific Aim 2 – Work cooperatively with the Administrative, Research, and DCM staffs to identify campus upgrades and renovations necessary to support the ongoing research goals of the University and ONPRC. This should include infrastructure upgrades to support anticipated changes in research methodology or desired animal housing refinements. Incorporate information into a comprehensive Campus Master Plan that will not only support the future needs of biomedical research but will also meet the requirements of the City of Hillsboro.

Specific Aim 3 – Working with the University's Design and Construction Department and Space Planning Group develop a clear understanding of the capital project planning process to assure timely identification and funding of future projects to support the ONPRC research and animal care mission.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Facilities_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

The Strategic Planning Facilities Infrastructure Task Force is developing a plan for the long term needs of the Center for major construction and/or remodel projects. The anticipated plan will include priorities, estimated costs and timeline to support the growth of research at the center.

To continue the efficient and productive aim for facilities operations, the Center will also be developing and implementing a new work order request system that will be available campus wide and accessible via mobile devices. The current way work order requests are received is very manual and not easily accessible to employees.

FACILITIES: ACCOMPLISHMENTS

To continue safe, efficient, productive and sustainable facilities operations, two monthly reports are used to track and monitor physical plant activity on campus. The first report, Facilities and Property Department Preventative Maintenance Schedule, is a comprehensive list that identifies specific area for regular service/testing and the specific employee responsible to do work. A Work Order List for Projects tracks specific project, requestor, preferred completion date and estimated cost. In addition, the center finalized and implemented an Energy Policy for the Center, ensuring energy is used efficiently and effectively throughout all aspects of the center's operations.

The Center has partnered with the university's Design and Construction (DesCon) department to clarify and agree on a specific capital budget process, identifying high priorities for the center. During capital budget season for the university, the center's Chief Operating Officer and the center's Facilities manager meets with DesCon to update needs and priorities that may have changed. The DesCon representative takes this information to the university's Space Planning committee in order for it to be included in their capital budget request with our priority level assessment. Timelines have been established and communicated by the university's Central Financial Services Budget Office.

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Unit Head	Institutional Base Salary	EFFORT			12,059.00	4,281.00	16,340.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **16,340.00**

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						
23	Unit Staff	32.69			132,456.00	47,022.00	179,478.00
23	**Total Number Other Personnel**					**Total Other Personnel**	**179,478.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**195,818.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	1,050.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**1,050.00**

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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	26,100.00
2. Publication Costs	0.00
3. Consultant Services	525.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	182,347.00
Total Other Direct Costs	**208,972.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**405,840.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	405,840.00	113,635.00
		Total Indirect Costs	**113,635.00**

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)	**519,475.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Information Systems

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Information Systems (IS) Manager is responsible for the IS service program at the ONPRC. The IS Program comprises IS staff directly reporting to the IS Manager, and the OHSU Information Technology Group (ITG) staff dedicated to the ONPRC but reporting to ITG Management. IS services include but are not strictly limited to: software applications, computational and database services, intranet websites, and multimedia support for all ONPRC seminars, videoconferences or symposia. ITG provides network and telecommunications infrastructure, workstation support, enterprise-wide core applications, resource hosting-management and customer support for the OHSU enterprise network.

Together, the IS Program is a comprehensive technical resource providing people, processes, and technology with a mission in support of ONPRC scientific, clinical and research programs; maintenance of animal resources; development of business applications; and technical integration with OHSU and other institutions. IS' vision is to achieve the most productive synergy between people and computing technologies.

IS specifically focuses on core strategic responsibilities and functions that provide key capabilities to the ONPRC research endeavor and leverage the OHSU IT infrastructure:
Software application support and development in line of business applications such as the integrated research and clinical information LabKey system platform called PRIMe; for office productivity workflows using Microsoft SharePoint; Research laboratory support in areas such as server/system configuration and hosting consultation; and Lab Information System (LIMS) or lab instrumentation interface development and integration
•Business process analysis to achieve improved informational and computational workflows
•Database administration; database and report design, consultation and migration
•Security and privacy of data along with business continuity, disaster recovery and capacity planning
•Service, quality and project management
•Audio-visual, conferencing and training content development support for local and offsite meetings
•NHP Consortium Participation including ONPRC representation for the Data Access Guidelines Group (DAGG) working group

Specific Aim 1. Continue progress in adoption of operational and industry best practices to deliver higher quantity and quality of service delivery to ONPRC and other stakeholders. Focusing on quality improves output. Becoming more efficient helps to lower or create more sustainable operating costs. Systems engineering and technology is getting more complex, not less, requiring prioritizing the highest value efforts.

Specific Aim 2. Leverage and exploit existing technology resources while adding technologies only as strategically needed. This will maximize the return on investments in technology resources, reduce risk in areas such as staffing, and to create a synergistic effect between systems resulting in more agile and scalable technical infrastructure, and ultimately more effective and efficient research, clinical and administrative operations that lead to better research.

Specific Aim 3. Provide support and expertise leadership for research and colony management informatics internally and at the national NHPRC level. Efforts such as creating interfaces to instrumentation allow for the streamlined and automatic capture of data. Facilitating the development of simulations and modeling, for example, help colony managers optimize a limited resource.

Specific Aim 4. Foster effective communications and collaboration internally and externally to, among other things, make it easier for stakeholders to find and use the right quality data in innovative ways. The future success of the NPRCs as a consortium will be increasingly based on collaborative work supported by Information Systems technologies.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-IS_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

Specific Aim 1 and 4: These aims, service level best practices and communication to stakeholders navigating to data, will be addressed in the Strategic Planning Infrastructure - Information Services Task Force. Metrics will be established to help measure the center's activity and performance against industry best practices

Specific Aim 2: Continuing to focus on deployment of enterprise wide solutions to data collection and sharing while providing increased training opportunities to the user community will allow us to get the most value from the resources available from the university.

Specific Aim 3: The planned deployment of wireless devices to aid in the entry of animal health data at its source will enhance our ongoing efforts to reduce errors and improve efficiency throughout the organization.

INFORMATION SERVICES: ACCOMPLISHMENTS

Specific Aim 1 and 4: These aims, service level best practices and communication to stakeholders navigating to data, will be addressed in the Strategic Planning Infrastructure - Information Services Task Force. Metrics will be established to help measure the center's activity and performance against industry best practices

Specific Aim 2: Continuing to focus on deployment of enterprise wide solutions to data collection and sharing while providing increased training opportunities to the user community will allow us to get the most value from the resources available from the university.

Specific Aim 3: The planned deployment of wireless devices to aid in the entry of animal health data at its source will enhance our ongoing efforts to reduce errors and improve efficiency throughout the organization.

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

RPPR - Core-6104

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			16,800.00	5,426.00	22,226.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **22,226.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Unit Staff	8.1			53,431.00	17,258.00	70,689.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**70,689.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**92,915.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	450.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**450.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	2,509.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	23,547.00
Total Other Direct Costs	**26,056.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**119,421.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	119,421.00	33,438.00
		Total Indirect Costs	**33,438.00**

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)	**152,859.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Research Library

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The ONPRC library provides all library services for ONPRC researchers, veterinarians, behavioral services team and staff with the major emphasis on NHP literature. Services include document delivery and interlibrary loan (ILL) of books and articles and reference services including in depth research projects; active assistance, information and advice ensure compliance with NIH public access policy. The librarian is also responsible for collection development and maintenance of the library's holdings of books and journals. The ONPRC library is closely associated with the OHSU main library to ensure that the needs of ONPRC and its NHP research mission are considered regarding access to e-journals and databases.

Through these functions the library:
• Ensures the ONPRC library collection meets the changing needs of ONPRC patrons and maintains its focus on NHP literature.
• Obtains requested articles and books that are not within the collection.
• Assists researchers and veterinarians in their mission of performing research on and maintaining the health and well-being of NHPs by performing in depth literature searches.
• Assists ONPRC authors to comply with NIH Public Access policy.
• Preserves the areas of the collection of historical significance to the center and unique NHP materials.
• Provides books and articles from its specialized collection of NHP literature to other primate centers, public, government and academic libraries, hospitals and research institutions in Oregon, throughout North America and even worldwide.

Specific Aim 1: Ensure the continued provision of efficient and effective services and maximize resources available for the needs of NHP researchers, veterinarians and support staff.

Specific Aim 2: Work closely with ONPRC Division of Comparative Medicine to provide assistance and support for their expanded educational and research role in Primatology.

Specific Aim 3: Preserve the unique NHP historical resources of ONPRC whilst making them more available to researchers and the wider community.

Specific Aim 4: Help ensure ONPRC authors comply with NIH public access policy in a timely manner.

Specific Aim 5: Develop training methods and techniques using new technologies and resources to effectively meet the needs of the ONPRC community and continue leveraging resources and connections with OHSU main library to ensure that ONPRC has access to any additional resources it needs to efficiently perform its mission of NHP research.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-ResearchLibrary_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

Specific Aim 1: The library will continue to provide current services whilst maintaining the high standards of speed and efficiency. Library services will be actively promoted particularly to new employees through brochures in the New Employee information packets, the CenterPage or by emails targeted at specific groups. In order to ensure the library is meeting the changing information requirements of researchers and veterinarians the library will conduct a survey to find if there are any unmet needs that the library can assist with.

Specific Aim 2: The library will increase outreach to DCM in order to increase awareness of the availability of current services but also to

identify if there are any unmet education needs. The library will offer individual training classes that are of special interest to DCM such as how to use PubMed with a focus on veterinary science.

Specific Aim 3: The library will focus on completing digitization of the Ito archive and increase its availability.

Specific Aim 4: The librarian will continue to act as a compliance monitor, running monthly checks of new publications and checking training sessions on NIHMS and promoting awareness through articles in the CenterPage, posts on the ONPRC Library bridge page and emails to researchers with potentially non-compliant publications and aid authors resolve problems.

Specific Aim 5: The librarian will continue to serve on Digital Collections and Collection Development Committee to represent ONPRC and ensure the needs of ONPRC veterinarians and researchers are met. The ONPRC library will continue to be involved in identifying problems and suggesting improvements in the SILS and Digital Commons. The library will also investigate new technologies and training classes relevant to the information needs of the ONPRC community.

RESEARCH LIBRARY: ACCOMPLISHMENTS

Specific Aim 1: The library provided literature searches, articles books and electronic resources for research purposes and day to day animal care to researchers, veterinary and support staff. The emphasis is on fast efficient service. Items obtained through Interlibrary loan (ILL) were usually obtained with 24 hours and document delivery items (available in the ONPRC library) often within 30 minutes of the request being received. Requests are filled electronically minimizing unnecessary printing and paper wastage. The library also provided articles and books to hospitals, universities, research institutions and public libraries throughout the USA and the world. Non OHSU researchers and members of the public accessed the library by appointment to use its specialized resources.

Specific Aim 2: The library has assisted veterinarians, interns, residents and other DCM staff in acquiring articles, books and other resources necessary to evaluate potential research projects and to study for professional examinations, including ACLAM. Library access is available 25/7 providing computer access to online resources and quiet study space.

Specific Aim 3: The online collection of rare historic primatology books has successfully transitioned to OHSU library's digital commons and there are now links from OHSU's catalog Primo, this has increased and improved access to the collection. Initial steps have been taken in a project to digitize the art generated by Medial Illustrator [redacted] during his over 40 years at ONPRC. The [redacted] collection is a unique collection of NHP art that will be appreciated by a wider community.

Excluded by Requester

Excluded by Requester

Specific Aim 4: The research librarian has been assigned a role as Public Access compliance monitor and is proactively alerting Authors to non-compliant publications and assisting them in the compliance process. The library has been involved in troubleshooting non-compliance issues and assisting PIs in the NIHMS process or submitting articles on their behalf.

Specific Aim 5: The librarian has worked closely with OHSU library on two major projects: the transition of digital collections to OHSU library's Digital Commons and the implementation of the new Shared Integrated Library Services (SILS) involving 37 library systems in the Northwest. SILS will increase visibility of ONPRC's unique NHP resources in particular to the other libraries and their patrons in the consortium. Both of these projects have changed the platform for accessing resources and involved extensive testing and troubleshooting to ensure ease of access.

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

RPPR - Core-6105

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Sala	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						
2	Unit Staff	3.6			8,708.00	3,483.00	12,191.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**12,191.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**12,191.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	113.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	16,425.00
Total Other Direct Costs	**16,538.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**28,729.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	28,729.00	8,044.00
		Total Indirect Costs	**8,044.00**

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)	**36,773.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Research Safety

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

A new organizational structure has been proposed for the Research Safety Program (RSP), which is part of the OHSU Environmental Health and Radiation Safety (EHRS) department and provides a broad spectrum of services to all ONPRC and other personnel. The RSP department formed in 2011 as a distinct program within EHRS, but reporting to the OHSU Research Integrity Office, with a direct reporting line to the Vice President for Research (VPR). This change was made in order to provide the organizational accountability for research safety by moving program authority to the VPR. This change in organization addresses comments made in the prior critique. The RSP/EHRS departments oversee programs and policies addressing biosafety, chemical safety, radioisotopes, medical waste, hazardous waste, worker safety, ergonomics, emergency response and occupational health programs are developed, administered and periodically updated. During program development, emphasis is placed on program functionality, cost control, and compliance with all federal, state, and local regulations. Training for ONPRC personnel is conducted as required by regulations and/or ONPRC Administration. RSP/EHRS personnel receive training needed to perform their assigned duties and maintain a network of contacts within the regulatory community. Requested funding is needed to maintain the ONPRC as an environmentally responsible member of the community and as a safe and healthy workplace.

The RSP/EHRS program consists of the Research Safety Manager/Biosafety Officer, Assistant Biosafety Officer, two Biosafety Specialists, Industrial Hygienist/Radiation Safety Officer, Industrial Hygienist/Safety Specialist, and an Administrative Assistant. To be hired is a new position that will serve as the Chemical Hygiene Officer for the OHSU campuses and that will report to the Research Safety Manager.

Specific Aim 1. Monitor and evaluate the efficiency and effectiveness of the new RSP/EHRS organizational structure with respect to ONPRC operations. As the proposed personnel arrangement represents a number of changes in the structure operating in the previous funding period, which itself was organized to address aspects of the previous critique, it will be important to continue assessment of the proposed new structure to ensure optimal levels of research safety.

Specific Aim 2. Improve laboratory safety awareness and compliance. In light of recent high-profile laboratory accidents and the resultant increased oversight of laboratory safety practices, it is essential to ensure that the ONPRC and its investigators and research staff are adequately protected from accidental injury and personal and institutional liability. The RSP/ERHS has begun to expand and improve laboratory safety monitoring and consulting by developing a laboratory safety audit program consistent with that developed by the University of California Center for Laboratory Safety. The goal of this program is to ensure that investigators are adequately informed about safety practices specific to the type of research being performed, and to assist them in maintaining compliance with all applicable federal, state, and local health and safety regulations.

Specific Aim 3. Continue to Strengthen the Occupational Health and Safety Program. The OHN has established working relationships with RSP/EHRS staff, Department of Comparative Medicine (DCM) staff, Risk Management, and the OHSU Employee Health department since she was hired in 2010.

Specific Aim 4. Continue to strengthen training and injury prevention strategies. The Research Safety Manager represents the ONPRC with the Occupational Health and Safety (OHS) Working Group. The stated goals of the OHS working group are to meet annually to share information critical to protection of personnel working with nonhuman primates. Preliminary efforts are expected to be completed by early 2014.

Specific Aim 5. Continue to strengthen Security and Biosecurity at the ONPRC. The RSP/EHRS works with the Oregon Health & Science University (OHSU) Department of Public Safety (DPS), DCM staff, facilities, local law enforcement, and first responders to improve Security/Biosecurity at ONPRC.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-ResearchSafety_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-ResearchSafety_Training.pdf

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

NOTHING TO REPORT

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

EHRS/RSP will continue to improve our Biosafety and Research Safety Programs using multi-media methods and working with all stakeholders of ONPRC.

RESEARCH SAFETY: ACCOMPLISHMENTS

A Chemical Hygiene Officer (CHO) is now reviewing chemical use by ONPRC personnel including those transferring chemicals, mixing chemicals, using cagewashes, and cage/habitat cleaning.

The laboratory safety audit program has been developed and is nearing the implementation stage. This audit program is an addition to our robust biosafety audit program and will integrate multiple areas safety oversight (IACUC, IBC, OSHA, etc.) and follow-up into a single program.

The Occupational Health and Safety (OHS) group met at ONPRC in 2014 and provided an opportunity to share experiences and risk mitigation in use at other NPRCs. Our OH Nurse (OHN) participated in this meeting along with select members of the EHRS staff.

The use of the SharePoint site to deliver the annual NHP Biosafety Refresher training allowed for transmission of training to a resource that can be used as convenient to the DCM staff and other personnel.

RESEARCH SAFETY: TRAINING & PROFESSIONAL DEVELOPMENT OPPORTUNITIES

The EHRS staff continues to refine and offer training to the ONPRC personnel for biosafety, BSL3, ABSL3, OSHA compliance (such as bloodborne pathogen training and facility safety), laboratory safety and biological materials shipping by both in-person and electronic methods.

The EHRS staff continues to receive training to increase their skills as well including hazardous materials handling, spill response (chemical, biological, and radiation), conflict resolution, and Communication methods.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

NOTHING TO REPORT

C.5.b Resource sharing

File uploaded: RPPR-ResearchSafety_ResourceSharing.pdf

RESEARCH SAFETY: RESOURCE SHARING

The EHRS/RSP works closely with the Occupational Health Working Group to exchange experiences and solutions for safety issues (PPE, Work Processes, engineering controls, and risk assessments) found at the NPRCS.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-6106

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			0.00	0.0 0	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						
2	Unit Staff	2.07			18,367.00	3,472.00	21,839.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**21,839.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**21,839.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	675.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	30.00
Total Other Direct Costs	**705.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**22,544.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	22,544.00	6,312.00
		Total Indirect Costs	**6,312.00**

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)	**28,856.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Comparative Medicine

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Division of Comparative Medicine (DCM) provides superior NHP animal models and research support services to the ONPRC by maintaining healthy, specific pathogen free (SPF) nonhuman primate (NHP) breeding and research populations. To ensure physically and psychologically healthy animals free from disease and genetically characterized, DCM also maintains a well-trained and experienced professional, technical and husbandry staff in a collaborative and cooperative posture with the Scientific Divisions.

To successfully accomplish this mission, the DCM will:

Specific Aim 1: Provide a reliable number of healthy, genetically defined and pathogen-free source of NHPs.

Specific Aim 2: Develop improved strategies for the socialization of NHPs.

Specific Aim 3: Train the next generation of veterinarians dedicated to the advances in the understanding and improvement of NHP models.

The DCM will continue to optimize NHP breeding consistent with physical infrastructure and the anticipated need and diversification of the ONPRC scientific programs. The Division will improve management of colony genetics, and continually strive for top quality animal resources by enhanced pathogen monitoring, screening tests and diagnostic technologies, to ensure Specific Pathogen Free (SPF) animals availability. DCM will also implement management strategies to increase breeding efficiencies and provide optimum holding facilities using a systems management approach to identify bottlenecks, leverage points, and potential animal resource management changes to improve breeding program performance.

The Guide has recently been updated and housing standards have been further enhanced for these sentient species. In addition, European Union guidelines will likely expand socialization requirements, which may well influence further such requirements in the U.S. Thus, DCM will explore new opportunities for social compatibility assessment and enrichment, ensure compliance and develop strategies to improve the quality of life for the animals at the Center. Strategies will include innovative and comprehensive approaches to improving the methods of managing medical and behavioral cases, and explore novel use of caging and the design of innovative housing systems to enhance animal welfare and socialization.

Finally, a relatively small number of veterinarians possess the clinical expertise to support NHP research models. Recognizing this fact, the ONPRC has entered into a Laboratory Animal Medicine (LAM) resident training consortium with OSU veterinary medical school and the OHSU medical center to provide opportunities to veterinarians that wish to pursue the important experience of using the NHP model. This non-NIH funded training program will give residents an integrated and comparative approach to the value and limitations of the wide array of NHP research models, and serve as a continuing education forum for DCM veterinarians and other ONPRC interested professional staff.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM_Training.pdf

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

We have disseminated the results of our findings through publications in peer-reviewed journals, poster presentations, and presentations in national and international conferences.

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

In order to advance service support, increase capacity and capabilities, DCM goals for the next grant year are both broad and ambitious:

Pending Support

• Optimize breeding and research NHP populations to meet an internal goal of an average of 15% surge capacity.

• Validate forecasting model; NHP Resources will utilize this tool to the extent possible for projecting breeding and holding strategies.

• Purchase Indian origin rhesus adult males with previous group experience to improve our colony heterogeneity.

• Pending Support

Pending Support

• Test a modified monkey chow in corral animals to validate nutritional needs based upon preliminary NHP data that demonstrated beneficial effects.

• Finalize hanging cage modifications and convert all to pairing capable. Also bar code all caging to improve change-out efficiency, monitor cage maintenance, and enhance repair history.

• Conduct veterinary-focused NHP research, using data collected via robust electronic health records and/or pilot grant funds, in addition to projects coordinated with scientific staff where possible.

• Expand and validate the competency-based training program for DCM and research staff.

• Continue to maximize IT technology to increase efficiency for data entry and review.

• Reduce the number of singly housed animals, and continue to improve methodologies to avoid breaking established pairs.

• Continue to utilize positive reinforcement techniques to train animals.

• Continue to implement new enrichment strategies for singly housed animals, and to reduce abnormal behaviors.

• Continue to provide timely and valuable pathology support both to our colony resource and the ONPRC research mission.

• Continue to prepare and publish manuscripts, including several case reports and papers in preparation including material and collaborative input from other NPRC members.

• Continue to provide comprehensive anesthesia, analgesia, and surgical services in support of the research activities on campus. Independent research will continue to be a focus with the development and expansion of research projects DCM veterinarians have initiated.

DIVISION OF COMPARATIVE MEDICINE: ACCOMPLISHMENTS

DCM Organizational Changes and Unit Accomplishments. To optimize resources and enhance service support, the Division disbanded the Research-Education-Training (RET) unit, and now consists of six operational units under the direction of the Division Chief: Resources-Facilities-Operations (RFO), Pathology Services (PSU), Surgical Services (SSU), Behavioral Services (BSU), Clinical Medicine (CMU), and the Small Laboratory Animal Unit (SLAU). The RET veterinary unit head position was converted to an additional CMU clinical veterinarian to support the growing and more complex research NHP population. Consistent with its collective importance to the Division, the Training Manager, Training Lead and just added Quality Assurance Specialist now report directly to the Division Chief. Other unit changes and accomplishments reflect a continuing effort to strengthen unit cohesion, facilitate optimization of resources, and provide improved services to the Center as reflected below:

Specific Aim 1: Provide a reliable number of healthy, genetically defined and pathogen-free sources of NHPs. This aim is focused primarily on the on-site breeding of Specific Pathogen Free (SPF) *Macaca mulatta*. The DCM has continued to maximize NHP breeding despite physical infrastructure limitations and increasing demand for SPF macaques. Although the approximate average daily census is approximately 4,800 NHPs, we have at times housed over 5,000 animals in 2014. The current ONPRC NHP population changes are displayed in the tables below. Table 1 displays NHP population by grant year and species; Table 2 presents NHP production, group formations, and disbanded rates by grant year; and Table 3 depicts the survival rate and fecundity of outdoor socially housed animals by year.

Table 1

	Year 50	Year 51	Year 52	Year 53	Year 54	Year 55*
Total NHPs	4593	4806	4886	5871	6024	5686
Macaca mulatta	4134	4348	4437	5259	5335	5103
Macaca fascicularis	46	50	87	198	251	170
Macaca fuscata	399	395	352	401	422	404
Papio anubis	8	13	10	9	12	9
Papio hamadryas	0	0	0	4	4	0
Chlorocebus sp.	6	0	0	0	0	0
Importation	76	102	71	160	207	123
Animal Sales	97	189	23	75	157	234
Project Assignments	1150	964	1288	1458	1466	1406

Table 2

	Year 50	Year 51	Year 52	Year 53	Year 54	Year 55*
Population	2324	2413	2588	2581	2669	2878
Production #	577	626	684	685	705	378
Production	25%	26%	26%	27%	26%	13%
New Groups Formed	10	12	18	11	31	30
Disbanded Groups	4	7	35	10	27	24

*Year 53 numbers are calculated through 1/22/15, lacking February through April data. These months fall within the heart of the birthing season, and commonly account for 60% of births for the year.

Table 3

	2009	2010	2011	2012	2013	2014
Survival rate up to 1 year old	0.85	0.82	0.80	0.80	0.84	0.89
Survival rate all other animals	0.98	0.97	0.96	0.93	0.96	0.97
Fecundity females 5 and up	0.71	0.70	0.68	0.75	0.73	NA**

**2014 fecundity not reported as not all animals born in 2014 have been recorded as of yet.

Over the past grant year, the ONPRC accepted Proprietary Info U24 (expanded-SPF, or SPF9) and Proprietary Info U42 (SPF, or SPF4) Indian-origin rhesus macaques from the NEPRC. These animals have just begun to be used as both breeding stock to improve genetic heterogeneity of the existing U24 and P51 colonies, and to support AIDS/HIV funded projects. We also imported Proprietary Info animals for approved ONPRC projects. In our effort to minimize the use of non-SPF NHPs, we made significant strides to lower our non-SPF group of caged animals. This cohort has dropped Proprietary Info this year, and we anticipate another Proprietary Info reduction for the next grant year. Finally, we sold more than Proprietary Info animals to other research institutions to help meet the national research needs for NHPs, significantly reducing our NHP colony overpopulation.

In our efforts to improve virology screening, the SPF Laboratory fully adopted the Intuitive Biosciences SPF4 and SPF9 microarray platform. Over 2,200 previously validated samples per viral pathogen were used to validate the new assay, and we also validated an SRV 2 & 5 western blot assay. For this reporting year, all animals in corrals (approximately 1,600 animals) were assayed on the SPF4 platform, and the shelter-based population (approximately 1,200 animals) will be tested on the new microarray in the next reporting year.

We continue to expand our use of the relatively new Primate Records and Information Management (PRIMe) electronic database for colony management and epidemiology efforts. An automated alert system provides daily updates on disease outbreaks in rooms and groups, behavior disruptions in groups, cage compliance information, pairing status, and required viral and tuberculin testing. Morbidity, mortality, and reproductive reports can be generated by date and location, allowing us to track and quickly respond to animal health issues. PRIMe information is also used to make objective decisions regarding group formation and animal success within the breeding colony.

In April 2014, the USDA asked the ONPRC to evaluate alopecia in our NHP colony. RFO immediately established an NHP alopecia task force composed of members from across the scientific, medical and veterinary community, including representation from husbandry, behavior, clinical medicine, pathology, endocrinology, outside consultants and other research investigators. The group is evaluating the endocrine, nutritional, behavioral, pathological, aged, seasonal, genetic, and housing components that may contribute to alopecia in the rhesus macaque. Data collected will be compared to housing density, housing type, season, and other parameters. We anticipate no less than a two year commitment to address this area of interest.

Finally, we continue to improve our animal housing facilities, aligning ONPRC infrastructure, space, and resources with the maintenance and husbandry requirements of each species we support.

- Received over $500K in funding for new cage purchases, cage modifications, cage repairs, manipulanda, and associated caging items (tunnels, transfer boxes, lifting stations, forage stations).
- Partnered with a new chemical supplier and animal facility sanitation expert, Specific Private Vendor Specific Private Vendor
- Partnered with a new exterminator company, Specific Private Vendor resulting in significant improvement in our pest monitoring and eradication capabilities.
- Upgraded animal flooring in all ten Harem runs, Feed area 3 & 4, and selected Colony runs. Several exterior corral feed pads were added, heating was improved in the Feed 1 area, and all external water lines were upgraded to stainless steel and made resistant to freezing.

- The Colony Annex phase 1 remodel was accepted for animal use. This immeasurably improved one large animal holding room, a procedure room and feed room and added two new behavioral group-housing rooms capable of constant video monitoring and individual animal food intake. The second phase of the remodel will begin in February 2015 to add another large procedure room and door upgrades to four rooms.

- Renovation projects for the ASB, Colony and Colony Annex buildings will result in additional capacity and capability. We expect all projects to begin construction within the first six months of 2015.

Specific Aim 2: Develop improved strategies for the socialization of NHPs. The ONPRC has increased the number of animals socially housed at the ONPRC. In 2014, approximately [redacted] of our population was singly housed, which includes those housed for clinical, behavioral and IACUC-approved scientific reasons. During the past year, the BSU attempted to pair house approximately [redacted] caged monkeys. Over [redacted] of these attempts were successful (i.e., the animals did not fight or show overt signs of aggression or fear). We also implemented pair observations in an effort to determine whether behaviors between partners following a pair attempt may predict later success or failure. Additionally, BSU continues to collaborate with other DCM units to oversee our outdoor groups, and have increased our level of monitoring as a result, in an effort to ascertain dominance relationships.

The incidence of abnormal behavior has decreased in our NHP population during this reporting period. Positive reinforcement techniques were successfully used to train over [redacted] monkeys to voluntarily cooperate with typical noninvasive procedures. The BSU and RFO units worked together to improve "Pole and Collar" training methods, and continued to examine factors that might influence trainability, including temperament and fear towards caretakers. Seeking to promote well-being and decrease situations known to compromise well-being, BSU continued to modify and improve our "Foster program," in which abandoned or orphaned infants are reared by a non-lactating female trained to allow the infant to drink from a bottle. We reared four infants in this fashion in the past year. As a result of this program, we have significantly reduced the need for nursery rearing, known to be a risk factor in the development of abnormal behavior.

Enrichment strategies were improved in 2014. Because cognitive enrichment is known to be of value to captive primates, several Kindle Fire tablets were purchased and evaluated for potential use. We discovered that monkeys readily adapted to the hardware and prefer programs that are interactive (e.g., a painting program) to those that are passive (e.g., colors or movies). We also established a "Human Interaction program" for caged animals, in which technicians spent time doing activities such as blowing bubbles or giving extra treats to the animals in their areas. This kind of positive interaction demonstrated improved relationship between caretaker and NHP, and as such should help improve the monkey's resiliency towards stressful stimuli and overall well-being. We have also procured new foraging enrichment items, including a "foraging tray" that will be attached to every cage. These trays are easy to fill and will allow us to provide additional enrichment to singly housed animals. In response to a USDA site visit, DCM developed the 'Alopecia Working Group", comprised of members from BSU, the Pathology Services Unit, RFO, and scientific staff, to examine underlying causes of alopecia. All veterinary and behavioral staff adopted the Behavioral Management Consortium alopecia scoring system to consistently measure alopecia across units when collecting data and tracking hair loss over time. Lastly, the Head of BSU reinitiated an ONPRC Enrichment Committee to provide an opportunity for scientific and DCM staff to work together as a collective response to improve enrichment at the Center.

Specific Aim 3: Train the next generation of veterinarians dedicated to the advances in the understanding and improvement of NHP models. With the departure of [redacted], a CMU clinical veterinarian also board certified in the laboratory animal medicine specialty, accepted the position of Program Manager for the ONPRC site of the Oregon State Laboratory Animal Medicine Residency Consortium. Under his leadership our third year resident, [redacted] is completing her research project for publication, and is expected to be fully board eligible in 2016. Dr. [redacted] from Oklahoma State University, joined DCM in July 2014 as a 3-year resident in the LAM residency program, and should be become board eligible in 2018. Notably, [redacted] successfully completed the 2014 ACLAM board examination and received the Henry & Lois Foster Award for Academic excellence for top score on the examination.

DCM continues to provide opportunities for undergraduate, graduate and postdoctoral training within the division. During the past year, clinical training was provided to 3 laboratory animal residents and 12 veterinary externs. A total of 640 hours of direct clinical instruction were provided in the Colony Hospital to residents, and an additional 144 hours of direct clinical instruction were provided to veterinary externs.

DIVISION OF COMPARATIVE MEDICINE: TRAINING AND PROFESSIONAL DEVELOPMENT

Collectively, DCM provided and participated in a myriad of training and professional development opportunities:

- Excluded by Requester participated in the Spring NPRC Directors Meeting, and Excluded by Requester attended the Fall NPRC Directors meeting.
- Excluded by Requester joined BSU as a postdoctoral fellow.
- PSU continues to support a one-year pathology fellowship. Excluded by Requester completed her one-year fellowship and was replaced by Excluded by Requester Additionally, PSU hosted a Pathology Assistant Master's candidate for a one week externship.
- A monthly training hour was established for CMU veterinary technicians and support staff consisting of both didactic lectures and wet labs for relevant duties.
- CMU is piloting an online CE service for technicians specifically designed to address common questions regarding clinical care.
- Excluded by Requester a CMU clinical veterinarian also board certified in the laboratory animal medicine specialty, presently serves as Program Manager for the ONPRC site of the Oregon State Laboratory Animal Medicine Residency Consortium. Excluded by Requester are the current ONPRC veterinary residents for this 3-year ACLAM approved program.
- Residents and veterinary clinicians give lectures at the Oregon State University College of Veterinary Medicine, and to a nationwide audience of laboratory animal veterinarians participating in Virtual Grand Rounds, an activity part of the NPRC Training Consortium.
- Excluded by Requester also leads the veterinary student externship program, which provides an in depth and unique experience working with NHPs in a research environment. Visiting veterinary students (see Table 4) spend time with each CMU veterinarian for mentorship and training, and in so doing gain a well-rounded perspective on the role of veterinary medicine in NHP-based research by rotating through the Colony Hospital, Surgical Services Unit, Behavioral Services Unit, and the Pathology Services Unit.

Table 4. Veterinary Externships at ONPRC

Title	School	Start Time	End Time
Excluded by Requester	University of Minnesota	4/28/2014	5/9/2014
	Ohio State University	5/27/2014	6/6/2014
	University of Wisconsin-Madison	6/2/2014	6/30/2014
	Oregon State University	6/23/2014	7/11/2014
	Private Source	6/30/2014	7/18/2014
	Oregon State University	7/14/2014	8/1/2014
	Oregon State University	7/21/2014	8/1/2014
	University of Missouri	8/4/2014	8/15/2014
	Oregon State University	8/11/2014	8/22/2014
	Oregon State University	8/18/2014	9/5/2014
	Oregon State University	9/22/2014	10/3/2014
	Oklahoma State University	12/1/2014	12/19/2014

- DCM as a whole conducts training and education for veterinary, husbandry, and research staff preparing for AALAS certification tests, and the CMU veterinarians participate in these educational events by giving didactic lectures on various medical, regulatory and husbandry topics.
- DCM veterinarians attended and presented (as speakers and posters) at continuing education conferences on relevant medical and regulatory subjects (e.g. AALAS, ACLAM forum, APV, PRIM&R, IACUC training); meetings also allow networking opportunities, cross facility collaboration and information sharing with other NPRC staff and research institutions.
  - Excluded by Requester presented posters at the national AALAS meeting in October of 2014. Excluded by co-authored an abstract presented at the NHP AIDS symposium in November 2014. Excluded by Requester attended the Breeding Colony Management Consortium Meeting in November.

- Excluded by R equester attended the OHSU New Manager Leadership Essentials training course, and also attended the 38th Meeting of the American Society of Primatologists where he gave two presentations.
- Excluded by R equester attended the Association of Primate Veterinarians meeting. Excluded by R equeste from CNPRC, presented "Monkey 101-Diarrhea management in Captive NHPs: Past, Present, and Future." presented "Blood Volume Measurement in Rhesus Macaques: Is the 10%:10% Rule Accurate?" Excluded by Requester
- Excluded by R equester also attended the Veterinary Emergency and Critical Care meeting in Indianapolis, and was selected to participate in the highly competitive 12-month "Lead Mentor" training program sponsored by the OHSU School of Medicine.
- Two BSU members attended the 2014 American Society of Primatologist meeting, and one attended the American Association of Laboratory Animal Science meeting.
- Excluded by R equester attended the Annual Meeting of the ACVP and Primate Pathology Workshop held in Atlanta, GA.
- Excluded by Requester attended the Workshop in Laboratory Animal Medicine, North Carolina State, NC.
- Excluded by R equester attended National AALAS in San Anton , TX. Excluded by R equester presented "Introduction to Malaria in Nonhuman Primates" and Excluded by Requester presented "Measurement of Blood Volume in Adult Rhesus Macaques."
- Excluded by Requester attended the European Primate Veterinarian Symposium, Seville, Spain to present "Obesity in Rhesus Macaques: Clinical and Surgical Challenges" and "Roux-en-Y Gastric Bypass Surgery in Obese Rhesus Macaques."
- Several DCM technicians attended the National AALAS meeting in San Antonio, TX, as well as the AALAS District 8 Conference in San Francisco, CA
- SSU technicians attended the Academy of Surgical Research Annual Meeting, Minneapolis; the Dove Lewis Emergency Animal Hospital Annual Conference, Portland; the National Veterinary Emergency Response Team Training, Anniston, AL; and the Northwest Veterinary Specialists Winterfest, Clackamas, OR
- Excluded by R equester was invited to give talks at seminars at the American Society of Primatology, and was also invited to give a public talk at the Oregon Museum of Science and Industry (OMSI) Science Pub.

- Excluded by Requester attended a one-day Grant Writing Workshop sponsored by OHSU OCTRI.
- BSU has a monthly journal club, and staff members attend webinars and seminars offered at the ONPRC.
- CMU veterinarians undertook 14 hours of on-site continuing education on ultrasound technique.
- Excluded by R equester from the CaNPRC spent a day with CMU staff to discuss cross-center collaboration and to provide specific information about our new electronic medical records system (PRIMe), based upon her experiences with the LabKey-based program at the WNPRC.
- Excluded by R equester the director of Covance Labs at Alice, TX (a large primate breeding and research facility) spent a day at the ONPRC, and met with the Heads of CMU and BSU to collaborate on enrichment and behavioral monitoring of animals.
- Excluded by R equester serves as an external advisory committee member for the Caribbean Primate Research Center in Puerto Rico.
- Excluded by R equester provided clinical training to 3 ACLAM residents, 12 veterinary externs, 2 summer interns, and 1 doctoral student. A total of 640 hours of direct clinical instruction were provided in the Colony Hospital to residents, and an additional 144 hours of direct clinical instruction were provided to veterinary externs. Additionally Excluded by provided 80 hours of support to summer and doctoral students, 32 hours of didactic support for students in the OHSU School of Medicine (SOM), and 50 hours of mentoring support to junior faculty.
- A local institution of higher learning, Portland State University (PSU) participates in the training of veterinary student clinical medicine externs as part of their comprehensive exposure to NHP medicine. They support the LAM residency program through provision of didactic lectures, rotations through pathology services, and monthly pathology-centered didactic lectures. PSU also provides lectures to the ONPRC Technician CE series coordinated by Excluded by and conduct weekly NHP histopathology rounds and weekly review of the Joint Pathology Center (JPC) Wednesday Slide Conference material open to all veterinarians and trainees.
- All DCM unit veterinarians actively participate in NPRC Consortium efforts, either as Chair, members or project leaders.

- DCM veterinarians, managers and technicians were active in ONPRC outreach efforts, and participated in various programs including Camp Monkey, Saturday Academy, Science Ambassadors, and the PCC Behavior Management of Zoo Animal course. Other activities include serving as information sources for on-site tours (e.g. when ONPRC hosted the NPRC Directors' meeting, and the National Association of Medical Examiners), presenting to school groups of all ages including Lewis and Clark Law School, Portland Community College, and local primary schools, and participating in local middle school science fairs.

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

Regulatory Compliance. We look forward to working with the other NPRCs and the USDA Western Regional Director to improve inspection strategies and outcomes.

Training and Personnel Development. Although a primary focus of the DCM, funding and workload constrains the development of skilled and proficient staff by limiting training opportunities to local attendance only.

Animal Rights. The ONPRC enjoys a regrettably high degree of exposure to animal extremist groups and continues to be targeted. The OHSU-ONPRC partnership has been crucial to assure adequate security and accuracy of public information, and we continue to work with the OHSU Strategic Communications (public affairs) office to maintain message continuity.

Infrastructure. The ONPRC has used strategic planning to develop targets for infrastructure needs. These include caging purchases, maintenance, equipment upgrades and facility improvements. Combination funding from NIH C06 and G20 grants has been very valuable, and we will increase containment capacity in 2015. Additional institutional and outside funding sources will be needed for future progress on this front. We have achieved efficiencies through improved processes for animal assignment, which include better models to project NHP research needs.

Staffing. The continued growth of scientific programs with the resultant need for sequester and containment housing has maximized holding capacity and increased labor requirements without a commensurate increase in program income to support the need. Additional funding, program restructuring, renovation and new construction of animal holding facilities and administration space are all necessary to avoid staff burnout and reversal of the progress made over the last five years.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			84,318.00	19,225.00	103,543.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **103,543.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Unit Staff	24.6			99,823.00	22,760.00	122,583.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**122,583.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**226,126.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	7,280.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**7,280.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	11,500.00
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. Other Expenses	28,887.00
Total Other Direct Costs	**40,387.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**273,793.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	273,793.00	76,662.00
		Total Indirect Costs	**76,662.00**

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)	**350,455.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Resources, Facilities, and Operations

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Non-human primates are critical animal models for basic and translational biomedical research. Supporting scientists who use NHP's in their research requires an integrated program of resource management, breeding, animal husbandry, and facilities oversight. To enhance the scientific utility, health, and well-being of ONPRC's animal resources, RFO coordinates programs of resource allocation and tracking, genetic and disease surveillance, animal husbandry and veterinary care. Working closely with other DCM units and across the ONPRC campus, RFO manages breeding colonies, animals and animal facilities, oversees animal care, animal assignment and utilization, and coordinates genetic and viral screening to ensure the health and well-being of our research resources.

Our long term goal is a population of pedigreed, disease-free animals of defined quality which matches current and future research needs. To achieve this, RFO must provide innovative resource management, excellent husbandry and clinical care, relevant genetic and viral screening, and utilize a centralized electronic health record system to document and track all aspects of animal care and management.

The specific aims for accomplishing this are:

Specific Aim 1: To support scientists who use NHP's in their research by providing state-of-the-art, comprehensive management of our animal breeding and acquisition programs and centralized coordination of animal breeding, allocation, assignment, and release.

Specific Aim 2: To operate animal housing and facilities, aligning ONPRC infrastructure, space and resources for maintenance and husbandry of species for which there is a major national demand.

Specific Aim 3: To provide exemplary care to our breeding population of NHP's through an integrated program of animal husbandry, genetic and viral screening, and veterinary clinical and preventative care.

The expected outcome is a physically and psychologically healthy population of NHP's sufficient to support current and future research needs for pedigreed, genotypically and phenotypically defined, disease-free animals.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-RFO_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-RFO_Training.pdf

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

We have disseminated the results of our findings through publications in peer-reviewed journals, poster presentations, and presentations in national and international conferences.

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

• The RFO will be purchasing up to eight Indian origin rhesus adult males with previous group experience. The founders of this troop were brought in from India years ago and have never genetically intermixed with our rhesus. We anticipate these animals will significantly improve our goal of improving our colony heterogeneity.

• Excluded by Requester have had multiple discussions with the Private Source and plan to submit a multi-division, multi-institutional Private Source is interested in developing an NHP model of human infant and juvenile infectious diarrhea. Our colony NHPs experience many similarities to human infants born in third world countries with exposure to Shigella sp. and Campylobacter sp. We hope to explore cognitive loss, growth retardation, and chronic diseases associated with exposure to these two pathogens in the young.

• RFO will be testing a modified monkey chow in the corral animals to validate nutritional needs based upon preliminary NHP data that

demonstrated beneficial effects from such a diet. The chow will have up-to-date essential fatty acid ratios and contain probiotics in order to achieve two measurable benchmarks: reduced diarrhea and alopecia. This will be a crossover study and is expected to take no less than two years to complete. Purina, our nutritional partner, is very interested in these studies and hopes to disseminate this information nationwide.

• The RFO has set the goal of finalizing all hanging cage modifications (>250) in 2015, both to make them safer for animals and staff, as well as to convert all to pairing capable. Additionally, we plan to bar code all caging to improve change-out efficiency, better monitor cage maintenance and enhance repair history of individual caging.

RESOURCES, FACILITIES, AND OPERATIONS: ACCOMPLISHMENTS

Specific Aim 1:
This aim includes resource planning, breeding, acquisition, and allocation. Several personal changes and committee appointments have been made to enhance our planning and breeding management capability.

Resource Planning: Staff members were appointed to several ONPRC strategic planning committees tasked with developing short and long-term goals for research, infrastructure, animal population, business processes and staffing. As part of the strategic planning process, we continue to develop recommendations for colony size based upon current infrastructure and staffing, as well as information gathered from staff scientists, clinical and behavioral services, and the husbandry staff. This effort included validation of all campus caging, space, and defining ideal animal populations for all types of campus housing. Monthly colony planning group meetings are used to continually refine and update colony population data. Collaborating with system scientist, we have developed and validated a colony simulation prediction model. NHP Resources has begun to use this forecasting tool to extract crude predictions for research demands of the rhesus colony. We anticipate further expansion of this forecasting tool to capture animal room utilization and caging as well.

Resource Management: Table 1 displays NHP population by grant year and species, Table 2 presents NHP production, group formations, and disbanded rates by grant year, and Table 3 depicts the survival rate and fecundity of outdoor socially housed animals by year.

Table 1

	Year 50	Year 51	Year 52	Year 53	Year 54	Year 55*
Total NHPs	4593	4806	4886	5871	6024	5686
M. mulatta	4134	4348	4437	5259	5335	5103
M. fascicularis	46	50	87	198	251	170
M. fuscata	399	395	352	401	422	404
Papio anubis	8	13	10	9	12	9
Papio hamadryas	0	0	0	4	4	0
Chlorocebus sp.	6	0	0	0	0	0
Importation	76	102	71	160	207	123
Animal Sales	97	189	23	75	157	234
Project Assignments	1150	964	1288	1458	1466	1406

Table 2

	Year 50	Year 51	Year 52	Year 53	Year 54	Year 55*
Population	2324	2413	2588	2581	2669	2878
Production #	577	626	684	685	705	378
Production	25%	26%	26%	27%	26%	13%
New Groups Formed	10	12	18	11	31	30
Disbanded Groups	4	7	35	10	27	24

*Year 53 numbers are calculated through 1/22/15, lacking February through April data. These months fall within the heart of the birthing season, and commonly account for 60% of births for the year.

Table 3

	2009	2010	2011	2012	2013	2014
Survival rate up to 1 year old	0.85	0.82	0.80	0.80	0.84	0.89
Survive rate all other animals	0.98	0.97	0.96	0.93	0.96	0.97
Fecundity females 5 and up	0.71	0.70	0.68	0.75	0.73	NA**

**2014 fecundity not reported as not all animals born in 2014 have been recorded as of yet.

Specific Aim 2:
We continue to improve our animal housing facilities, aligning ONPRC infrastructure, space, and resources with the maintenance and husbandry requirements of each species we support.

Facility Improvements:

- Received ove[Proprieta Info]in funding for new cage purchases, cage modifications, cage repairs, manipulanda, and associated caging items (tunnels, transfer boxes, lifting stations, forage stations). These purchases improved animal pairing, safety of staff and animals, animal handling efficiency, and overall quality of life for all NHPs.

- Partnered with a new chemical supplier and animal facility sanitation expert. This company shift has led to a vast improvement in our in place sanitation, group housing cleaning program and cage/rack washer disinfection and maintenance program. We have purchased new sanitation equipment (foamers, sprayers, scrubbers) and significantly upgraded our sanitation monitoring ability.

- Partnered with a new exterminator company, resulting in significant improvement in our pest monitoring and eradication capabilities. Overall, both our indoor and outdoor pests have been markedly reduced because of this change.

- Upgraded animal flooring in all ten Harem runs, Feed area 3 & 4, and selected Colony runs. Several exterior corral feed pads were added, heating was improved in the Feed 1 area, and all external water lines were upgraded to stainless steel and made resistant to freezing.

- The Colony Annex phase 1 remodel was accepted for animal use. This immeasurably improved one large animal holding room, a procedure room and feed room. It also added two new behavioral group housing rooms capable of constant video monitoring and individual animal food intake. The second phase of the remodel will begin in February 2015 to add another large procedure room and door upgrades to four rooms.

- Received approval to finalize and submit G20 grant draft proposal for a state-of-the-art upgrade of the group and cage housing area between corrals 4 & 5. An underutilized area for over thirty years, this renovation will be used for new group formations, visualization and recovery of sick and injured animals with their natal troop, and create the ability to add nutritional support for young corral animals. We have had multiple successes with re-introductions of sick and injured animals when they can visualize their groups during recovery in the shelter groups; this modification would allow us to carry the success into the corral groups.

Resource Improvements:

- Accepted[Proprietary Info]U24 and[Proprietary Info]U42 Indian-origin rhesus macaques from the NEPRC. These animals will be used as both breeding stock to improve genetic heterogeneity of the existing U24 and P51 colonies, and to support AIDS/HIV funded projects. In collaboration with[ ](previously NEPRC, now TNPRC), we collected serum for cortisol levels and feces for microbiome analysis over two time points (arrival and 6 months) on the U42 group of animals. Additionally we imported[ ]animals for approved ONPRC projects.[Exempted by Requester][Proprietary Info]

- Made significant strides to lower our non-SPF group of caged animals. The colony size has dropped 30% this year, and we anticipate another 25% reduction for this coming year.

- Sold over[Propr ietary Info]NHPs to other research institutions to help meet the national research needs for NHPs. These sales significantly reduced our NHP colony overpopulation; income generated facilitated upgrades to our outdoor corral-associated support facilities (Feed Area 7 heating, feed pad to Corral 3, pea gravel around all corrals).

Specific Aim 3:
We continue to provide exemplary animal care, maintaining an integrated program of animal husbandry, genetic and pathogen screening, and veterinary clinical and preventative care. In support of this aim, additional personnel were added, our viral screening process was updated, and our colony health program was integrated with the PRIMe electronic database.

Personnel:

- To meet increased cage and housing sanitation requirements, we promoted a Cage Crew Manager and two additional Cage Crew staff were hired. These staff enhancements have improved sanitation and cage repair efficiency, strengthened communication with investigative staff and other DCM units, and reduced our out-of-service cage repair from 10% to 5%.

- RFO will hire one permanent and one temporary Veterinary Research Health Technician in February 2015 to support the significant new research demands on the colony nursery. Historically, the colony nursery managed 10-20 research infants/year, but is now expected to care for more than 80 infants/year for the next 3 years.

- The RFO will hire an additional clinical veterinarian for Colony Medicine. As shown in table 4, 2500 clinical cases from our outdoor housing groups received treatment in 2014; the caseload has remained at this level since 2010, thus additional veterinary support is needed. The change will also allow the unit to continue essential colony epidemiology and clinical medicine research projects.

Table 4: Colony Medicine Caseload from 1/1/2014 to 12/31/2014.

	Corrals (2234 animals)		Shelters (2327 animals)		Jmac (253 animals)		All (4814 animals)	
Master Problem	**Unique**	**Total**	**Unique**	**Total**	**Unique**	**Total**	**Unique**	**Total**
Dermatopathy	4	4	7	7	0	0	7	11
GI-Diarrhea	127	153	173	233	7	8	248	394
GI-Other	38	38	38	40	10	11	61	89
MS Abnormality	11	13	19	19	1	1	21	33
Neurologic Abnormality	3	3	0	0	4	4	8	7
OBGYN condition	12	12	27	29	1	1	31	42
Ophthalmic abnormality	6	6	6	7	0	0	7	13
Respiratory abnormality	8	8	6	6	0	0	6	14
Routine or Preventative	126	141	178	220	3	3	226	364
Urogenital	1	1	3	3	0	0	3	4
Weight loss	48	54	56	63	3	3	69	120
Wound	343	402	648	975	30	32	1037	1409
Total by case type	727	835	1161	1602	59	63	1724	2500

Refinements to Virology Screening Program:

- The Specific Pathogen Free Laboratory (SPF Lab) fully adopted the Intuitive Biosciences SPF4 and SPF9 microarray platform. Over 2200 previously validated samples per viral pathogen were used to validate the new assay. We also validated an SRV 2 & 5 western blot assay. This reporting year all animals in corrals (approximately 1600 animals) were assayed on the SPF4 platform and the shelter-based population (approximately 1200 animals) will be tested on the new microarray in the next reporting year. This new platform has greatly improved our diagnostic efficiency. As expected we discovered a few STLV1 positive animals in the corrals that were quickly removed from breeding. In addition, the SPF9 assay has been fully adopted for the U24/Expanded-SPF animal colony. Total testing performed for both P51 and U42 populations are depicted in the Table below.

Total tests performed per year for the ONPRC P51 colony		2012	2012	2013	2013	2014	2014
Test Type	Virus	Negative	Positive	Negative	Positive	Negative	Positive
ONPRC	Simian Betaretrovirus (SRV) #$^	3490	16	3464	26	5781	48
ONPRC	Simian Immunodeficiency Virus (SIV) #	18	0	17	0	1357	0
ONPRC	Simian T-Cell Lymphotrophic Virus (STLV) #	18	0	21	0	1350	7
ONPRC	Macacine Herpesvirus 1 (Herpes B) #@	2626	38	2565	25	3158	140
ONPRC	Measles Virus (Paramyxovirus) #	14	0	12	9	1304	53
Confirmatory	Simian Betaretrovirus (SRV) +	231	13	337	6	133	5
Confirmatory	Simian Immunodeficiency Virus (SIV) +	143	2	207	0	132	0
Confirmatory	Simian T-Cell Lymphotrophic Virus (STLV) +	137	6	211	1	127	9
Confirmatory	Macacine Herpesvirus 1 (Herpes B) *	447	62	557	27	438	22
Confirmatory	Measles Virus (Paramyxovirus) +	122	19	131	75	71	66

Total tests performed per year for the ONPRC U42 colony		2012	2012	2013	2013	2014	2014
Test Type	Virus	Negative	Positive	Negative	Positive	Negative	Positive
ONPRC	Simian Betaretrovirus (SRV) #$^	1044	0	982	0	1378	6
ONPRC	Simian Immunodeficiency Virus (SIV) #	0	0	17	0	170	0
ONPRC	Simian T-Cell Lymphotrophic Virus (STLV) #	0	0	19	0	169	1
ONPRC	Macacine Herpesvirus 1 (Herpes B) #@	935	4	878	5	717	4
ONPRC	Measles Virus (Paramyxovirus) #	0	0	15	4	169	1
Confirmatory	Simian Betaretrovirus (SRV) +	26	0	20	1	12	0
Confirmatory	Simian Immunodeficiency Virus (SIV) +	24	0	18	0	12	0
Confirmatory	Simian T-Cell Lymphotrophic Virus (STLV) +	24	2	22	0	12	0
Confirmatory	Macacine Herpesvirus 1 (Herpes B) *	75	1	73	2	58	1
Confirmatory	Measles Virus (Paramyxovirus) +	24	0	16	2	12	0

Total tests performed per year for the ONPRC U24 colony		2012	2012	2013	2013	2014	2014
Test Type	Virus	Negative	Positive	Negative	Positive	Negative	Positive
ONPRC	Lymphocryptovirus (LCV) #			6	64	80	324
ONPRC	Macacine herpesvirus 1 (Herpes B) #@	584	0	419	0	404	0
ONPRC	Measles Virus (Paramyxovirus) #			57	13	386	18
ONPRC	Rhesus Cytomegalovirus (CMV) #@	987	2	1404	5	1562	2
ONPRC	Rhesus Rhadinovirus (RRV) #@	986	23	1405	5	1548	16
ONPRC	Simian Betaretrovirus (SRV) #@^$	344	0	503	0	832	3
ONPRC	Simian Foamy Virus (SFV) #@	984	7	1432	11	1560	4
ONPRC	Simian Immunodeficiency Virus (SIV) #			70	0	404	0
ONPRC	Simian T-Cell Lymphotrophic Virus (STLV) #			70	0	404	0
Confirmatory	Macacine herpesvirus 1 (Herpes B) +*	1163	2	304	12	382	6
Confirmatory	Measles Virus (Paramyxovirus) +	157	12	140	6	178	12
Confirmatory	Rhesus Cytomegalovirus (CMV) +	161	0	146	0	190	0
Confirmatory	Rhesus Rhadinovirus (RRV) +	161	0	146	2	190	1
Confirmatory	Simian Betaretrovirus (SRV) +	162	0	147	0	194	1
Confirmatory	Simian Foamy Virus (SFV) +	160	2	146	0	190	0
Confirmatory	Simian Immunodeficiency Virus (SIV) +	161	0	151	0	197	0
Confirmatory	Simian T-Cell Lymphotrophic Virus (STLV) +	161	1	150	0	195	0

KEY
Intuitive Biosciences Colony Surveillance Assay
$ IFA
^ Western blot
@ ELISA
+ Pathogen Detection Laboratory, Davis CA
* National B Virus Resource Center, Atlanta, GA

Colony Health Program:

- We continue to expand our use of the relatively new Primate Records and Information Management (PRIMe) electronic database for colony management and epidemiology efforts. An automated alert system provides daily updates on disease outbreaks in rooms and groups, behavior disruptions in groups, cage compliance information, pairing status, and required viral and tuberculin testing. Morbidity, mortality, and reproductive reports can be generated by date and location, allowing us to track and quickly respond to

animal health issues. PRIMe information is also used to make objective decisions regarding group formation and animal success within the breeding colony.

- Proprietary Info

Proprietary Info The vaccine was safety tested in rodents this winter, and will undergo the next phase 2-week NHP safety trial in rhesus beginning in February 2015. If the vaccine is proven to be safe, an efficacy trial is scheduled for March 2015 in over 120 group-housed animals. The objective is to lower the acute and chronic incidence rate of C. coli diarrhea. Additionally, Pending Support

Pending Support

- In April 2014, the USDA asked the ONPRC to evaluate alopecia in our NHP colony. RFO immediately established an NHP alopecia task force composed of members from across the scientific, medical and veterinary community, including representation from husbandry, behavior, clinical medicine, pathology, endocrinology, outside consultants and other research investigators such as Excluded by Requester from the University of Massachusetts & NEPRC who has extensively studied alopecia in NHPs. The group is evaluating the endocrine, nutritional, behavioral, pathological, aged, seasonal, genetic, and housing components that may contribute to alopecia in the rhesus macaque. We are currently scoring alopecia in our outdoor-housed animals over several time points and collecting hair samples at the same time for cortisol determination. These data will then be compared to housing density, housing type, season, and other parameters. This will be, at a minimum, a two-year commitment to address this area of interest.

To prevent competition and food-related fighting, all group-housed animals are fed in excess. This common practice has apparently contributed to an increase in obesity of our Japanese macaque troop. Because Purina has had great success with their Mazuri NHP zoo food, a low glycemic diet which leads to weight reduction, we intend to test this diet on one group of Japanese macaques for palatability in February 2015. If successful in this small cohort, the diet will be slowly integrated into the larger Japanese macaque troop in the spring of 2015.

RESOURCES, FACILITIES, AND OPERATIONS: TRAINING

Training: Excluded by Requester provided clinical training to three ACLAM residents, 12 veterinary externs, two summer interns, and one doctoral student. A total of 640 hours of direct clinical instruction were provided in the Colony Hospital to residents, and an additional 144 hours of direct clinical instruction were provided to veterinary externs. Additionally, [redacted] provided EFFORT of support to summer and doctoral students, EFFORT of didactic support for students in the OHSU School of Medicine (SOM), and EFFORT of mentoring support to junior faculty.

Professional development: During the period, Excluded by Requester attended the Breeding Colony Management Consortium Meeting in November, and presented on the Campylobacter vaccine development program. Excluded by Requester attended the Primate Center Directors meeting that same month, and supported a workshop on the PRIMe electronic health record system. [redacted] attended the OHSU New Manager Leadership Essentials training course, and also attended the 38th Meeting of the American Society of Primatologists where he presented "Does nearby construction increase aggression in outdoor, socially housed macaques?" and "Development of a touchscreen testing apparatus to assess recurrent perseveration in rhesus macaques (*Macaca mulatta*)." [redacted] attended the Association of Primate Veterinarians meeting, and jointly with [redacted] from CNPRC, presented "Monkey 101-Diarrhea management in Captive NHPs: Past, Present, and Future." [redacted] also attended the Veterinary Emergency and Critical Care meeting in Indianapolis, and was selected to participate in the highly competitive 12-month "Lead Mentor" training program sponsored by the OHSU School of Medicine.

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 RFO Unit continues to follow the plan for caging purchases, maintenance, and upgrades, as well as equipment upgrades and facility improvements. RFO staff meets with the Business Office and Administration leadership on a regularly scheduled basis to facilitate problem-solving and to assure that the goals are met.

The RFO Unit, NHP Resources in particular, have presented and will continue to emphasize capacity, repair and maintenance needs at monthly meetings of the Animal Utilization Committee (AUC), Executive Leadership Committee and the IACUC. Our target is to build 15% flex/surge space (empty rooms and caging) by the end of calendar year 2015 to be available for maintenance or emergencies, and ONPRC leadership fully supports this proposed program.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			48,960.00	16,793.00	65,753.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **65,753.00**

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						
80	Unit Staff	430.32			1,428,086.00	577,448.00	2,005,534.00
80	**Total Number Other Personnel**					**Total Other Personnel**	**2,005,534.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**2,071,287.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	5,100.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**5,100.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	117,755.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	78,872.00
Total Other Direct Costs	**196,627.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**2,273,014.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	2,273,014.00	636,444.00
		Total Indirect Costs	**636,444.00**

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)	**2,909,458.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Pathology Services
Component Project Lead Information:
Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Anatomic and clinical pathology expertise and services are key elements of ONPRC's veterinary care program dedicated to the maintenance of self-sustaining populations of genetically characterized, disease-free NHPs for research. They are also essential for meeting the objectives of our research programs. The primary goals of the Pathology Services Unit (PSU) are to provide disease diagnostic and surveillance services that promote the health and safety of ONPRC's animal resources and provide research support services that strengthen the research infrastructure and contribute directly to the mission of ONPRC through participation in multidisciplinary research programs.

The specific aims for accomplishing this:

Specific Aim 1: To provide disease diagnosis and surveillance for ONPRC's animal resource through diagnostic necropsies, biopsies, clinical pathology and maintenance of databases for epidemiologic queries.

Specific Aim 2: To participate in the research mission of ONPRC by providing pathology support for research projects through necropsies, tissue distribution, clinical laboratory services and participation in study design; and through characterization of spontaneous NHP diseases potentially useful as models for human diseases.

Specific Aim 3: To act as a national resource for NHP pathology through maintenance of archived tissues, slides and blocks, databases of biological data and images.

Specific Aim 4: To serve as a resource for educating veterinarians, laboratory animal professionals and investigators, about primate pathology by participation in publication, teaching and presentation in local, national and international settings.

The expected outcome is a highly productive resource for the support of the research mission and the NHP population through centralized provision of pathology services and expertise.

TISSUE DISTRIBUTION PROGRAM SPECIFIC AIMS
The nonhuman primate (NHP) is, and will always remain, a limited and valuable research resource. Continued efforts to maximize distribution of NHP tissues to biomedical investigators will ensure the best possible use of this resource. Centralized coordination of tissue requests with scheduled necropsies permits support for increased numbers of biomedical research efforts with less impact on the primate resource.

Specific Aim 1: Ensure maximum and efficient utilization of the unique primate resource through continued and expanded promotion of the Tissue Distribution Program (TDP)

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-Patho_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-Patho_Training.pdf

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

NOTHING TO REPORT

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

We will continue to provide timely and valuable pathology support both to our colony resource and the ONPRC research mission. Much of the ongoing review of archival material for inclusion in the PPID, and as a basis for case series publications, will also serve as the foundation for advanced work in the identification and characterization of disease phenotypes for use as models of human disease. We

have several manuscripts in preparation for several case series, and additional case material being analyzed for additional publications. Several case reports in preparation include material and collaborative input from other NPRC members.

PATHOLOGY SERVICES: ACCOMPLISHMENTS

The Pathology Services Unit (PSU) continues to provide pathology support for the animal resource and research mission through necropsies, tissue distribution and clinical pathology laboratory services. During the reporting period, the histology laboratory generated 12,197 H&E stained slides, 2,883 slides for recuts and special stains, 518 slides for immunohistochemistry, and 242 slides for evaluation of surgical biopsies. The Clinical Pathology Laboratory performed 8,755 complete blood cell counts, 3,285 serum biochemistry profiles, 1,213 fecal microbiology cultures, 595 general cultures and an additional 3, 544 miscellaneous tests in-house and through external laboratories including urinalyses, glycosolated hemoglobin, clotting profiles, anaerobic cultures, and antibiotic sensitivity profiles.

The Tissue Distribution Program (TDP) is administered by the Pathology Services Unit to maximize the availability and use of NHP tissues and minimize the number of NHPs required for research. As part of the NHP TDP, 33 ONPRC/OHSU investigators received 5,263 tissue specimens and 12 non-OHSU investigators received 581 specimens prepared according to their specifications. An additional 285 tissues were distributed for use in tissue banks administered at ONPRC. Of 6,129 total tissue samples distributed, 4,631 tissues were received by investigators from animals assigned to them as part of terminal research protocols.

A major way in which ONPRC serves as a national resource for NHP pathology is through participation in the Primate Pathology Image Database. During the 2014-15 reporting period, an additional 269 scanned digital microscopic slides and gross images from the ONPRC archives were curated and published to the database. The number of registered academic users rose from 53 to 164 and now represents more than 50 institutions.

PSU served as a resource for educating veterinarians, laboratory animal professionals and investigators, about primate pathology through the publication of five case reports and case series in peer-reviewed journals, serving as co-authors for an additional three papers published by ONPRC researchers, and coauthor on a poster presented at a national meeting. Excluded by Requester lectured on NHP Pathology at the 41st Annual CL Davis Foundation Gross Pathology Review Course held in East Lansing, Michigan. Excluded by Requester served as a member of the Ad Hoc General Pathology Committee for the American College of Veterinary Pathologist's (ACVP) Examination Committee and has accepted a position on the ACVP Certifying Examination Board. Excluded by Requester each presented cases at the Primate Pathology Workshop held in conjunction with the ACVP Annual Meeting in Atlanta, GA. They also prepared and presented three cases for the Pathology Working Group Virtual Slide Conferences.

PATHOLOGY SERVICES: TRAINIING AND PROFESSIONAL DEVELOPMENT

The Pathology Services Unit (PSU) supports a one year training fellowship in NHP Pathology. During the current reporting period, Excluded by Requester DVM, MPH, completed her one year fellowship and has begun a residency in veterinary anatomic pathology at UC Davis College of Veterinary Medicine with specialization in laboratory animal pathology. Our current trainee Excluded by Requester DVM has been accepted to the residency in veterinary anatomic pathology at University of Florida College of Veterinary Medicine to begin in July 2015 at the end of her one year fellowship. We are currently recruiting for the next year's fellow. Additionally, we have hosted a Pathology Assistant Master's candidate for a one week externship.

PSU participates in the training of veterinary student clinical medicine externs as part of their comprehensive exposure to NHP medicine. We support the Laboratory Animal Medicine residency program through provision of didactic lectures, rotations through pathology services, and monthly pathology-centered didactic lectures. We provide lectures to the ONPRC Technician CE lecture series coordinated by Excluded by Requester Additionally, we conduct weekly NHP histopathology rounds and weekly review of the Joint Pathology Center (JPC) Wednesday Slide Conference material open to all veterinarians and trainees.

Excluded by Requester attended the Annual Meeting of the ACVP and Primate Pathology Workshop held in Atlanta, GA. Excluded by Requester attended a one day Grant Writing Workshop sponsored by OHSU OCTRI in November 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

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Unit Head	Institutional Base Sallary	EFFORT			72,269.00	24,065.00	96,334.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **96,334.00**

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	Unit Staff	70.5			335,112.00	112,390.00	447,502.00
12	**Total Number Other Personnel**					**Total Other Personnel**	**447,502.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**543,836.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	74,790.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	67,234.00
Total Other Direct Costs	**142,024.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**688,860.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	688,860.00	192,881.00
		Total Indirect Costs	**192,881.00**

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)	**881,741.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Surgical Services Unit

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Surgical Services Unit is a specialized, unified team delivering centralized, reliable, and consistent surgical services in a state-of-the-art surgical facility. Complete surgical service and expertise that include procedural planning and development, anesthesia, analgesia, and post-operative animal care are essential for meeting the objectives of the research programs at ONPRC, as well as supporting a comprehensive clinical care program. The primary goal of SSU is to provide superior surgical expertise while ensuring compassionate care for animal patients and the scientific integrity of research objectives. The specific aims in support of this goal are:

Specific Aim 1. To provide surgical support for research projects through comprehensive surgical, anesthetic, analgesic and post-operative care. Research support includes collaboration with investigators to refine surgical procedures through careful planning, proper training, and optimal instrumentation to minimize invasiveness and discomfort to the animal subjects. We will continue to provide and refine anesthesia and analgesia modalities tailoring them for specific surgical procedures, subject size, age, and species while also accommodating for physiologic factors that may compromise anesthesia, such as obesity. We will continue to find ways of providing these services while maximizing efficiency through work flow analysis and computational automation.

Specific Aim 2. To support colony health maintenance by providing diagnostic, therapeutic, and emergency surgical services for spontaneous or experimentally induced diseases or conditions. SSU provides support for colony health maintenance through the provision of aseptic surgical suites equipped with quality anesthesia machines, instrumentation, endoscopic equipment, and experienced surgical veterinarians available for referral procedures or consult. Specific examples of routine colony health support we will continue to provide include intestinal resection and anastomosis for intestinal neoplasia, emergency Caesarian section, orthopedic fracture repair, diagnostic endoscopy and laparoscopy, and critical care.

Specific Aim 3. To serve as a resource for training veterinary students, residents, technicians, and veterinarians as well as investigative staff in all aspects of non-human primate surgical techniques, anesthesia, and analgesia practices. A significant part of this training is continued proficiency evaluation of personnel performing surgeries on animals. We will work closely with the RETU in developing interactive, software-based means of training and competency evaluation to compliment the traditional hands-on training and observational modalities currently in use. Intraoperative imaging will continue to be a primary component of the preparatory materials personnel must review prior to hands-on training, as well as a key aspect of continued proficiency assessment after initial certification.

Specific Aim 4. To expand collaborative and independent research with the goal of refining practices to minimize adverse physiological sequelae that may result from experimental interventions for the betterment of animal welfare and science. SSU will explore long-acting analgesic modalities to reduce subject distress associated with frequent post-operative injections. Current collaborations to determine the physiological effects of various anesthesia modalities on neonatal and pregnant rhesus macaques will continue. Finally, we have applied for funding to develop a means of measuring the total blood volume of rhesus macaques.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-SSU_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-SSU_Training.pdf

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

Excluded by Requester "Clinical Research Overview" was presented by [redacted] to the Science Ambassadors, a group of high school students with special interest in careers in science.

"Introduction to Basic Surgical Instruments and Suturing Skills", a wet lab and lecture for 6th grade students from Health and Science High School. Instruction provided by Excluded by Requester of SSU.

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

SSU will continue to provide comprehensive anesthesia, analgesia, and surgical services in support of the research activities on campus.

New techniques and refinements will be adopted as they are developed. A neonatal MCA occlusion model is being anticipated, as well as the development of a macaque surgical preeclampsia model. Independent research will continue to be a focus with the development and expansion of research projects the SSU veterinarians have initiated. Longitudinal studies of blood volume changes throughout pregnancy, as well as a cross-sectional study of blood volume as function of age are planned. Additionally, a study assessing neuroapoptosis caused by sevoflurane, remifentinil, and dexmedetomidine in neonatal macaques is planned.

SURGICAL SERVICES: ACCOMPLISHMENTS

Specific Aim 1: The Surgical Services Unit (SSU) is projected to complete over 7,500 surgical cases by the end of this reporting period. This is an increase of over 22% from the previous reporting period. Notably, this increase in case load was accomplished with 15% fewer staff members than the previous reporting period. The gain in efficiency is the direct result of computational integration and automation of SSU processes. Web forms continue to be developed that streamline data entry into animal health records (PRIMe) as procedures are completed. This improves accuracy and reduces error. Systems that integrate with PRIMe crosscheck each surgical procedure for case, post-operative rounds, and post-operative analgesic entries. These technological advancements and the transition to PRIMe have freed our staff to spend less time doing data entry tasks and more time providing excellent animal care. Several new surgical procedures have been developed during this reporting period in support of approved experimental protocols. New procedures include MRI-guided intracranial injection using the Clearpoint system that allows specific targeting of brain regions and real-time image feedback of target region perfusion of injected materials. SSU will also be taking over the aorto-iliac graft procedures that were previously performed by a human vascular surgeon [Excluded by Requester] is currently providing training and feedback in this technique. Additionally, an ovarian perfusion and venous blood collection technique has been developed that involves placing a vascular clamp on the contralateral utero-ovarian vein in order to prevent cross-contamination from the contralateral ovary. Finally, SSU collaborated closely with the Advanced Imaging Resources Center to refine neonatal anesthesia and monitoring protocols. This has allowed several investigators to add fMRI of neonates as young as 5 days of age to their protocols.

Specific Aim 2: Approximately 100 procedures were performed over this reporting period in support of colony health maintenance and not as part of any experimental protocol. These procedures included 10 exploratory laparotomies that resulted in intestinal resection and anastomosis as treatment for GI adenocarcinoma, a common neoplasia of older rhesus macaques; 37 wound repairs; and 12 emergency cesarean sections. Miscellaneous other procedures performed included bone fracture repairs, tail amputations, and several herniorrhaphies.

Specific Aim 3: Surgical training has been provided to five veterinarians; two veterinary residents; 20 veterinary student externs; 11 veterinary technicians; 24 members of investigative staff; and one visiting journalist. Surgical training is typically multimodal and includes a written SOP, guideline, and/or surgical narrative, PowerPoint presentation, observation, hands-on training, and follow-up proficiency assessments. A list of surgical task certification by employee is maintained in PRIMe. SSU staff also collaborates with other units within DCM to standardize and centralize training.

Specific Aim 4: During this reporting period, considerable independent research was conducted by the SSU veterinary staff. A publication describing the physiological effects of ketamine, isoflurane, or propofol anesthesia on neonatal rhesus macaques was completed and published by [redacted] Additionally, funding was obtained to compare two methods of measuring blood volume in adult rhesus macaques. This study was completed by [redacted] and a manuscript describing the experiment and findings has been submitted to a publisher. Both of these studies were novel, innovative, and highly relevant to the field. Both contribute information intended to significantly refine current practices for the betterment of animal welfare and science.

SURGICAL SERVICES: TRAINING AND PROFESSIONAL DEVELOPMENT

The SSU veterinarians attended the following meetings and seminars:
Workshop in Laboratory Animal Medicine, North Carolina State, NC
Association of Primate Veterinarians Annual Workshop, San Antonio, TX
American Association for Laboratory Animal Science National Meeting, San Antonio, TX
European Primate Veterinarian Symposium, Sevilla, Spain

The SSU technicians attended the following meetings and seminars:
American Association for Laboratory Animal Science, District 8 Conference, San Francisco, CA
Academy of Surgical Research Annual Meeting, Minneapolis
Dove Lewis Emergency Animal Hospital Annual Conference, Portland
National Veterinary Emergency Response Team Training, Anniston, AL
Northwest Veterinary Specialists Winterfest, Clackamas, OR
SSU technicians also attend Technician Continuing Education lectures that are available on the ONPRC campus

The following professional certifications were achieved:
Diplomate, American College of Laboratory Animal Medicine (LDM)
Surgical Research Technician, ASR (TS)
Surgical Research Specialist, ASR (VS)

The following awards were received:
Henry and Lois Foster Award for Academic Excellence in Laboratory Animal Medicine (LDM)
Barry Sauer Award for attaining the highest SRT exam score (TS)
Oregon AALAS Technician of the Year Award (TS)

Publications:
Excluded by Requester 2014. "Effects of Anesthesia with Isoflurane, Ketamine, or Propofol on Physiologic Parameters in Neonatal Rhesus Macaques (*Macaca mulatta*)." *Journal of the American Association for Laboratory Animal Science* 53(3):290-300.

Submitted

The following oral presentations were given:
Excluded by Requester 2014. "Blood Volume Measurement in Rhesus Macaques: Is the 10%:10% Rule Accurate?" *Association of Primate Veterinarians 41st Annual Workshop Program*. San Antonio, TX.

Excluded by Requester 2014. "Introduction to Malaria in Nonhuman Primates" *American Association for Laboratory Animal Science 65th National Meeting*. San Antonio, TX.

Excluded by Requester 2014. "Obesity in Rhesus Macaques: Clinical and Surgical Challenges." *14th Annual European Primate Veterinarian Symposium*. Sevilla, Spain.

Excluded by Requester 2014. "Roux-en-Y Gastric Bypass Surgery in Obese Rhesus Macaques." *14th Annual European Primate Veterinarian Symposium*. Sevilla, Spain.

The following poster was presented:
Excluded by Requester 2014. "Measurement of Blood Volume in Adult Rhesus Macaques." [Poster] *American Association for Laboratory Animal Science 65th National Meeting*. San Antonio, TX.

Consortium Activities
Excluded by Requester continues to chair the Clinical and Surgical Techniques Working Group. This group, part of the

NPRC Consortium, has met once monthly via webinar for the past three years. The goals of this group are to improve procedural competency and repertoire as well as improve workflow efficiencies associated with procedures that are commonly performed among the NPRCs. A website is maintained that serves as a reference library of past presentations. All of the NPRCs are represented at the monthly meetings which consist of approximately 50 veterinarians and veterinary technicians.

Lectures given to the Oregon Laboratory Animal Medicine Residency Consortium:
NHP Taxonomy, Biology, and Use in Research (LDM)
NHP Anesthesia (LDM)
Large Animal Surgical Models in Biomedical Research (LDM)
Biomedical Ethics in NHP Research (TH)

Veterinary Technician Continuing Education Program Lectures given:
NHPs in Malaria Research (LDM)
Obesity in NHPs, tips to keep anesthesia boring (TH)

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Unit Head	Institutional Base Salary	EFFORT			32,952.00	10,413.00	43,365.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **43,365.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
8	Unit Staff	20.79			108,812.00	34,384.00	143,196.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**143,196.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**186,561.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	750.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**750.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	39,563.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	4,771.00
Total Other Direct Costs	**44,334.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**231,645.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	231,645.00	64,861.00
		Total Indirect Costs	**64,861.00**

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)	**296,506.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Behavioral Services Unit

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Behavioral Services Unit (BSU) is a service unit in the Division of Comparative Medicine. The BSU is responsible for overseeing behavioral management of nonhuman primates (NHPs) at the ONPRC. As such, the BSU plays a major role in ensuring that the ONPRC is compliant with both the Animal Welfare Act and the Guide for the Care and Use of Laboratory Animals. The primary objectives of this unit are to provide social opportunities and environmental enrichment promoting species-typical behaviors for the monkeys, to assess and attempt to decrease abnormal behaviors and promote animal well-being by using and developing techniques, devices and procedures that contribute to their psychological health. Pursuant to these objectives, the specific aims of this unit are:

Specific Aim 1. Reduce the number of single housed animals. A major goal of the ONPRC is to further reduce the number of single housed animals. Social housing increases the opportunity for animals to engage in many species typical behaviors, including play, feeding, and grooming, and is considered one of the best ways to promote their psychological well-being. We will continue to explore and further define the factors that positively influence pair or group success.

Specific Aim 2. Improve and expand upon our NHP training program. Training animals to cooperate with procedures such as injections or blood draws reduces the stress associated with these procedures. In addition, by reducing the stress associated with husbandry and handling procedures, inter-individual variation in stress response may also be reduced, enhancing the use of NHPs as research subjects. Training can also allow experimental animals to be housed in social groups as opposed to cages. Therefore, a major objective of our program is to expand upon our Positive Reinforcement Training, including training group housed monkeys to come to the front of their pen for injection or blood draw. We are currently undertaking studies geared at increasing training success, and will continue to investigate ways to improve and expand these efforts.

Specific Aim 3. Improve well-being and decrease abnormal behavior in NHPs. Abnormal behaviors, including self-injurious behavior and stereotypical behavior, can be indicators of compromised well-being in captive NHPs. Therefore, a major goal of the BSU is to reduce the occurrence of abnormal behaviors in our NHPs by improving conditions that promote well-being and decreasing situations known to compromise well-being (such as nursery rearing). To achieve this aim, we plan to: 1) Improve early rearing for orphaned infants by providing opportunities for them to be with foster females (i.e., non-lactating females trained to allow infants to feed from a bottle); 2) Provide a wider variety of enrichment options to NHPs, particularly for singly housed monkeys; and 3) Work with the Clinical Medicine Unit, the Behavioral Management Consortium and others to develop novel treatments for these behavioral problems.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-BSU_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-BSU_Training.pdf

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

Excluded by Requester

In 2014 [redacted] was invited to give talks at seminars at the American Society of Primatology and the American Association of Laboratory Animal Science meetings. She was also invited to give a public talk at the Oregon Museum of Science and Industry (OMSI) Science Pub. Members of the BSU were active in outreach, and participated in various programs including the Camp Monkey, Saturday Academy, Science Ambassadors, and the PCC Behavior Management of Zoo Animal course, as well as various ONPRC tours.

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

In the coming year, we plan to continue to work on our specific aims.
1. We will continue to work with RFO and others to help reduce the number of singly housed animals, and to avoid breaking established pairs. We are investigating whether variables such as temperament can affect pairing success.
2. We will continue to utilize positive reinforcement techniques to train animals to more willingly cooperate with procedures. We hope to have more operations technicians involved with this process.
3. We will continue to examine ways to help reduce abnormal behavior. In particular, we plan to continue to implement new enrichment strategies, particularly for single housed animals. Such enrichment might include exercise and different Kindle programs.

BEHAVIORAL SERVICES: ACCOMPLISHMENTS

Specific Aim 1: Our specific objective in this aim was to increase the number of animals socially housed at the ONPRC. Results: Social housing was a focus of the BSU in the past year. In 2014, the BSU attempted to pair house approximately 1,350 caged monkeys. Over 82% of these attempts were successful. We also implemented pair observations in an effort to determine whether behaviors between partners following a pair attempt may predict later success or failure. Technicians conduct focal observations on members of the pair immediately following the attempt, and again one day and one week after the pair attempt. These data will help us to make more compatible pairs. We have also continued to work with other DCM units to oversee our outdoor groups. And we have increased our level of monitoring in an effort to ascertain dominance relationships. Outcomes: We presented two abstracts on social housing at the 2014 American Society of Primatology meeting. We will continue to try to identify factors that may influence group stability.

Proprietary Info

Specific Aim 2: Our objective was to expand our training program. Results: In 2014, we used positive reinforcement techniques to train over [redacted] monkeys to voluntarily cooperate with noninvasive procedures including remaining stationary for vaginal swabbing and presenting a body part for venipuncture. We have also worked closely with the Resources-Facilities-Operations (RFO) unit to improve the method by which "Pole and Collar" training (moving animals from their home cage to a primate chair for procedures) is performed. We also continued to examine factors that might influence trainability, including temperament and fear towards caretakers. Outcomes: Results from these studies were presented at the 2014 AALAS meeting.

Specific Aim 3: Our specific objective was to decrease the incidence of abnormal behavior in our population. The focus of this aim has been to prevent abnormal behaviors by improving conditions that promote well-being and decreasing situations known to compromise well-being.Results: 1) We have continued to modify and improve upon our "Foster program", in which abandoned or orphaned infants are reared by a non-lactating female trained to allow the infant to drink from a bottle. We reared four infants in this fashion in the past year. As a result of this program, we have significantly reduced the need for nursery rearing. No infant was nursery reared for husbandry (as opposed to scientific) reasons in 2014. 2) We also improved upon our enrichment strategies in 2014. Because cognitive enrichment is known to be of value to captive primates, we purchased several Kindle Fire tablets, and evaluated their use. We found that monkeys prefer programs that are interactive (e.g., a painting program) to those that are passive (e.g., colors or movies). We also established a "Human Interaction program" for caged animals, in which technicians spent time doing activities such as blowing bubbles or giving extra treats to the animals in their areas. This kind of positive interaction has been shown to help improve the relationship between caretaker and NHP. We are currently evaluating the use of this enrichment. We have also procured new foraging enrichment items, including a "foraging tray" that will be attached to every cage. These trays are easy to fill and will allow us to provide additional enrichment to singly housed animals. In the past year, we were also involved in the 'Alopecia Working Group", comprised of members from BSU, the Pathology Services Unit, RFO, and scientific staff, to examine underlying causes of alopecia. All veterinary and behavioral staff have adopted the Behavioral Management Consortium alopecia scoring system; we are therefore measuring alopecia consistently across units, which allows us to collect data and track hair loss over time. Lastly, we started an Enrichment Committee, to provide an opportunity for scientific and DCM staff to work together to improve enrichment at the ONPRC. 3) We have started to examine the efficacy of using positive reinforcement training to reduce stereotypical behavior. Outcomes: We are currently submitting two abstracts to the 2015 American Society of Primatologists meeting with the results of the Kindle study as well as preliminary results from our alopecia study.

BEHAVIORAL SERVICES: TRAINING

Two BSU members attended the 2014 American Society of Primatologist meeting, and one attended the American Association of Laboratory Animal Science meeting. In addition, the BSU has a monthly journal club, and staff attend webinars and seminars offered at the ONPRC.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

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

We intend to increase the amount of NHP enrichment, including exercise. This will require additional staff, or additional involvement from others, in order to achieve this goal.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-6114

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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			34,511.00	13,079.00	47,590.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **47,590.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
8	Unit Staff	47.4			162,295.00	61,510.00	223,805.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**223,805.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**271,395.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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	0.00
Total Travel Cost	**1,500.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	7,244.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	3,620.00
Total Other Direct Costs	**10,864.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**283,759.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	283,759.00	79,453.00
		Total Indirect Costs	**79,453.00**

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)	**363,212.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Clinical Medicine Unit

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

What are the [specific aims] of the project?
Non-human primates are critical animal models for basic and translational biomedical research. Enhancing the scientific utility, health, and well-being of these populations requires an integrated program of clinical care, animal husbandry, genetics, and psychological health. Working closely with other DCM units, the Clinical Medicine Unit (CMU) maintains animal health through preventative and clinical care, ensuring the health and well-being of ONPRC NHP research resources while supporting breeding populations of genetically characterized, disease-free NHPs.

CMU's long term goal is efficient and humane management of ONPRC's NHP colonies using innovative techniques and procedures to identify, treat, and manage disease and abnormalities. To achieve this, the CMU must provide disease surveillance, diagnosis and treatment, work with ONPRC investigators to ensure experiments are well-planned and have clear scientific and humane endpoints, provide veterinary emergency care both during working hours and afterhours, and utilize a state-of-the art electronic health record system for documenting and managing animal care.

The specific aims for accomplishing this are:

Specific Aim 1. To provide preventative care and clinical care to ONPRC's laboratory animals through annual physical examinations, reproductive health monitoring, geriatric wellness programs, and weight management programs; and to provide rapid diagnosis and treatment of disease, illness, and injury.

Specific Aim 2. To provide clinical veterinary support for NHP related research, including technical assistance with protocol development, protocol review, animal model development, veterinary medical research, and resource management to optimize the NHP resource for current and future research use.

Specific Aim 3. To serve as a resource for educating pre- and post-graduate veterinarians, researchers, and technicians about clinical veterinary care and veterinary support of NHP research, including teaching, mentoring, collaborating, and presenting in local, national and international settings.

The expected outcomes are physically and psychologically healthy animals for support of biomedical research, and a population of disease free, genetically characterized NHP's sufficient to support current and future research needs. These outcomes support scientists who use NHPs, while ensuring the highest level of veterinary care for all NHP species at ONPRC.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-CMU_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-CMU_Training.pdf

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

All CMU veterinarians regularly participate in outreach events. These activities include serving as information sources for on-site tours (e.g. when ONPRC hosted the NPRC Directors' meeting, and the National Association of Medical Examiners), presenting to school groups of all ages including Lewis and Clark Law School, Portland Community College, and local primary schools, and participating as a judge in local middle school science fairs.

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

Conducting veterinary-focused NHP research using data collected by the electronic health records or pilot grant funds, in addition to projects coordinated with scientific staff where possible, will help us fulfill our goal of expanding basic knowledge of our important animal models. Excluded by Requester have ongoing projects that should be complete by grant end In Preparation In Preparation and it is anticipated that other projects will be initiated and concluded in the five-year time frame of the base grant.

Partnering with ONPRC investigators to produce publishable data that specifically contributes to the basic knowledge and understanding of NHP medicine and husbandry, and authored by the veterinarians, continues to be a primary CMU goal.

The competency-based training program for DCM and research staff will continue to expand and become more formalized and better documented over the next several years. This process will help ensure consistent skill levels for those performing procedures, and also validate the parameters for “trained individuals” at each skill level.

We will continue to use IT technology to help decrease time needed for reviewing information and data entry. It is anticipated that as our electronic medical records (PRIMe) becomes more refined and specifically adapted to ONPRC requirements, CMU will continue to discover additional ways to utilize this powerful program to streamline processes and improve efficiency.

We will work to bring information regarding scientific projects to the DCM staff by partnering with the researchers to create short, layperson targeted presentations about the important research occurring at the Center. We strongly believe this link will improve staff loyalty and job satisfaction, by explaining the value of the seemingly mundane or repetitive husbandry tasks.

CLINICAL MEDICINE UNIT: ACCOMPLISHMENTS

The purchase of a new ultrasound machine this last year has significantly increased the number of diagnostic ultrasounds performed at ONPRC. The number of ultrasounds for specifically diagnostic purposes (243) nearly equaled the combined total (274) of both diagnostics and research-driven ultrasounds of the previous grant year. Importantly, this singe capability has improved our animal care is by allowing earlier diagnosis of the most common spontaneous tumor of rhesus, GI adenocarcinoma.

We refined our physical examination practices by standardizing processes and improving preventive and aging care (e.g. earlier dental cleanings, radiographic evaluation of common joint and cardiac issues, routine evaluations for endometriosis), and partnered with investigators to ensure the healthiest animals possible for study by performing thorough evaluations of animal health and history prior to assignment (e.g. complete blood count or serum chemistry evaluation prior to starting PK studies).

The addition of a consulting radiologist using digital transfer of radiographs and additional technological/software advances have improved veterinary care and streamlined common tasks, including record entry reviews by veterinarians and NHP weight management by the technical staff. Pre-formulated software alerts ensure that no significant weight drops or gains go unnoticed, and that entries into an animal record are reviewed by a veterinarian in a timely fashion. These technologies have reduced the time required for oversight, resulting in more time available for staff to perform clinical work rather than combing through records for information.

We developed a required anesthetic monitoring training process for research staff, which involved clinical and surgical veterinarians and utilized both didactic and hands-on training. We have also significantly refined our requirements for provision of heat support of anesthetized NHPs, including temperature monitoring and approved mechanisms of heat support for all staff handling anesthetized animals.

We partnered with the Behavioral Services Unit (BSU) to create a more integrated care program for animals with behavioral abnormalities, and work closely with that group to ensure a holistic view of animal care for determining appropriate treatment methods and research and illness endpoints. BSU and CMU frequently collaborate to increase positive reinforcement training and reduce single housing of animals for clinical purposes whenever possible. Regularly scheduled meetings of involved personnel now occur between research, clinical, husbandry and behavioral staff working with specific animal groups to ensure consensus about best practices for animals with ongoing behavioral or clinical issues.

Aim 2:
An important refinement has been the realignment of paraprofessional staff responsibilities to ensure entry-level tasks are primarily handled by entry-level staff. This has allowed our highly skilled certified veterinary technicians to perform more appropriate skill level tasks, which then frees the veterinarians to handle complex cases and provide an increased level of research support. In addition, two new full time entry-level technicians were hired to handle tasks that do not require a certified veterinary technician, such as medication preparation and administration, surgical instrument cleaning and pack wrapping, collecting animal weights, and assisting with phlebotomy.

Our clinical staff continues to provide technical research support to scientists by performing complex procedures where the health of the animal could potentially be impacted (e.g. bronchioavelor lavages, lymph node biopsies, and CT scans).

The addition of a clinical veterinarian for research support now permits sufficient time for all CMU veterinarians to consult with PIs on protocol techniques, animal models and welfare issues, thereby ensuring improved clinical coverage for animal care. Optimum clinical workload distribution also allows [Excluded by Requester] to enhance their leadership duties as CMU unit head and Project Manager for the Oregon State Laboratory Animal Medicine Residency Consortium, respectively.

During the grant year, CMU veterinarians reviewed 144 protocols (new protocols, 3-year renewals, and modifications to existing protocols) prior to IACUC approval. Through this process, CMU veterinarians ensured

the best possible animal welfare, health and safety. Examples of protocol refinements initiated by DVMs include:

- Establishment of an intensive supportive care protocol for animals undergoing total body irradiation and hematopoetic stem cell transplantation.
- Initiation of a pilot study for a test article that had not been given via injectable routes prior to proceeding with the full study.
- Development and refinement of appropriate feeding and growth monitoring practices for juvenile animals undergoing a study requiring daily 18 hour fasts.
- Development of a supportive care protocol for PK studies using test articles that are known to cause nausea and vomiting.
- Development of appropriate monitoring parameters for pregnant animals undergoing a protein deficient trial per protocol.
- Improved monitoring for unexpected adverse events resulting from test article administration.
- Refinement of diabetic treatment modalities and monitoring protocols for obese resource animals.
- Refinement of infant supportive care for anesthesia while undergoing MRI.
- Refinement of diet manipulation projects to require calorie consumption calculation per animal rather than setting standard feed amounts for all animals.
- Refinement of protocols previously requiring single housing to allow pairing using novel housing options.

Aim 3: See Training and Professional Development.

CLINICAL MEDICINE UNIT: TRAINING AND PROFESSIONAL DEVELOPMENT

The CMU group has significantly increased the number of formal training opportunities provided for technicians and research staff over the past year. Provided by CMU veterinarians, a monthly training hour was established for CMU veterinary technicians and support staff consisting of both didactic lectures and wet labs for relevant duties. Topics covered include: dental extractions, management of periodontal disease, proper use of analgesics, common drug interactions, proper radiographic technique, clinical and systemic effects of tissue trauma, I-stat value interpretation, and appropriate suture selection.

Working in conjunction with the DCM Training Coordinator, the CMU Head, Manager, and Lead Technicians developed a formally documented training process, which will also include additional training documentation enhancements such as competency-based checklists for most skills. As a part of this process, all job descriptions were revised to specifically include an advancement path regarding skill acquisition for CVTs. In addition, CMU is piloting an online CE service for technicians, specifically designed to address common questions regarding clinical care. While the videos are based on small animal emergency practice, many of the procedures are provided at the ONPRC. We anticipate this online modality will increase access to NHP-specific training relevant to technicians, particularly as it applies to trauma care.

Excluded by Requester a CMU clinical veterinarian also board certified in the laboratory animal medicine specialty, presently serves as Program Manager for the ONPRC site of the Oregon State Laboratory Animal Medicine Residency Consortium. He develops and oversees the extensive training of LAM residents at the ONPRC, training which is also available to all CMU veterinarians. The program provides didactic lectures on medical, regulatory, and husbandry topics for the residents of the consortium, as well as hands-on training and mentoring for residents during their CMU rotations at the ONPRC. Residents and veterinary clinicians give lectures at the Oregon State University College of Veterinary Medicine, and to a nationwide audience of laboratory animal veterinarians participating in Virtual Grand Rounds, an activity part of the NPRC Training Consortium. The resident training program also provides support to any ONPRC staff veterinarian seeking ACLAM board certification, by allowing them to participate in resident educational activities, and by allowing protected time and financial support for board preparation activities, exam fees and travel costs.

In addition, Excluded by Requester also leads the veterinary student externship program, which provides an in depth and unique experience working with non-human primates in a research environment. Visiting veterinary students spend time with each CMU veterinarian for mentorship and training, and in so doing gain a well-rounded perspective on the role of veterinary medicine in NHP-based research by rotating through the Colony Hospital, Surgical Services Unit, Behavioral Services Unit, and the Pathology Services Unit. The externship program also provides NHP clinical and surgical experience to veterinarians enrolled in laboratory animal medicine training programs not affiliated with the Oregon State Laboratory Animal Medicine Residency Consortium.

DCM as a whole conducts training and education for veterinary, husbandry, and research staff preparing for AALAS certification tests, and the CMU veterinarians participate in these educational events by giving didactic lectures on various medical, regulatory and husbandry topics. Additionally, CMU veterinarians provide on-site RACE-certified continuing education seminars for ONPRC veterinary technicians.

CMU veterinarians regularly attend continuing education conferences on relevant medical and regulatory subjects (e.g. AALAS, ACLAM forum, APV, PRIM&R, IACUC training), which also allow networking opportunities, cross facility collaboration and information sharing with other NPRC staff and research institutions. Both Excluded by Requester presented posters at the national AALAS meeting in October of 2014. Excluded by Requester co-authored an abstract presented at the NHP AIDS symposium in November 2014. CMU veterinarians undertook 14 hours of on-site continuing education focused on ultrasound technique (primarily hands-on and provided by a certified ultrasonagrapher), to improve our use of this important diagnostic imaging modality.

CMU hosted several guests from outside facilities for collaborative purposes. Topics included:

- Discussion of cross-center collaboration and to provide specific information about our new electronic medical records system (PRIMe). These discussions allowed us to make specific improvements, as well as better understand the capabilities of the system.
- Collaboration on enrichment and behavioral monitoring of animals, and to discuss the possibilities of providing OSLAMRC veterinary residents with industry experience on public outreach strategies, general NHP health care, and management of veterinary staff in large primate facilities.
- Excluded by Requester additionally serves as an external advisory committee member for the Proprietary Info Primate Research Center, located in Proprietary Info

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

RPPR - Core-6115

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			51,000.00	18,921.00	69,921.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:									**Total Senior/Key Person**	**69,921.00**

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						
20	Unit Staff	112.8			492,028.00	182,542.00	674,570.00
20	**Total Number Other Personnel**					**Total Other Personnel**	**674,570.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**744,491.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	2,400.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,400.00**

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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	26,476.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	17,236.00
Total Other Direct Costs	**43,712.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**790,603.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	790,603.00	221,369.00
		Total Indirect Costs	**221,369.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**1,011,972.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Obese NHP Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Obese NHP Resource is closely linked with the newly established Division of Diabetes, Obesity, and Metabolism, and exploits the macaque model of diet-induced obesity (DIO) developed at ONPRC to provide qualified internal and external investigators access to metabolically characterized animals and clinical samples for a variety of studies in metabolism, obesity, pre-diabetes, and co-morbidities. Through provision of the services and expertise supported by this Resource, it fulfills the mandate of the ONPRC to serve as a national resource for valuable NHP models. In furtherance of this goal, the Resource will pursue the following Specific Aims:

Specific Aim 1. Maintain a healthy and well-characterized DIO macaque colony. Since diet-induced obesity is a serious disease state, the animals become more susceptible to health complications when maintained on the Western-style diet used to produce weight gain. Therefore, the progression of disease state is accomplished through the quarterly measurement of body weight, adiposity (by DEXA), and glucose tolerance (through intravenous glucose tolerance tests and HbA1C determinations).

Specific Aim 2. Expansion of animal availability. There is an ever-expanding demand, both locally and nationally, for the macaque DIO model. Resource constraints will be addressed by targeting short-term studies supported by industry to maintain animals during phenotype development and the establishment of a cynomolgus DIO model.

Specific Aim 3. Increased collaboration with the ONPRC Primate Aging Resource. Most current ongoing studies using the Obese NHP Resource focus on early developmental programming or the young adult. However, one of the major challenges that clinicians will face in the future is the management of aging, obese patients. To address this issue, Obese Resource staff will cooperate with Aging Resource personnel to evaluate the metabolic status of aged animals as well as making older Obese Resource animals available for studies as they reach the appropriate age.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-ObeseResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-ObeseResource_Training.pdf

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

NOTHING TO REPORT

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

The focus on the next period will be to further characterize the DIO model in the NHP. In addition, we are increasingly involved in grant applications that will utilize the animals in the resource or require technical assistance from the resource.

OBESE NHP RESOURCE: ACCOMPLISHMENTS

Our first goal for this resource was the establishment of a plan to closely monitor the development of obesity and associated diseases in the nonhuman primate. This was accomplished by performing quarterly measurements of body weight, glucose tolerance (fasting glucose, in vitro glucose tolerance tests, HbA1c), insulin sensitivity (fasting insulin and insulin tolerance tests), body composition via DEXA scanning (lean mass, fat mass and bone mass) and lipid profiles (HDL, LDL, Cholesterol, Triglycerides). We have expanded on these outcomes by adding retinopathy. A large cohort of animals received baseline eye scans and will be followed over time to determine the rate and level of retinopathy in response to obesity and/or diabetes.

We also developed the cynomolgus macaque as a DIO model by placing a cohort of cynomolgus macaques on the western style diet. These animals are slated to be used in both academic research and research sponsored agreements with industry. Currently, we have one animal that has been made available to the Aging Resource. We expect this number to increase over time as the DIO colony ages and more animals reach the appropriate age for being entered into the Aging Resource.

OBESE NHP RESOURCE: TRAINING AND PROFESSIONAL DEVELOPMENT

The Obese Resource provides both technical assistance, as well as training for investigators that are interested in measuring metabolic changes in their studies. We have trained research staff from several investigators to perform their own metabolic analyses. In other cases, the obese resource staff will provide technical support to perform these measures.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

During this last year, we have replaced the DEXA scanner with a new model due to malfunction of the old unit. The new scanner will provide for greater reliability in the scanning of smaller, juvenile monkeys, which is of great importance to studies that investigate the impact of maternal high-fat diet on development. In addition, the new scanner will allow for differentiation between subcutaneous and visceral fat.

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: RPPR-DCM-ObeseResource_ResourceSharing.pdf

OBESE NHP RESOURCE: RESOURCE SHARING

The Obese Resource provides NHP samples to internal and external users based upon published rates. Reagents and other resources developed through NIH-funded studies are shared according to NIH guidelines.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Limited. As part of the distribution program, we have provided samples from obese animals to pharmaceutical industry, as well as academic partners at different universities.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

Some turnover in the division has resulted in personnel changes. The departure of Excluded by Requester resulted in the promotion of Excluded by Requester into the position of Director of the Obese Resource. We have already recruited new technicians and little to no disruption is expected in the functionality of the Obese Resource.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			11,000.00	4,477.00	15,477.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **15,477.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
4	Unit Staff	17.64			59,976.00	24,410.00	84,386.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**84,386.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**99,863.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	880.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**880.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	27,520.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	5,160.00
Total Other Direct Costs	**32,680.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**133,423.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	133,423.00	37,358.00
		Total Indirect Costs	**37,358.00**

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)	**170,781.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Primate Aging Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Primate Aging Resource (PAR) has been in existence since 1999 and manages the Primate Aging Study (PAS) colony, which is a NIA-supported nonhuman primate resource at ONPRC. The PAS colony serves the research community by identifying, maintaining, and supplying projects with aged Indian rhesus macaques. To further facilitate this process and strengthen the resource for the future we propose the following specific aims:

Specific Aim 1. Formalization of organizational ties with the Division of Comparative Medicine (DCM). To integrate the goals of the PAR with DCM operations, strong and direct connections of PAR with senior management in animal resources, facilities, research, clinic, surgery and pathology departments will be necessary for smooth PAR operations.

Specific Aim 2. Leveraging of Information Services (IS) and other computational resources. The ongoing evolution and expansion of the IS department will be highly beneficial for PAR and will result in the development of management tools for tracking of replacement animals, database management (LabKey project) and the data mining of archival animal records.

Specific Aim 3. Enhancement of husbandry practices. Physicals exams (PE) of old animals are more frequent (biannual) and will now be used to capture biomarkers of inflammation and evaluate the prevalence of aging pathology, arthritis and obesity. This data will better define the model and inform clinical practice.

Specific Aim 4. New model development. We will use PE results to discover the extent and level of arthritis in the PAS colony and evaluate the possibility of model development. A second project leverages on-campus expertise and scientific collaborations to develop a model of alcohol abuse in aged animals.

Specific Aim 5. Expansion of archival projects. Continuation of one of the long-term projects in PAR is the collection tissues for our archives. Moreover, we propose to continue to build our archive of MRI brain images to better define the patterns of normative aging.

Specific Aim 6. Data mining. A great deal of descriptive data whose analysis is valuable for primate model development and husbandry is available for extraction. Programming for the extraction and then analysis of such data is being pursued.

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

Yes

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-AgingResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-AgingResource_Training.pdf

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

NOTHING TO REPORT

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

Fundamentally, continue the work initiated in the past year. One exciting aspect of the process is the continued development of IS tools that should assist in a gain of efficiency with workloads, along with the possibility of database search engines to yield information on the aging process in the nonhuman primate model.

AGING RESOURCE: ACCOMPLISHMENTS

Specific Aim 1. The Primate Aging Resource has developed optimized procedures for animal enrollment into the Resource with Division of Comparative Medicine (DCM) senior staff. For example, DCM generates a list of candidates for enrollment into the resource from which final selections are made, based upon anticipated need. The working ties with the Behavioral Sciences Unit, Surgery, Pathology and Clinical Medicine Units are strong, and improved lines of communication for issues and solutions that deal with animal health, care, surgery and pathology have been put into place.

Specific Aim 2. The resource has worked with members of the Information Systems (IS) staff managing the Primate records and Information Management (PRIMe) system to create and then populate a database describing the aging tissue archive. The same group is also creating tools for easier management of the Primate Aging Resource animals, including creation of documents for census monitoring and identification of replacement animals for the resource.

Specific Aim 3. Animals in the Primate Aging Resource will receive biannual physical exams in order to more readily capture age-related health problems, which are more amenable to early intervention. A byproduct of these exams is that blood samples will also be collected and processed into the serum tissue archive for future considerations, such as biomarker research.

Specific Aim 4. We have discussed and are working on options to examine aging biomarkers and pathology in the aging colony, an effort that is bolstered by data from the ORIP database search engine (see below). Additionally, the measurement of specific markers may be feasible due to the recent purchase of a tandem mass spectrometer by the Endocrine Services & Technology Core.

Specific Aim 5. The collection of tissue for age-comparisons has continued, and biopsies have been distributed for studies locally and internationally. For the latter effort, ONPRC scientists will collaborate with scientists in Australia and the United Kingdom in an effort to determine genetic and structural changes as an effect of aging.

Specific Aim 6. The Aging Resource was recently advised by the Office of Research Infrastructure Programs (ORIP) to list its involvement with the generation of research tools for mining of the ONPRC animal database. The generality of the methodology may encourage intra- and extra-Center usage for groups seeking similar solutions. The NPRCs maintain extensive animal records that can be mined for valuable data. We recently extracted past records of thousands of brain weights to address age-related change. We were able to demonstrate a mild loss of brain weight in older males only, but not on the order of catastrophic changes seen with human neurodegenerative disease. This suggests that macaques model normative brain changes seen clinically with advanced age.

AGING RESOURCE: TRAINING AND PROFESSIONAL DEVELOPMENT

The Head of the Primate Aging Resource attended two conferences: 1. The 2014 American Aging Association meeting; and, 2. The 2014 Society for Neuroscience meeting. These two meetings afforded the opportunity to see first-hand the current finding in two fields of primary interest and the opportunity to talk with collaborators.

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 most transferable technologies are the search algorithms that arise from the database search effort. It is noted that some modifications of the search program might be required on a site-by-site basis, as each institute has their own variation of hardware and software configurations that make up their records system.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

File uploaded: RPPR-DCM-AgingResource_OtherProducts.pdf

C.5.b Resource sharing

File uploaded: RPPR-DCM-AgingResource_ResourceSharing.pdf

AGING RESOURCE: OTHER PRODUCTS

Last year, Excluded by Requester participated on several papers on aging and neurodegeneration and is currently working on drafts of two additional papers, one on the topic of hormone replacement therapy in aged females and the effect on cognition and also a report on the brain weight as a function of age and gender gleaned from the ONPRC database query.

- Excluded by Requester
- Excluded by Requester (2014) Impact of moderate calorie restriction on testicular morphology and endocrine function in adult rhesus macaques (*Macaca mulatta*). *AGE* 36:183-97. PCMID: PMC3889886
- Excluded by Requester (2014). Androgen supplementation during aging: development of a physiologically appropriate protocol. *Rejuvenation Res* 17:150-3. PCMID: PMC3995436
- Excluded by Requester (2014) Toll-like receptors and ischemic brain injury. *J Neuropathol Exp Neurol.* 73:378-386. PCMID: PMC4115675
- Excluded by Requester (2014) Testosterone increases circulating dehydroepiandrosterone sulfate levels in the male rhesus macaque, *Front in Endocrinol* 5:101. PCMID: PMC4070064

AGING RESOURCE: RESOURCE SHARING

Sharing by the resource includes samples from the tissue bank archive, animals requested for projects, and more recently, requests for aging phenotypes that can linked to genetic background.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			69,683.00	28,988.00	98,671.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **98,671.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
2	Unit Staff	18.0			52,647.00	21,902.00	74,549.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**74,549.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**173,220.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	5,600.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	215,552.00
Total Other Direct Costs	**221,152.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**396,372.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	396,372.00	110,984.00
		Total Indirect Costs	**110,984.00**

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)	**507,356.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Infectious Disease Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

This is a resource not described in the prior funding period that brings together a number of assets and capabilities that were previously in other Center entities, but which shared a focus on infectious disease research. In light of the significant focus on this research area and the concurrent presence of specialized SPF colonies supported by U24 and U42 grants, as well as the SIV-infected long-term survivor cohort, this resource provides professional and technical expertise to investigators who are performing infectious disease research in nonhuman primates and who would benefit from assistance with project performance as well as specialized SPF colonies supported by U24 and U42 grants. The Resource managed 44 infectious disease study protocols in nonhuman primates utilizing 12 Risk Group 2 and 3 infectious agent models for 11 investigators totaling 687 macaques in calendar year 2014.

Specific Aim 1. Model development.
Development of a Plasmodium knowlesi (Pk) challenge model.
The Plasmodium knowlesi (PK) challenge model in rhesus macaques will be developed with the assistance of Excluded by Requester Naval Medical Research Center (11). Macaques will be intravenously inoculated with 100 sporozoites obtained 14 days after Anopheles dirus mosquitos are fed on a Pk-infected macaque using the Ozaki method. Beginning 6 days after sporozoite challenge, blood will be taken daily by ear prick at 1 pm. Pk infections are highly synchronized in the blood. Daily ear prick blood (10 µL) will be used for a PCR blot onto filter paper and for thin and thick malaria smears stained with Giemsa stain to quantify the percent of infected red blood cells according to standard procedures. When parasitemias exceed 2%, monkeys will be treated by IM injection of chloroquine 15 mg/kg on days 1, 3, and 5, and a single IM dose artesunate (AS; 5 mg/kg) to prevent death.

Specific Aim 2. Development of an autologous bone marrow transplant model.
This rhesus macaque model will be developed with the assistance of Excluded by Request and his transplant staff at the Private Source Private Source (12, 13). Briefly, macaques will be habituated to a jacket-tether system. Recombinant human granulocyte colony-stimulating factor (rhG-CSF, 100 µg/kg) will be given daily as subcutaneous injections for 5 days. On day 5, bone marrow will be harvested from the humeri and/or femora and cryopreserved. In preparation for transplant, a femoral vein catheter will be placed for continuous intravenous (iv) hydration with continuous iv administration of broad-spectrum antibiotics (cetazadime, vancomycin, gentamicin) and an antiviral agent (acyclovir) and the animals will receive myeloblative total-body irradiation. Twenty-four hours after transplantation, the animals will be started on intravenous G-CSF at 100 µg/kg daily until the animals have attained stable neutrophil engraftment with an absolute neutrophil count of greater than 0.5 × 109/L (500/µL). Standard supportive care, including blood product transfusions, fluid and electrolyte management, and antibiotics will be given as needed.

Specific Aim 3. Development of state-of-the-art immunological assays and analysis. We will make services available to support subcontracted grant work in the NHP model (design and implementation of full immunological studies), custom sample processing (isolation, counting, and cryopreservation of cells, fluids, and nucleic acids), performance of optimized and validated flow cytometric assays (phenotype staining, ICS, CFSE, tetramer, TruCount), specialized and customized high-throughput analysis, economies-of-scale reagent purchasing, and archiving of cryopreserved samples. This operation was previously the Cellular Immunology Unit of the Immunology Support Core during the previous grant period, but was felt to be more appropriate to function as a component of the IDR, and will continue to be managed by Excluded by Requester

Specific Aim 4. Maintenance of a National AIDS Macaque Resource. The resource will maintain a pool with an average census of 60 clinically stable and immunologically and virologically characterized SIV-infected macaques that have completed their initial research assignment. This pool of animals represents a unique and increasingly valuable research resource because of their value for priority research to identify strategies to eliminate HIV reservoirs (14). These animals will be made available to the US AIDS research community along with sufficient virologic and immunologic data to permit the identification of animals that are suitable for inclusion in additional studies. To maintain adequate immunologic characterization, animals in the pool will be bled and bronchoalveolar lavage will be performed at three week intervals to obtain serum, plasma, peripheral blood leukocytes and lung lymphocytes for virus-specific antibody, cellular immune, cellular proliferation and virus load analyses. The immunologic assays will be performed by the IDR. The ONPRC Molecular Virology Service Core will perform real-time PCR assays to quantify plasma SIV RNA.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-IDResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DCM-IDResource_Training.pdf

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

NOTHING TO REPORT

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

Specific Aims 1 & 2. Model development.
Future activities to develop the Plasmodium knowlesi challenge model.will focus on acquiring the expertise to maintain Anopheles dirus and infect them to eliminate the need to ship Pk-infected mosquitos. Future activities to develop the bone marrow transplant model will focus on modifying the myeloblative irradiation dose to achieve heterologous engraftment and initiate autologous bone marrow transplants, in rhesus macaques to support studies aimed at eliminating the SIV reservoir that remains after anti retrovirus therapy as a model for eliminating the HIV reservoir.

Specific Aim 3. Development of state-of the art immunological assays and analysis.
The laboratory unit's future activities will continue to focus on providing professional and technical expertise to support immunological studies for collaborative investigators utilizing nonhuman primate infectious disease models.

Specific Aim 4. Maintenance of a National AIDS Macaque Resource.
Future activities will focus on managing the resource to maintain a cost effective balance between the numbers of animals maintained and projected investigator need for the animals.

Enhanced Resource Staffing.
Additional staff recruitments will be necessary to support recently funded grants that will increase the number of animals on study and to support the challenge phases of funded and ongoing malaria and mycobacterium tuberculosis vaccine studies.

INFECTIOUS DISEASE RESOURCE: ACCOMPLISHMENTS

Specific Aim 1. Model development.
Development of a Plasmodium knowlesi (Pk) challenge model.
With the Assistance of [Excluded by Requester] Naval Medical Research Center the Infectious Disease Resource (IDR) staff acquired the expertise to complete its first [Pro prietary] macaque Pk vaccine challenge study. Plasmodium Knowlesi-infected Anopheles dirus mosquitos were obtained from the Naval Medical Research Center, sporozoites were harvested from them using the Ozaki method and the macaques were inoculated intravenously with 100 sporozoites. Parasitemia was quantified daily using Giemsa-stained thin blood smears and the animals were treated with chloroquine and artesunate when parasitemias exceeded 2% resulting in clearance in 100% of the animals. Therefore, the initial goals of this specific aim were achieved. The study provided evidence for partial vaccine efficacy and follow-up studies are planned.

Specific Aim 2. Development of an autologous bone marrow transplant model.
With the Assistance of [Excluded by Requester] and his transplant staff at the [Private Source] [Private Source] the IDR. staff acquired the infrastructure, equipment and expertise to complete its first survival allogeneic bone marrow transplant in a cynomolgus macaque. A matched donor was mobilized with recombinant human granulocyte colony-stimulating factor, 1.5x109 donor peripheral blood mononuclear cells were obtained using apheresis on day 5 post-mobilization and infused into a recipient maintained in a jacket-tether system following myeloblative total-body irradiation. Post-transplantation intensive care of the recipient consisted of continuous antibiotic infusion, treatment with rhG-CSF and infusion of irradiated matched donor platelets until its granulocyte numbers exceeded 0.5 × 109/L (500/µL. The allograft in this animal failed; however, the initial technical goals of this specific aim were accomplished.

Specific Aim 3. Addition of state-of-the-art immunological assays and analysis.
The IDR Laboratory unit (LU) finalized protocols to test the efficacy of a computationally designed peptide, VG1177, as a therapeutic drug for treatment of SIV in rhesus macaques. This project will managed by the IDR-LU, utilize the LU'S portfolio of immunological assays and utilize SIV infected macaques from the National AIDS Macaque Resource.

Specific Aim 4. Maintenance of a National AIDS Macaque Resource.
The IDR maintained an average census of [Proprietary Info] clinically stable and immunologically and virologically characterized SIV-infected macaques in the National AIDS Macaque Resource. The average census of macaques maintained in the resource was reduced from the initially proposed target [ ] due to a budget [Proprietary Info] reduction [Prop rietary Info] of the animals were assigned to a research project to test a therapeutic strategy to reduce or eliminate the SIV reservoir. Assignment of additional animals to a protocol to study the effect(s) of an additional therapeutic strategy to reduce or eliminate the SIV reservoir is pending final protocol approvals. The overall goal of this specific aim was achieved The SIV-infected macaques made available from the resource reduce overall use of rhesus macaques and provided a substantial cost savings to grants over infecting naive animals and maintaining them for 1-2 years to obtain a project-usable animal.

Enhanced Resource Staffing.
A Veterinary technician and an additional research technician were added to the IDR staff to keep pace with the growth in the number of nonhuman primates assigned to infectious disease protocols managed by the resource and the increases in procedure complexity. The average daily census for protocols managed by the Resource was [Proprietary Info] macaques in calendar year 2014. Resource staff obtained 14,246 blood samples, 5,497 bronchoalveolar lavage samples, 395 intestinal mucosal biopsy samples, 331 lymph node biopsy samples, 443 bone marrow samples, 1,210 urine samples, and 402 mucosal secretion samples; and performed 856 infectious agent administration procedures, 24,955 drug administrations, 44 necropsies and 5,174 Complete blood counts in support of these protocols. With the addition of [ ] the initial goal of recruiting [Excluded by Requester] additional professional expertise has been achieved. Additional staff recruitments will be necessary to support recently funded grants that will increase the number of animals on study, and to support the challenge phases of funded and ongoing malaria and mycobacterium tuberculosis vaccine studies.

INFECTIOUS DISEASE RESOURCE: TRAINING AND PROFESSIONAL DEVELOPMENT

One-on-one training is provided to all members of the IDR with the goal of achieving a completely cross-trained staff. Formal class room training was provided for nonhuman primate apheresis to the IDR staff as well as some of the Center's veterinary clinicians and veterinary technicians. Formal class room training in the use and applications of the Leica Bond® RX was provided to IDR laboratory staff. The IDR routinely provided one-on-one nonhuman primate protocol management and procedures training for graduate students and postdoctoral fellows from investigators laboratories.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Apheresis: The resource acquired a Spectra Optia® apheresis system and completed intensive training on the application of the system for nonhuman primate leukophoresis. The unit now performs leukophoresis procedures supporting bone marrow transplantation and large scale determination of T cell epitope specificity and major histocompatibility restriction of vaccine-induced T cell responses. Approximately 109 lymphocytes can be obtained in a single procedure permitting determinations to be completed on a single large cell sample, thereby eliminating the variability inherent in determinations from multiple blood samples and markedly reducing the number of blood sample experiences for the animals. The projected project use of leukophoresis is approximately 150 procedures annually.

Immunohistochemistry/in situ hybridization: The resource recently acquired a Leica Bond® RX and supporting equipment to add high throughput immunohistochemistry and in situ hybridization to its infectious disease research support repertoire. Protocols for multi-labelled immunohistochemistry and combined immunohistochemistry.in situ hybridization are being developed for precisely defining cells in tissues infected with study agents and vaccine vectors.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Unit Head	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Unit Staff	19.5			112,718.00	36,859.00	149,577.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**149,577.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**149,577.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	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. Other Expenses	25,000.00
Total Other Direct Costs	**25,500.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**175,077.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	175,077.00	49,022.00
		Total Indirect Costs	**49,022.00**

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)	**224,099.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Japanese Macaque Resource

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The ONPRC Japanese Macaque Resource is increasingly recognized as an important reservoir of animals with unique phenotypes (presumably resulting from specific genetic susceptibilities) relevant to multiple sclerosis and age-related macular degeneration.

To maintain an appropriate population to exploit these features, the Resource is pursuing the following steps in the next funding period:

Specific Aim 1. Expand breeding production, by rebalancing the demographic distribution, using best practices to optimize colony and genetic health.

Specific Aim 2. Employ Information Systems (IS) capacities to model and inform JMR colony management decisions.

Specific Aim 3. Characterize colony members for pedigree relationships and risk for genetic diseases.

Specific Aim 4. Maintain centralized genetic and phenotypic records of the JMR to inform colony management decisions.

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

Yes

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DCM-JMacResource_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

Japanese macaque user groups were participants in the planning process, to ensure that the selected animals for breeding achieved the desired goals without impacting other JM-resourced programs.

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

Continue to support genetic and phenotypic characterization, breeding colony management and harem housing goals to re-balance the population.

JAPANESE MACAQUE RESOURCE: ACCOMPLISHMENTS

We established two breeding harem groups to propagate genetic disease models (JME, Macular Degeneration) outside of the main colony. This effort is intended to preserve and expand the number of unique disease model subjects by breeding selected animals retired from other studies.

Colony genetic analysis and breeding management support were provided to address the sex and age imbalances present in the larger breeding colony population. Initial phenotypic surveys of breeding colony members began and will continue at each semiannual round-up. Data records on JME and macular degeneration status were updated accordingly. New caging was purchased to better meet needs for short-term JM containment (such as for health care or staging for harem housing).

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: RPPR-DCM-JMacResource_ResourceSharing.pdf

JAPANESE MACAQUE RESOURCE: RESOURCE SHARING

Sharing by the resource includes samples from the tissue bank archive and animals requested for projects.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salar y	EFFORT			5,795.00	1,890.00	7,685.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **7,685.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Unit Staff	0.96			4,100.00	1,337.00	5,437.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**5,437.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**13,122.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	17,500.00
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. Other Expenses	31,546.00
Total Other Direct Costs	**49,046.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**62,168.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	62,168.00	17,407.00
		Total Indirect Costs	**17,407.00**

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)	**79,575.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Assisted Reproduction Technology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The overall objective of the ONPRC Assisted Reproductive Technologies (ART) Support Core is to provide ONPRC researchers as well as national and international scientists the expertise and materials necessary for the efficient use of nonhuman primates (NHPs) in studies relevant to human health and disease. Specifically, the ART Core offers investigators the means to acquire difficult to obtain NHP ovarian specimens (granulosa cells, follicular fluid), germ cells (sperm, oocytes), and embryos for research purposes. Embryos are generated by the ART Core using established in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) techniques. Additionally, the ART Core provides the expertise and technical support necessary to perform embryo transfers, such that the developmental potential of experimentally manipulated embryos can be evaluated based on the presence or absence of a successful pregnancy. Established ART Core embryo transfer and cryopreservation protocols also allow investigators to maintain animal lineages with valuable genotypes/phenotypes. Lastly, the ART Core also provides researchers with media and reagents that are necessary to culture nonhuman primate germ cells and embryos.

To ensure that the ART Core possesses the most up-to-date means to provide the aforementioned services in an efficient and cost-effective manner, continual refinement of existing protocols and the development of new technologies are required. Thus, the Core strives to be at the cutting edge of NHP ART by developing new techniques and protocols that will fully support ONPRC scientists and collaborators focusing on primate reproduction and development. An active technology-development arm of the Core enables the addition of services and expertise that advance the use of the NHP as a manipulatable and translationally relevant model system.

Therefore, to attain the same level of high quality and cutting-edge services provided in the previous funding interval, the ONPRC ART Core proposes the following objectives through the next 5-year period of support:

Specific Aim 1: To provide an efficient, responsive, and transparent operating structure that allows for the delivery of high-quality NHP ART services and support. The Core aims to offer the necessary services and expertise for researchers seeking to utilize NHPs as models for the treatment of diseases and regulation of fertility in humans. To achieve this goal, the Core will focus on maintaining current high standards of service and quality control, ensuring an uninterrupted source of nonhuman primate gametes, embryos, ovarian materials, and germ cell/embryo culture media. Regular review of resources, personnel training and performance, as well as quality of services offered will be performed by the Core director, oversight committee, and the ONPRC Associate Director for Research to ensure continued success of the Core.

Specific Aim 2: To develop new ART reagents, services, and expertise that advance the use of the NHP as a translationally relevant model system. The Core will develop the following tools and resources to advance the utility of NHP ART for ONPRC and external research projects. Technology development objectives for the next funding interval include: a) the identification of biomarkers in ovarian follicles that yield oocytes with the greatest potential to undergo fertilization and embryonic development; b) the development and optimization of ART protocols in cynomolgus macaques, an NHP species that is emerging as a valuable model system at ONPRC, as well as; c) to apply state-of-the-art molecular methodologies to the manipulation of the NHP genome, which will allow for the development of models of human disease critically important for advancing reproductive, regenerative, and stem cell-based medicine.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-ART_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Core-ART_Training.pdf

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

NOTHING TO REPORT

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

With service and research objectives already well in progress, continuation of ART Core goals will be seamless. User surveys have been reviewed along with funded grants indicating a continued demand for ART Core services through the end of the breeding season in 2016

(May). Periodic review of routinely collected data (i.e., project income, animal expense, oocyte retrieval and embryo production rates) will provide an assessment of service quality and quantity provided to investigators. Updates to routine protocols will be evaluated through literature review and discussions with colleagues to ensure the optimal services are being provided to investigators.

Research goals will continue as proposed in Specific Aim 2. When the metabolomics data is returned, bioinformatic inquiry will identify the essential regulators of a healthy ovarian follicle and competent oocyte. These regulators will then be subject to further interrogation by assessing their value as biomarkers of oocytes capable of producing healthy embryos, a technology highly sought after in the ART Core, as well as human IVF clinics, where selection of the embryo that has the greatest potential to yield a live birth is paramount.

Incorporation of ART protocols specific to cynomolgus macaques will be initiated and refined to determine optimal recovery and culture conditions of oocytes and embryos. The practice of sedated epididymal semen recovery from genetically valuable males will be validated, a technique similar to procedures already in place at the Washington National Primate Research Center and not yet utilized at the ONRPC. This will allow us to expedite the process of generating live cynomolgus monkeys with the unique genetic background while the animals undergo training to accommodate non-sedated semen acquisition.

Initial data obtained from CRISPR/TALEN studies collected in collaboration with investigators at MIT will be published with the goal to not only introduce the technique in terms of NHP model development, but to also promote the capabilities of the ART Core to create valuable, higher-order animal disease models. Production of the CRISPR and TALEN constructs will also be tested and validated with the ART Core to move the procedure “in house” so that it may be offered as a service to investigators. Additionally, embryos identified as genetically modified are scheduled for transfer into a surrogate at the end of 2015 with the goal of producing the first modified NHP in the US.

ASSISTED REPRODUCTION TECHNOLOGY (ART): ACCOMPLISHMENTS

All specific aims are currently on track and/or being developed.

Aim 1: Research services including controlled ovarian cycle stimulations, oocyte retrievals, in vitro fertilization, embryo culture, embryo cryopreservation, blastocyst biopsy, semen cryopreservation, and embryo microinjection were performed by the ART Core for 11 ONPRC investigators and 3 external investigators (Excluded by Requester University of California Los Angeles; Excluded by Requester National Institutes of Health). A cohort of adult female rhesus macaques [illegible] male rhesus monkeys were managed by the Core to ensure the services and requested samples were available to meet investigator needs. Major equipment acquisition included an objective mounted laser to insure the Core could provide up-to-date, technically advanced, ART-associated services that included manipulating oocyte and pre-implantation embryos (i.e., performing trophectoderm biopsies or embryonic blastomere sampling). With input from members of the ART Core Oversight Committee, improvements to existing protocols were made with respect to updating and optimizing culture conditions to maximize the ability of rhesus macaque embryos to develop into implantation-stage blastocysts. Improved methods for macaque sperm cryopreservation were tested based on consultation and advice from Excluded by Requester at the California National Primate Research Center. The ART Core also provided external investigators with information and input into conducting NHP ARTs. The ART Core consulted with and advised Excluded by Requester a clinical investigator in the National Institute of Child Health & Development, with regard to the optimal protocols for performing rhesus macaque ovarian stimulation, sperm cryopreservation and thawing, as well as IVF. The Core's protocols for ovarian stimulation, IVF and ICSI were provided to Excluded by Requester at the Tulane National Primate Research Center to help in their development of an NHP ART program.

Aim 2: Significant progress advancing the NHP as a transnationally relevant model was made in three major areas. First, follicular fluid was collected for a large-scale metabolomic analysis to elucidate the key regulators present in the mature follicle that are predictive of those oocytes that will develop into healthy blastocyst embryos following in vitro fertilization and culture. Bioinformatic interrogation of the results will be performed upon receipt of the data (in progress) to identify biomarkers that distinguish a healthy and developmentally competent oocyte. Second, collaboration with an internal investigator was established to optimize ART protocols in a unique subspecies of cynomolgus macaque. Since propagation of this subspecies is critical for investigations into HIV-related therapies, protocols for gamete retrieval and in vitro culture were developed and are currently being tested. Third, utilization of the CRISPR/TALEN directed genome-editing systems were tested and validated using rhesus macaque zygotes. Both CRISPR and TALEN systems induced the anticipated genetic alterations in the resultant blastocysts. An external collaboration with investigators at the Private Source is currently underway to assess the feasibility of generating genetically modified rhesus macaques. By injecting CRISPR guide RNAs/Cas9 and TALEN constructs that target a gene (*SHANK3*) known to be mutated in individuals with autism-spectrum disorder, we have verified successful modification of the embryonic genome in such a way that eventual transfer of these embryos into a surrogate would likely produce affected macaques and, thereby, serve as a useful model for future studies of autism and related neurological disorders. Further, we have developed a protocol whereby the trophectoderm of CRISPR/TALEN modified embryos is biopsied at the blastocyst stage. The biopsied blastocyst is cryopreserved until genome analysis of the biopsy confirms the appropriate gene editing occurred. This approach will allow for the transfer of only those embryos that possess the mutation or genetic modification of interest are transferred to surrogates, greatly reducing the number of animals needed to obtain a genetically modified NHP.

ASSISTED REPRODUCTION TECHNOLOGY (ART): TRAINING & PROFESSIONAL DEVELOPMENT

Members of the ART Core staff oversaw the training of six users of ART Core services in techniques ranging from sperm collection and cryopreservation, oocyte retrieval, IVF, and embryo culture, to embryo microinjection. Additionally, a visiting Ph.D. student from Brazil is spending a one-year fellowship supported by her home institution [Private Source] to learn and optimize methods of NHP sperm vitrification and recovery.

Professional development was provided for [Excluded by Requester] who attended the Keystone Symposia "Precision Genome Engineering and Synthetic Biology" at Big Sky, Montana in January 2015. Data was presented that was generated under Specific Aim 2 comparing CRISPR and TALEN genome editing efficiencies in rhesus macaque embryos, the first of its kind to be reported.

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 feasibility of developing unique NHP biomedical models through the use of recently developed genome editing techniques was determined by the ONPRC ART Core. Moreover, the Core developed a protocol whereby manipulated embryos are biopsied and cryopreserved for storage while the biopsied material is analyzed for the desired genomic changes. Embryos determined to be appropriately modified by next generation sequencing of the biopsied material are then available for embryo transfer into a surrogate, ensuring any resultant offspring would possess the desired genetic alteration. To date, this process of selective embryo screening prior to embryo transfer has not been reported for genetically altered NHP embryos.

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: RPPR-Core-ART_ResourceSharing.pdf

ASSISTED REPRODUCTION TECHNOLOGY (ART): RESOURCE SHARING

All data relating to the development of CRISPR and TALEN modified rhesus monkey embryos was reported as an abstract at the 2015 Keystone Symposia "Precision Genome Engineering and Synthetic Biology". During this conference external investigators were encouraged to contact the Director of the ART Core to discuss the use of the NHP in their own projects centered on genome modification.

Additionally, all research data collected for the metabolomics and genomic editing projects will be submitted for publication in peer-reviewed journals.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			11,415.00	4,064.00	15,479.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **15,479.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Unit Staff	14.7			62,309.00	22,142.00	84,451.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**84,451.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**99,930.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	76,490.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	62,497.00
Total Other Direct Costs	**138,987.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**238,917.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	238,917.00	66,897.00
		Total Indirect Costs	**66,897.00**

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)	**305,814.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Endocrine

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The goal of the ONPRC Endocrine Technology and Support Core (ETSC) is to provide intramural (ONPRC and OHSU) and external (academic and industry) scientists with the expertise and facilities necessary for obtaining quality data supporting clinical and pre-clinical research using nonhuman primates (NHPs) and other species in studies relevant to human health and disease. Specifically, the ETSC provides services and support in traditional and new assay technologies, including radioiodination, radioimmunoassay (RIA), organic solvent extraction (Ext), Sephadex LH-20 liquid chromatography (LC), immunochemiluminescense technology using automated clinical platforms, XMAP-based technology (i.e., Luminex 200) for multiplexing protein assays, enzyme immunoassays (EIA), enzyme-linked immunosorbent assay (ELISA), enzyme-linked fluorescent immunoassay (ELFA), and unique bioassays such as those developed for mouse interstitial cell testosterone bioassay (MICT) and monkey luteinizing hormone (LH). Furthermore, the ETSC supports continuous developments in NHP research by validating commercial or existing assays using human antibodies, by developing new assays with antibodies generated in academia, and by partnering with companies to develop and validate single or multiplex assay panels specifically for NHPs. Regular review of resources, personnel training and performance, as well as quality of services offered will be performed by the Core director, oversight committee, and the ONPRC Associate Director for Research to ensure continued success of the Core.

To continue the high-quality services for NHP and non-NHP research provided in the previous funding period, the ONPRC ETSC proposes the following objectives through the next 5-year period of support:

Specific Aim 1: To provide a transparent operating structure for efficient and responsive services for NHP research programs with quality and validated analyses. This will be achieved through cooperation between the Core Director and his staff, the Core Oversight Committee, and the ONPRC Business office. Over the past 40 years, the ETSC has developed or validated more than 50 assays suitable for NHP serum, plasma, cell culture medium, or tissue extract samples. We expect to continue the high standards of service by maintaining close attention to all reagents and procedures, including multiple internal quality controls in all assays, and by enhancing our operation with electronic interactions with users, including sample requests, assay schedules, assay protocols, assay analysis, data reports, and invoicing. Immediate data-return, within an hour or less if necessary, is provided for time-dependent research projects, such as daily monitoring of the menstrual cycle in female NHPs. Regular review of resources, fee structure, performance and quality of services will be performed by the Core Director, the Core Oversight Committee, and the ONPRC Business office to ensure continued success of the Core.

Specific Aim 2: To support internal and external programs for clinical and basic sciences research. The ETSC focuses on providing scientists and clients with state-of-the-art equipment, knowledge, experience, reliability, skills, reasonable rates and well-proven technologies. The Core has acquired and validated assays on both a bench-top (e411) and a high-throughput (e170) Roche clinical automatic platform for analyzing large number of primate samples in clinical and basic research. The Core will continue to provide the capacity to analyze multiple steroid or protein hormones for primate and non-primate species, using chromatography and Luminex technologies, respectively, and to analyze a single steroid or protein parameter by traditional RIA and EIA methods following isolation and purification as necessary.

Specific Aim 3: To develop NHP-specific assays and share with NPRCs and other scientific institutions. The ETSC has initiated cooperation or partnership with academic laboratories or commercial companies to develop NHP-specific assays or panels, including custom-made multiplex monkey cytokine kits, appropriate multiplex metabolic hormonal panels, as well as steroid biosynthesis panels to monitor steroid intermediates and products in a single serum sample. The results of these developments will be shared with all NPRCs as well as the scientific community through specific organizations, NIH-sponsored programs, scientific annual meetings, and on our website.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Endocrine_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Core-Endocrine_Training.pdf

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

NOTHING TO REPORT

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

During Year 56 (May 2015-April 2016) we plan to develop methods for assaying 15 steroid hormones and 5 synthetic steroid hormones in NHP serum and plasma. This will result in the lab ultimately transitioning away from our in-house extraction-RIAs and extraction-chromatography-RIAs for steroids by the end of 2015, as these assays will be completely replaced by LC-MS/MS methods. We also plan to develop LC-MS/MS methods for measuring LH and FSH in NHP serum. The ETSC will also work with [redacted] on further developing and validating NHP assays for the Luminex platform, and other companies including [redacted] to validate ELISA kits for NHP.

Specific Private Vendor

Specific Private Vendor

ENDOCRINE CORE: ACCOMPLISHMENTS

During the 12-month period from December 2013 to November 2014, the ETSC served 32 internal investigators (ONPRC/OHSU) and 37 external investigators to process 56,473 tests for 79 different assay types with chargeback income of $514,630.76. For the period in Year 55 from May 2014 to January 2015 covered in this progress report, the ETSC has served 28 internal investigators and 30 external investigators, including 12 new investigators. We have performed 42,685 tests, with about 75% of these for internal clients with chargeback income of $367,520.75 to date. We anticipate that during Year 55 chargeback income will surpass $500,000 and approximately 57,000 tests will be completed for investigators.

Technologies Update: We continue to work with Specific Private Vendor to develop and validate cytokine platforms for nonhuman primates (NHP). We are currently in the final stages of validating a 9-plex inflammatory cytokine kit. The ETSC has also performed a number of Luminex assays for investigators using commercially available NHP kits from Specific Private Vendor and Millipore. We have validated an Specific Private Vendor activin A ELISA kit for NHP and are currently in the process of validating a Specific Private Vendor glucagon ELISA kit for use in NHP and continue to work with the company on development of other ELISA kits for use in NHP. We hope to replace our commercial RIA offerings (e.g., glucagon, leptin) with commercial ELISAs in the near future. The ETSC also receives frequent requests for NHP LH and FSH measurement by traditional iodination RIA. The ETSC validated four new assays for NHP on our Roche Cobas e411 and modular E-170 platforms, and 11 new ELISAs for either NHP or rodents. We will be installing an LC-MS/MS platform which we anticipate will be functional early in Year 56, during Spring 2015. We plan to move all steroid hormone assays currently available by in-house extraction-RIA or extraction-chromatography-RIA to LC-MS/MS and offer high-throughput, affordable LC-MS/MS methods for quantifying these hormones to our clients.

Investigator Base and Scientific Interactions: The ETSC continues to expand its client base. For the 12-month period from December 2013 through November 2014 we served a total of 79 investigators at the ETSC. In the current project year from May 2014 through January 2015 we have served a total of 58 investigators, including 12 new investigators. We also continue to advise clients on assays and experimental design in the areas of reproduction, aging, metabolic disease, and cancer research among others. We strive to serve our client base by providing assay services that focus on sensitivity, specificity, and selectivity.

Reduction of Manual Operations and Mistakes: The ETSC is still in the process of implementing LabKey data management software or another data mangement system. This has been temporarily suspended due to a reduction in the budget this fiscal year, but we continue to investigate data management options for the lab. We have instituted a data checking process for all assays, in which staff will audit all data generated by the Roche automated platforms before they are reported to investigators. Excluded by Requester reviews all data from RIA and ELISA platforms before they are reported to investigators.

ENDOCRINE CORE: TRAINING & PROFESSIONAL DEVELOPMENT

Excluded by Requester retired on December 31, 2014 and Excluded by Requester has taken over as Director of the ETSC effective January 1, 2015. There was a four-month overlap period for training, in which [redacted] gained a complete understanding of the operations of the ETSC including the lab's assays, philosophy, and approach to business. Staff attended a training course for the Proprietary Info platform at Specific Private Vendor in Indianapolis, IN in January 2015, a training session for the upcoming Proprietary Info platform at Specific Private Vendor headquarters in Columbia, MD.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

We have successfully validated an Specific Private Ve activing A ELISA for NHP, we are in the process of validating a glucagon ELISA for NHP Specific from and are in the final stages of validating a 9-plex NHP cytokine kit from Life Technologies. We also validated an Private Vendor additional four assays on the Proprietary Info for NHP (now total of 19), and 11 commercial ELISA kits for either NHP or rodents.

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

RPPR - Core-6121

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			11,250.00	4,230.00	15,480.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **15,480.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Unit Staff	12.48			33,189.00	12,479.00	45,668.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**45,668.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**61,148.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	237.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**237.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	15,622.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	6,300.00
Total Other Direct Costs	**21,922.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**83,307.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	83,307.00	23,326.00
		Total Indirect Costs	**23,326.00**

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)	**106,633.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Flow Cytometry

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Flow Cytometry Support Core was created during the mid-1980s in response to the increase in non-human primate AIDS research. Both the technical capabilities and user base of this Core have significantly expanded in the intervening years, and the Core is now used by researchers from each of the ONPRC's scientific research divisions, animal care staff from the Division of Comparative Medicine, and collaborators from outside institutions.

The Specific Aims of the Flow Cytometry Core are:

Specific Aim 1: Provide an efficient, responsive, and transparent operating structure. Starting in 2012, the Core Director directly interacts with the users, the Core Oversight committee, the ONPRC business office, and manufacturers. In the last funding period, the Flow Cytometry Core was a unit of the Immunology Support Core, which also included the Cellular Immunology Unit, under the overall direction of [Excluded by Requester]. The latter unit has been transferred to the Infectious Disease Resource and the flow cytometry component has resumed its historical status as an independent support core. This new organization improves the efficiency, responsiveness and transparency of the Core's operation. As Core Director [Excluded by Requester] will interact with the Core oversight Committee, the Associate Director for Research, and the ONPRC Business Office to ensure appropriate provision of core services, regular assessment of chargeback fees, and assessment of technology needs.

Specific Aim 2: Provide, maintain, and upgrade the Flow Core's equipment. The Flow Core currently has the same flow cytometers it had at the beginning of the 5-year grant; i.e., two BD FACS Calibur analyzers, two BD LSR2 analyzers, and a BD Aria II cell sorter. The analyzers will be available to all users on a self-serve basis, while the sorter will be available only to a limited number of well-trained users. We will continue to have a full maintenance contract with BD to keep the cytometers in peak working condition. During the coming 5-year grant period, we will explore efforts to replace the two aging BD FACS Caliburs with a BD Verse and add to our cell sorting capabilities by purchasing a cell sorter that can sort very large cells.

Specific Aim 3: Train users to operate the equipment in the Flow Core. We will continue training personnel to operate the analyzers on a self-service basis. The analyzers are available on a 24/7 basis to the users. Since the beginning of the Flow Core, the cell sorter has been operated by Flow Core personnel only. However, starting in 2009, we started training selected laboratory personnel to operate the Aria II sorter. The Aria II proved to be much easier to operate than the FACS Vantage. This change made the sorter available for longer sorting runs, some of which ended in early morning.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-FlowCytometry_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Core-FlowCytometry_Training.pdf

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

[Excluded by Requester] has incorporated lessons from the Aria training into a special version of the 'Flow 101' course, and has created checklists for instrument operations, and also written up new basic SOPs. By discussions with interested Core users, [Excluded by Requester] has disseminated information about apoptosis and RNA expression staining.

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

In the next reporting period, the Core's three-laser BD LSR-II will have its violet laser upgrade completed. This will allow users of the Core to dramatically increase the number of fluorophores they use in their staining panels. [Excluded by Requester] will optimize the PMT voltages to minimize spectral overlaps, and then hold several class sessions teaching interested users how to make use of the new Brilliant Violet fluorophores. [Excluded by Requester] is also planning to discard the obsolete reservation system, and replace it with a modern construction with new useful features (e.g., access to resource information).

FLOW CYTOMETRY CORE: ACCOMPLISHMENTS

Specific Aim 1: Provide an efficient, responsive, and transparent operating structure. [Excluded by Requester] retired at the end of March, 2014, and was replaced as Director by [Excluded by Requester] has overseen the sophisticated, high-throughput (>205 thousand samples in 2014) flow cytometry operations of the [Excluded by Requester] Lab since 2002, and was appointed to oversee Core operations on a part-time basis. Dr. [Excluded by Requester] is assisted part time by a staff member, who is the flow cytometry team leader of the [Excluded by Requester] Lab, in that capacity overseeing the daily function of three cytometers, and supervising 4 full time cytometry technicians. Together, [Excluded by Requester] and staff bring new attention to QA/QC aspects of the Flow Core operations, and also real-world, cutting-edge technical advise to other users of the Core. [Excluded by Requester] has personally met with nearly every established user of the core, discussed operational concerns, and has improved the reservation and time-logging systems.

Specific Aim 2: Provide, maintain, and upgrade the Flow Core's equipment. Regarding equipment maintenance: [Excluded by Requester] implemented a system of daily, weekly, and monthly QA/QC chores that staff enacts. These include regular cleaning, frequent running and assessment of CST (Cytometer Setup and Tracking) beads, system flushes, and database backups and dumps.

Regarding equipment upgrades: The two oldest instruments of the Core, the 4-color FACS Calibur analyzers have both been decommissioned because of obsolescence and hard-to-repair equipment problems. This has freed up service contract money to fund upgrades to the other instruments. The three remaining instruments have had full computer and software upgrades (to FACS Diva 8), and the three-laser BD LSR-II in VGTI Rm 1211 is scheduled to have its violet laser trigon upgraded to an octagon, to take advantage of the many new 'Brilliant Violet' fluorophores revolutionizing flow cytometry. Also, two new FlowJo dongles were acquired, that have been loaned out to Core users, allowing them to do analysis in their offices. Also, new hard drives have been purchased to allow backup systems to be permanently tethered to each of the instrument's computers. A proposal was submitted in October 2014, to the OHSU 'Emerging Technology Fund', to use $500K to buy a Sony SP6800 Spectral Analyzer, which represents a radical new way of doing flow cytometry, but the funds went to a different proposal.

Specific Aim 3: Train users to operate the equipment in the Flow Core. [Excluded by Requester] created a 5hr course titled 'Flow 101'. Day 1 is a classroom overview of the theory of flow cytometry, and the theoretical considerations of trouble-shooting, compensation, and panel design. Day 2 is a practicum at a cytometer (either analyzer or sorter), and goes over specific hardware and software operation. A Day 3 is available to any users who request it, and involves direct assistance with the setup of actual templates and the first running of samples from novel experiments.

FLOW CYTOMETRY CORE: TRAINING & PROFESSIONAL DEVELOPMENT

Excluded by Requester received formal training on the operation and care of the BD Aria-II cell sorter, attending a four-day course in San Jose, CA. In addition, Excluded by Requester and staff enrolled in a web-based class titled 'Optimizing Sort Efficiency' offered by Becton Dickinson. Both the Director and staff have also takens several free online courses, regarding the analysis of apoptosis and RNA expression by flow cytometry.

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

RPPR - Core-6122

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			36,114.00	13,398.00	49,512.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **49,512.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Unit Staff	2.7			8,550.00	3,172.00	11,722.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**11,722.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**61,234.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	3,750.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	21,954.00
Total Other Direct Costs	**25,704.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**86,938.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	86,938.00	24,343.00
		Total Indirect Costs	**24,343.00**

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)	**111,281.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Imaging and Morphology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The overall goal of the Imaging and Morphology Support Core (IMSC) is to provide the ONPRC scientific community access to state-of-the-art instruments, expertise, and services in support of their light microscopy image acquisition and analysis needs. The IMSC offers advanced imaging, specialized for the needs of nonhuman primate (NHP) research, at the molecular and cellular level. Major groups of services include confocal microscopy and derived fluorescence techniques for studies of molecular localization and interactions, stereology for quantitative analysis of morphometric tissue features, and laser-capture microdissection for gene expression analyses in specific cells. Major instruments used to support IMSC goals include a Leica SP5 AOBS confocal (Leica Microsystems, Wetzlar, Germany), a Marianas digital workstation (Intelligent Imaging Innovations, Denver, CO), an MBF Bioscience system (Williston, VT) and an ArcturusXT (Life Technologies, Carlsbad, CA). Core personnel provide expertise in experiment planning and choice of most adequate instrument and method, training for instrument use customized for each specific need, technical support in image acquisition and troubleshooting, and image analysis and stereology.

Specific Aim 1. Provide an efficient, responsive, and transparent operating structure. This will be achieved through cooperation between the Core Director and her staff, the Core Oversight Committee, and the ONPRC Business office.

Specific Aim 2. Provide state-of-the-art instruments that satisfy the major, most common needs for advanced microscopy techniques NHP studies. To this aim, the core is responsible for identifying instrument needs, procuring funds, and purchasing instruments. The Core currently offers a Leica SP5 AOBS confocal, a 3I's Marianas Imaging workstation, and an MBF Bioscience system. All instruments are covered by service contracts and undergo stringent periodical quality-control procedures to ensure optimum function. For each instrument, users receive a minimum three hours of one-on-one training before gaining independent access.

Specific Aim 3. Provide expertise, tools, and training for quantitative image analysis. To this goal, the IMSC has developed stereology and digital image processing and automated analysis expertise. The MBF system and the Marianas are the most appropriate tools for running a stereology-based analysis as they have the routines for uniform systematically subsampling large areas and (particularly the StereoInvestigator within MBF) collections of probes for estimating numbers, lengths of fibers, surface area, volumes, etc. Neurolucida is used for neuron tracing and analysis. ImageJ and FIJI are the tools of choice for image analysis for which the core offers basic and advanced training and automation macros. Volocity is used primarily for advanced 3D rendering.

Specific Aim 4. Provide expertise, training, and access to laser-capture microdissection (LCM) for the isolation of pure populations of cells. To this goal, IMSC maintains a list of protocols for tissue processing, an Arcturus XT LCM system and a close collaboration with ONPRC's Cell and Molecular Support Core and OHSU's Microarray Core to facilitate downstream applications for the microdissected materials.

Specific Aim 5. Act as an expert resource in microscopy and digital image analysis by providing consultation in experiment planning and execution, general microscopy and image-analysis knowledge, benefiting primarily the ONPRC and OHSU communities, but also serving as a regional resource in the field. To this goal, the IMSC keeps up-to-date with new methods, tools and applications, organizes periodic seminar and workshops and hosts trainees and student interns.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Imaging_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Imaging_Training.pdf

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

NOTHING TO REPORT

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

The current core director is leaving for another position and recruitment is underway for a replacement staff scientist. In the interim, Dr.

Excluded by Requester	who is an expert in the microscopy platforms in the IMSC, will provide user training and assistance.

IMAGING AND MORPHOLOGY SUPPORT CORE: ACCOMPLISHMENTS

IMSC was used by 30 Principal Investigators, contributing to the quality and depth of their work. Instrument use was: 736 hours for the confocal, 166 hours for the Marianas, 19 hours for the MBF Bioscience and 44 hours for the Laser Capture Microdissection system.

IMAGING AND MORPHOLOGY SUPPORT CORE: TRAINING & PROFESSIONAL DEVELOPMENT

Within the seven months of the last grant cycle, 24 new users were trained to use the instruments of the IMSC. Training involved explanations on the theory of image formation, fluorescence as well as the design and preparation of an imaging experiment.

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 IMSC has invested time and minimal reagents for the development of new protocols: LCM for single cell genomic analysis and confocal for long term imaging of developing embryos.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

File uploaded: RPPR-Imaging_OtherProducts.pdf

C.5.b Resource sharing

NOTHING TO REPORT

IMAGING AND MORPHOLOGY SUPPORT CORE: OTHER PRODUCTS

Macros for FIJI image analysis.

Publications:

Excluded by Requester 3D structure tensor analysis of light microscopy data for validating diffusion MRI. Neuroimage. 2015 Feb 7. pii: S1053-8119(15)00088-9. doi: 10.1016/j.neuroimage.2015.01.061. PMID:25665963

Excluded by Requester Spatiotemporal dynamics of triglyceride storage in unilocular adipocytes. Mol Biol Cell. 2014 Dec 15;25(25):4096-105. doi: 10.1091/mbc.E14-06-1085. Epub 2014 Oct 8. PMID:25298400. PMCID: PMC4263452.

Excluded by Requester

Excluded by Requester Measuring cone density in a Japanese macaque (Macaca fuscata) model of age-related macular degeneration with commercially available adaptive optics. Adv Exp Med Biol. 2014;801:309-16. doi: 10.1007/978-1-4614-3209-8_39. PMID:24664712. PMCID: PMC4332712.

Excluded by Requester Fluorescence-based laser capture microscopy technology facilitates identification of critical in vivo cytomegalovirus transcriptional programs. Methods Mol Biol. 2014;1119:217-37. doi: 10.1007/978-1-62703-788-4_13. PMID:24639226.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			35,439.00	9,568.00	45,007.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **45,007.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Unit Staff	1.08			3,277.00	885.00	4,162.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**4,162.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**49,169.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	675.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**675.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	2,925.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	28,683.00
Total Other Direct Costs	**31,608.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**81,452.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	81,452.00	22,807.00
		Total Indirect Costs	**22,807.00**

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)	**104,259.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Molecular & Cell Biology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Molecular and Cellular Biology Support Core (MCBSC) provides services in support of molecular biology and cell culture for ONPRC investigators. The goal of the MCBSC is to provide flexible, state of the art, time-effective, cost-effective services to facilitate ONPRC investigators' utilization of molecular and cellular biology. Such services are absolutely fundamental to cutting-edge nonhuman primate research. Molecular biology services include both NextGen and capillary DNA sequencing, high-throughput genotyping, high-throughput real-time quantitative PCR, digital PCR, preparation of monkey genomic DNA, generation of monkey-specific cDNAs, establishment of monkey-specific, real-time quantitative PCR assays, large-scale plasmid and phage preparation, fully automated small-scale DNA and RNA preps, and supply of a limited number of reagents and training. Cell biology services include preparation of lentiviral vectors, specialized media and reagents, storage, freezing and amplification of cell lines, preparation of coated culture ware and cover slips, transfection and cloning of cell lines, establishment of primary cell lines, training and access to specialized equipment including liquid handling robots, real-time quantitative PCR platforms, scanning fluorometer, bioanalyzer and plate readers.

The focus of the next grant period will include continued delivery of existing services, provision of more automated and high-throughput services, delivery of medium-scale NextGen sequencing services utilizing the core's newly acquired Illumina MiSeq, working closely with the ONPRC primate genetics program for ancestry, parentage and MHC genotyping, and meeting new needs of primate center investigators. Our specific aims for the next period are as follows:

Specific Aim 1: To provide an efficient, responsive, and transparent operating structure.

Specific Aim 2: To provide state-of-the-art, competitively priced molecular biology services.

Specific Aim 3: To provide state-of-the-art, competitively priced cell biology services.

Specific Aim 4: To work closely with the Primate Genetics Program to enhance colony management.

Specific Aim 5: To work closely with similar cores at the OHSU main campus and Oregon State University to leverage delivered services.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-MCB_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Core-MCB_Training.pdf

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

NOTHING TO REPORT

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

Continue to work closely with our customers to ensure we are meeting their needs. This will be accomplished by direct conversations and surveys. We will continue to monitor technologies being developed and as appropriate and cost-effective bring those technologies into the core. We will continue to have frequent meetings with personnel from the Primate Genetics Program to ensure we are meeting their needs and will develop new technologies as indicated to meet those needs.

MOLECULAR AND CELL BIOLOGY SUPPORT CORE: ACCOMPLISHMENTS

This has been a record project and revenue year for the MCB core. The core has reach new levels of delivered services to investigators. This reflects the increased focus on next-generation sequencing in terms of library construction, quantitation, quality control, training and sequencing. The core is also working with multiple primate center investigators to develop new methods to further the genetic characterization of the primate center colony and to facilitate new research directions in general. High numbers of lentiviral vectors have also been delivered to facilitate gene expression and knockdown studies. Emphasis on excellent customer service with timely delivery and cost effectiveness continues.

MOLECULAR AND CELL BIOLOGY SUPPORT CORE: TRAINING AND PROFESSIONAL DEVELOPMENT

Emphasis on training of all services that the molecular core delivers continues. Particular emphasis on DNA sequencing, RNA and DNA quantification, viral vector and cell culture training continues. A new area of emphasis is training in preparation and quality control of libraries for Next-Gen sequencing.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Improved techniques for Next-Gen library construction and application of GBS (genotyping by sequencing) to primate genetics.

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

RPPR - Core-6124

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			7,332.00	2,066.00	9,398.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **9,398.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Unit Staff	16.32			80,956.00	24,669.00	105,625.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**105,625.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**115,023.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	1,260.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**1,260.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	20,400.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	36,225.00
Total Other Direct Costs	**56,625.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**172,908.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	172,908.00	48,414.00
		Total Indirect Costs	**48,414.00**

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)	**221,322.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Molecular Virology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The overall purpose of the Molecular Virology Support Core (MVSC) is to provide high quality, affordable, and state-of-the-art virology services to support the local and national mission of the Oregon National Primate Research Center (ONPRC) that is centered on non-human primate (NHP) research. NHPs are an invaluable model for studies of viral pathobiology and immunology and for the evaluation of recombinant vaccines and viral gene therapies. The Core supports investigators through an array of specialized virology services and the provision of technical expertise. Key focus areas are 1) custom production and quality control of viral vectors, viral stocks, and antigens; 2) sensitive viral diagnostic assays to study virus spread after infection, to monitor viral tissue distribution, and to assess viral antibodies; and 3) provision and development of key reagents and standardized assays. In addition, the Core offers user training in virology techniques and safe handling of infectious agents, and assists in maintaining proper compliance with local institutional biosafety requirements.

In the previous grant period, the MVSC underwent structural and programmatic changes in order to position itself for success in a rapidly changing research environment and to best meet the virology needs of the local scientific community. In particular, the Core has made improvements to its management and infrastructure and has begun developing an array of new state-of-the-art virology services that capitalize on its expertise in viral production and diagnostics. Early indicators of success have been an increase in service utilization and user diversity. During the next grant period, we will continue building on these gains by further improving and tailoring our services to the programmatic needs of the ONPRC. To that end, the following specific aims are proposed:

Specific Aim 1. Provide an efficient, responsive, and transparent operating structure. This will be achieved through cooperation between the Virology Core Director and staff, the MVSC Oversight Committee, and the ONPRC Business office. The MVSC will further improve lab efficiency and administration in order to facilitate core operations, service use, and information flow. Key efforts will be 1) continuation of current efforts to standardize methods and improve efficiency in the MVSC laboratory through optimized protocols and automated procedures; 2) development and implementation of a viral load service module in the new campus-wide LabKey animal record and scientific database system to facilitate service requests, data analysis, and data sharing; and 3) evaluation of other potential LabKey service and administrative modules (e.g., billing, laboratory notes, inventory and freezer management, internal data storage, etc.) that would most benefit the Core and users.

Specific Aim 2. Provide high-quality virology services and to appropriately expand services and expertise in support of ONPRC's mission. The Core will continue to implement and improve its ongoing and new services, focusing on areas that foster growth of ONPRC's scientific programs and that are most important to investigators. These include cytomegalovirus (CMV) and HIV/SIV AIDS research, as well as gene transfer and gene therapy using adenoviral and adeno-associated virus (AAV) vectors to support diverse research areas such as neuroscience, reproduction, and metabolic disease. The goals, progress, service quality, and organization of the MVSC will be regularly reviewed by the MVSC Director, the Core Oversight Committee, and the Associate Director for Research.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Virology_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

The MVSC director has been invited to local schools and has conducted outreach events with students. The topics have ranged from the basic "What makes us sick?" (elementary school level) to the advanced "Turning Germs into Gene Therapy" (high school level).

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

The MVSC will continue responding to user needs by performing appropriate services and developing and improving services and capabilities as needed and in consultation with the core oversight comittee.

MOLECULAR VIROLOGY: ACCOMPLISHMENTS

In core grant year Yr.55, the MVSC has continued the tremendous growth that was started in the previous grant period. The user base has broadened to a total of 19 investigators (14 OHSU/ONPRC, 5 external) that have utilized MVSC services so far this year. In the area of viral diagnostics, the largest service increase has occurred in simian-immunodeficiency virus (SIV) viral load (1,439) assays, and in the related plasma (1,061) and tissue processing (997) services. Viral production services have increased most for rhesus cytomegalovirus (RhCMV) (132) and adeno-associated virus (AAV) (26) vectors. Other notable services provided were virus co-cultures (379) and adenoviral vector productions (7). The number of MVSC laboratory technicians has recently been increased to 5.0 FTE to cope with the much increased demand.

New and improved services have been added based on investigator needs. For example, the recently developed AAV vector production service was expanded. Large-scale production capability (in addition to the existing medium-scale) was added and permits the generation of sufficient quantities of AAV vectors for non-human primate (NHP) experiments. AAV neutralizing antibody (NAb) assays have started to be developed (initially for AAV1, 2, 9) for pre-screening and selection of study animals and for antibody titer determinations. SIV diagnostics are critical for AIDS pathogenesis and vaccine studies and have been expanded to include tissue viral load assays. A state-of-the-art ultrasensitive SIV ("nested digital") qPCR assay (initially developed by Excluded by Requester at the QMDC, NCI Frederick, MD) is currently being introduced that significantly increases sensitivity and permits in-depth viral biodistribution and reservoir studies. These high-throughput studies are helped by the recent purchase of a modern Quantstudio 6 (Thermofisher/ABI) real-time quantative PCR system. This instrument has joined the existing ABI 7500 machine in the MVSC laboratory, which allows simultaneous assay runs on two machines. It provides advanced capabilities, such as FAST thermal cycling (reducing assay time to just over thirty minutes) and a 384-well block capability.

The MVSC continues to be a designated core component for a multi-investigator HIVRAD P01 (AI094417-01 Excluded by Requester (PI), "Development of an Effector-Memory T cell AIDS Vaccine"; provides % Effort salary support for MVSC Director). The core is closely involved with several current CMV and HIV research grants to different ONPRC investigators, which increasingly make use of its recently developed service capabilities for large tissue processing and ultrasensitive virus detection by nested qPCR. One example is a recently funded R01 on SIV reservoirs (HD080459-0 Excluded by (PI), "Reducing Latent Viral Reservoirs in Infant Macaques"; provides % Effort salary support for MVSC Director).

One important goal has been to better integrate MVSC service requests, data analysis, and sharing of results with users. To that end, the MVSC has been working closely with ONPRC's IT unit to develop new and customized software modules in LabKey (a.k.a. ONPRC's PRIMe database). The SIV viral load service was selected as the initial target, due to its central importance for local AIDS researchers and the regular and growing usage of the service. In the past, SIV viral load results had to be manually exported, reformatted in Excel, and then emailed to individual investigators. A customized PRIMe module for automated SIV viral load data processing and reporting was designed and has now been put to routine use in the MVSC, automating SIV viral load reporting and improving data sharing with investigators.

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Unit Head	Institutional Base Salary	EFFORT			44,914.00	14,490.00	59,404.00
Total Funds Requested for all Senior Key Persons in the attached file													
Additional Senior Key Persons:			File Name:									**Total Senior/Key Person**	**59,404.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Unit Staff	26.85			97,272.00	31,859.00	129,131.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**129,131.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**188,535.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	525.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**525.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	50,809.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	5,282.00
Total Other Direct Costs	**56,091.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**245,151.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	245,151.00	68,642.00
		Total Indirect Costs	**68,642.00**

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)	**313,793.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: MRI

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Magnetic Resonance Imaging Support Core (MRISC) operates a Siemens Magnetom Tim Trio 3T whole-body MRI system housed in a free-standing, 2500-sq. ft. facility in close proximity to the Animal Services Building. The MRISC's objective is to capitalize on the translational value of MRI-based investigations in non-human primate (NHP) research. The Core's mission is to enhance existing ONPRC research programs by providing flexible MRI facilities and expertise that are optimized for NHP subjects, enabling investigators to undertake strategies analogous to human clinical practices, and to utilize the close similarity between human and NHP anatomy and physiology to develop new MRI research and in vivo diagnosis techniques and applications. In order to facilitate these goals, the MRISC relies heavily on a mutually beneficial relationship with the OHSU Advanced Imaging Research Center (AIRC), in which the MRISC supports the efforts of several AIRC faculty and staff to provide infrastructure and technical support of the ONPRC MRISC.

The fundamental service provided by the MRISC to ONPRC investigators is assistance performing MRI exams of sedated NHP subjects. MRISC staff are available for each exam. Equipment and supplies for anesthesia and MRI-compatible physiological monitoring and regulation are provided by the MRI facility. A veterinary "on-call" system has been arranged with ONPRC surgical staff to address complications such as adverse reactions to anesthesia or experimental procedures immediately prior to, or during, the MRI exam. Imaging infrastructure services provided by the AIRC include safety and operator training sessions for ONPRC scientists, the construction of MRI-related instrumentation specialized for NHP MRI experiments, maintenance of computer resources for data access and archiving, quality/assurance oversight for the system, interface with ONPRC facilities staff to manage system requirements (such as electrical power, chilled water, etc.), and maintenance of a web-based scheduling system.

The overall goal of the MRISC is to provide ONPRC investigators state-of-the-art magnetic resonance imaging and spectroscopy services through pursuit of the following specific aims:

Specific Aim 1: Organization. Provide an efficient, responsive, and transparent operating structure. This will be accomplished by providing access to projected fees for MRISC for a 5-year period extending 5 years and through regular meetings with the MRISC oversight committee.

Specific Aim 2: Project Design. Provide the ONPRC research community with consultation and advice on appropriateness and/or feasibility of MRI experiments, and to assist with optimizing experiment design.

Specific Aim 3: Data Acquisition. Assist researchers in the development of data acquisition procedures, most typically through the development and implementation of imaging protocols.

Specific Aim 4: Data Analysis. Assist users of the ONPRC MRISC in the development of data analysis procedures, and train ONPRC personnel, either within the MRISC or within an investigator's laboratory, in implementation of the data-analysis plan.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-MRI_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

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?

Continued support of ONPRC MRI core staff to provide services to ONPRC and OHSU investigators.

In order to accommodate increased needs for imaging neonatal and juvenile animals, it is planned to purchase a smaller (11 cm inner-diameter) 8-channel radiofrequency coil for improved sensitivity with these subjects.

MRI: ACCOMPLISHMENTS

The MRI core has provided data acquisition and analysis services to support laboratories from all four ONPRC scientific devisions, as well as multiple additional OHSU departments.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

New MRI data acquisition and analysis strageties are continually being implemented at the ONPRC MRI support core. Example data acquisition strategies include high-reslolution T2-weighted imaging (SPACE), improved spatial resolution in diffusion tensor imaging protocols. Example data analysis strategies include network analyses of resting state fMRI and diffusion tensor imaging data.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

File uploaded: RPPR-Core-MRI_OtherProducts.pdf

C.5.b Resource sharing

File uploaded: RPPR-Core-MRI_ResourceSharing.pdf

MRI: OTHER PRODUCTS

In collaboration with Excluded by Requester (ONPRC Division of Neuroscience core scientist), instrumentation has been purchased from ClearPoint to perform MRI-guided neurosurgical manipulations. Plans are underway to provide general training for this instrumentation for ONPRC scientists through the core and the Excluded by Requester laboratory.

MRI: RESOURCE SHARING

The ONPRC MRI core supports the development of resources which are shared, such as a rhesus macaque brain atlas which available through the NITRC data repository, and the nonhuman primate aging resource.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			12,373.00	4,157.00	16,530.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **16,530.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
6	Unit Staff	14.22			71,598.00	24,057.00	95,655.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**95,655.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**112,185.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	500.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**500.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	2,750.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	8,210.00
Total Other Direct Costs	**10,960.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**123,645.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	123,645.00	34,621.00
		Total Indirect Costs	**34,621.00**

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)	**158,266.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Primate Genetics

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The rapid development of the scope and sophistication of a number of capabilities in the Primate Genetics Program over the past funding period has justified their incorporation into a new Primate Genetics Support Core. The focus of the next grant period will include the systematic delivery of these services, using state-of-the-art methods to meet the expanding emphasis on genetic analysis in NHP management and research. Incorporation of next-generation sequence (NGS) methods and high-throughput genotyping analysis will continue to require integration to insure the seamless and efficient use of service resources. Our specific aims are as follows:

Specific Aim 1: Provide an efficient, responsive, and transparent operating structure. This will be achieved through cooperation between the Core Director and their staff, the Core Oversight Committee, and the ONPRC Business office.

Specific Aim 2: To collect and manage a comprehensive ONPRC NHP DNA Bank. The DNA Bank is a centralized resource to insure the availability of high quality genomic material for both colony and research analysis.

Specific Aim 3: To provide state-of-the-art genotyping services. Genotype assays to establish macaque parentage, ancestry and MHC expressed allele haplotypes inform colony management decisions. Additional genotype analyses, such as for TRIMCyp and 5-HTTLPR, are available as needed.

Specific Aim 4: To provide state-of-the-art bioinformatics services. Dedicated bioinformatics personnel provide state-of-the-art support for the analysis of high-density data, such as MHC expressed-allele analysis, user support for the Illumina MiSeq sequencer (operated by the MCBSC), and ONPRC genomics research applications.

Specific Aim 5: To provide comprehensive colony genetic analysis. This critical service informs ONPRC colony management decisions for breeding group formation and potential animal sale or research assignment, and to evaluate genetic diversity overall.

Specific Aim 6: To provide biostatistics support. This service leverages the Core's biostatistics expertise to evaluate NHP health measures and treatment efficacy, as well as pre- and post-award research grant support.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Core-Genetics_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

We will continue to use cutting edge technologies to characterize the ONPRC macaque colonies. We will expand the genomic information available through PRIMe-Seq and continue to make Bioinformatics and Biostistics services available to ONPRC staff.

PRIMATE GENETICS: ACCOMPLISHMENTS

The ONPRC macaque breeding colony genetic characterization was carried out using state-of-the-art ancestry (n=48) and MHC assays (n=580). Due to our updating the parentage assay from microssatlellite to SNP genotyping this year, we needed to regenotype all potential parents. Proprietary Info Proprietary Info Proprietary Info and Biostatistics services were were utilized by 16 different investigators. Colony genetic management services were provided to guide the assembly of corral and shelter house macaque breeding groups.

A new ONPRC database was established to provide a common resource to analyze or access genomic information gathered on the ONPRC macaques. PRIMe-Seq is now available for automated RNAseq analysis, variant calling methods, and to search for previously identify variants identified within ONPRC macaques.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

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: RPPR-Core-Genetics_ResourceSharing.pdf

PRIMATE GENETICS: RESOURCE SHARING

Genotype data are deposited into PRIMe for access by ONPRC staff.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			17,384.00	6,293.00	23,677.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,677.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
10	Unit Staff	39.72			198,356.00	69,722.00	268,078.00
10	**Total Number Other Personnel**					**Total Other Personnel**	**268,078.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**291,755.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	3,880.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**3,880.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	23,864.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	37,621.00
Total Other Direct Costs	**61,485.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**357,120.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	357,120.00	99,994.00
		Total Indirect Costs	**99,994.00**

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)	**457,114.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Neuroscience

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Division has established itself as a national and international leader in the fields of pubertal development, addiction, metabolic disease, healthy aging, macular degeneration, neurodegenerative diseases and primate genetics. Further, we have emerging expertise in therapeutic neural stem cell biology, motor system dysfunctions, epigenetics, primate informatics, in vivo MRI/MRS imaging and gene therapy in NHPs.

This research is organized within the Division along the lifespan of the organism, from in utero to advanced age. Scientists in this Division utilize NHP models of human disease processes as well as normative studies of NHP to understand fundamental aspects of brain development, puberty, biological rhythms, immune senescence, and cognitive decline. The Division produces and utilizes specific technologies that optimize the information obtained from our NHP models, including novel methods to acquire in vivo imaging data, measure cognitive performance, introduce and assess genetic therapeutics, provide functional neuroanatomical links to behavior, and identify informative phenotypes for genetic analysis of traits. Our longitudinal approaches in the NHP models provide a key translational bridge between animal models and human diseases based in nervous system dysfunction where baseline values or the impact of environmental variables are difficult if not impossible to measure/control in humans. This translational effort involves clinical partners at both our parent institution OHSU and in other national clinical centers. With the numerous high-throughput and repeated phenotypic measures gathered across all laboratories, the Division provides an unprecedented opportunity to provide tissue/data repositories as national resources for primate nervous system disorders. Further, these extensive phenotypic measures provide an opportunity to identify specific and sensitive biomarkers for disease progression or response to treatment.

The Division of Neuroscience also provides specialized training to graduate students, postdoctoral research fellows, and visiting scientists and these activities increase our interactions with the basic science departments at OHSU. Our faculty members hold appointments in, and actively contribute to, the three main OHSU Graduate Programs, namely, the Department of Behavioral Neuroscience (BNS) graduate program and the cross-departmental graduate programs in Neuroscience (NGP) and in Molecular and Cellular Biosciences (MCB). Finally, the Division serves as a regional, national and international resource for integrative neuroscience research because of its unique capabilities to conceptually and experimentally link neural functions of invertebrate and other vertebrate laboratory animal models to those of nonhuman and human primates.

To advance our knowledge of primate nervous system development, function and disease we had the following specific aims:
Aim 1: Develop and use NHP models of a human nervous system disease/disorders as well as normative processes to provide a deeper understanding of our primate neuroscience.
Aim 2: Identify potential therapeutic target(s) to alter the course of the disease/disorder
Aim 3: Promote the further development and implementation of specialized technologies that will uniquely inform NHP research.
Aim 4: Continue to train the next generation of research neuroscientists using NHP models.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Neuro_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Neuro_Training.pdf

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

We disseminate research findings through national and international conference presentations, publications in peer-reviewed journals, data repositories, and invited lectures. Since May 2014, we have 63 journal publications representing an average of about 8 publications per year per laboratory. These publications have been in top rated journal including Nature, Nature Neuroscience, Science, Proc. Nat. Acad. Sci., J. Neuroscience, Bio. Psychiat. etc. We also have two tissue banks (R24) based on monkey models of disease awarded to Division scientists that disseminate tissue and data nationally to requesting laboratories. We participate in all ONPRC outreach activities, in OHSU outreach activities and in community outreach, particularly the annual “brain fair” at the Portland Museum of Science and Industry. Finally, we participated in two congressional staff visits last year.

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

In order to advance our NHP neuroscience into a deeper understanding of neural circuitry, we will hire a new Scientist with expertise in brain imaging, multi-unit recording and optical imaging of single cell firing in behaving monkeys. This will add to every research area listed above. We will expand our in vivo brain imaging, already represented in the addiction, neurodegeneration, and aging groups. We will likely begin trials of neuron specific gene therapeutic approaches to treat neurodegenerative disorders and extend this approach to our addiction models. We will expand our cognitive testing in NHP models with the anticipated remodeling of our behavioral suites to include a selection of on-line cognitive tasks for investigators to choose from and download to the computer controlled touch screens. Finally, we will continue to publish high quality papers and applications for NIH and foundations funding.

DIVISION OF NEUROSCIENCE: ACCOMPLISHMENTS

1) Major Activities:
The Division has Integrated information across multiple levels of analysis and scientific disciplines, become a leading center for neuroscience research at OHSU, created resources for local, national and international neuroscience research, established clinical partners at OHSU and other universities and health centers to validate NHP model, helped to train the next generation of scientists, successfully maintained a strong funding base, published our research finding in top tier neuroscience journals, extensively disseminated our research finding at international, national, regional and local neuroscience scientific meetings.
2 & 3) Specific Objectives and Significant Results: the Division functions by focus groups that use common NHP models, common technologies and/or address common scientific approaches. Our objectives and results are best described within each of these scientific groups:

The genetics group: Leveraged the power of the ONPRC pedigreed macaque population and state-of-the-art genomic approaches to discover the genetic determinants of human diseases. They made considerable progress in building the informatics infrastructure necessary to begin large scale genomic and epigenomic characterization of the NHP populations. This group tackled the arduous task of colony-wide phenotypic characterization. They have identified specific genes of interested and epigenetic changes of high relevance to alcohol addiction, macular degeneration, demyelinating disease. They continue to show the uniqueness of the gibbon for understanding transposable elements in chromosomal rearrangements that may provide breakthrough findings in cancer, cardiovascular disease, arthritis, anxiety disorders, obesity/adiposity, age-associated cognitive decline. Faculty in the group are also the core director of the Primate genetics program

The neuroendocrine group: Leveraged NHP models of normal development disease such as pubertal development and neuroendocrine dysfunction caused by alcohol addiction, age-related disorders, neurodegenerative diseases, and nutritional challenges. Newly emerging focus has been on neuroendocrine disorders caused epigenetic misinformation, environmental toxins impacting neuroendocrine development, treatment of neuroendocrine and central nervous system disorders using modified viruses as delivery vectors for gene therapy.

The neurodegenerative group: Leveraged the power of the ONPRC rhesus and Japanese macaque population and state-of-the-art imaging, histological and surgical approaches to discover mechanisms underlying the initiation and progression of neurodegenerative diseases and to develop experimental therapies for these diseases. This group has made progress in understanding multiple sclerosis, Huntington's disease, Batten's disease, age-related macular degeneration, age-related cognitive decline, vascular cognitive impairment, chemotherapy-induced cognitive dysfunction, and alcohol-induced cognitive dysfunction. Progress was made towards translational gene therapeutics for Huntington and Batten's disease, the development of novel neurosurgical strategies to deliver viral vectors to the primate brain and the development of a non-human primate model of Huntington's disease.

The addiction group: Leveraged the translational significance of nonhuman primates with the Division of Neuroscience's expertise in addiction models to create a local, national and international resource for addiction research for biomedical (NIH), regulatory (FDA) and Industry research into the causes and cures for substance use disorders. This group has developed state-of-the-art operant drinking and cognitive testing panels with computer automation. They are currently extending the NHP model to include nicotine self-administration and in utero models of fetal alcohol syndrome disorders. They have published extensively on longitudinal evaluations of brain damage through *in vivo* structural and functional MRI imaging, ex vivo slice recordings, and neuroimmune assessments of brain and organ damage. Through the Monkey Alcohol Tissue Research Resource (www.matrr.com), they have provided high quality tissues to over 32 laboratories to advance the understanding of the NHP model. Progress was made towards expanding new touch screen technology and the electronic infrastructure, with the goal of applying this to novel social group housing for assessing addictive behavior within a social setting. Faculty in this group is also the director of the molecular biology core.

The aging group: Used an integrated multidisciplinary approach to elucidate the mechanisms that underlie normal and pathological aging in order to help develop of safe and effective therapies for human age-related disorders. This group made considerable progress in showing environmental and dietary factors that can influence the development of age-related neuropathologies. Specific projects of focus were age-related disruption of circadian rhythms and sleep-wake cycles, age related cognitive impairment, postmenopausal behavioral changes, and immune senescence. Progress was made on understanding the neurobiological basis of post-menopausal hot flashes, sex differences in cognitive decline and pathologies of the skeleto-muscular system and metabolism. Faculty in the group is also the Director of the DCM Aging resource.

4) Key outcomes: An arguably key metric of outcome on a Divisional level is the amount of funding secured through the peer-review process, disease-specific foundation support and industry applications. Below is the current funding level of the Division of Neuroscience.

Our funding portfolio is diverse, reflecting the 5 major scientific groups represented in the Division:

NINDS	NIAAA	NHLBI	NEI	NIA	NIAID	Foundations	Industry	Other
R01	R00	R01 (2)	R01	R01 (3)	R01	NSF	Private Source	U of W
R00	P60	NRSA	Subcontract (1)	Subcon (3)	subcont	OHSU		
subcontract (3)	R01	R01		T32		Private Source		
	U01 (3)							
	R24							
	R13							
	NRSA							

In addition to funding in hand, progress can be measured by the success rate of our Scientists. Since May 2104 the Division Scientists applied for 44 grants, Pending Support and 10 were funded. Therefore of the 31 grants submitted in the past 8 months, we have a 33% hit rate. This is an outstanding success rate given the pay lines of NIH and Foundations.

DIVISION OF NEUROSCIENCE: TRAINING

The Division provides training and professional development encompassing summer internships for high school students, high school teachers, and undergraduates. We also have five graduate students from the Behavioral Neuroscience graduate program that are conducting their doctorate research in the laboratory of a Division Scientist. The Division has a total of eight post-doctoral trainees in seven different laboratories. There are nine junior faculty on the non-core track that receives close mentoring by their lab chiefs. At each level, training encompasses different activities, but at the student level, Division scientists teach in graduate courses at the medical center. Our Scientists are members of NIH funded training grants (aging, alcohol and drug abuse), with the training grant Principal Investigator a member of our Division. We also provide lectures to student interns during the summer program. The Division has a seminar series that meets three times a month where students and trainees are expected to present their research progress. This seminar series also has guest presenters from OHSU and other Universities that provide new research and ideas to our community and help foster collaborations. Faculty is encouraged to have active roles in national and international societies and present their data at important scientific conferences. We help critique each other's grants, particularly helping junior investigators to secure their independent funding base. Finally, ever faculty member (core or non-core) receive a yearly evaluation from the Chief of the Division and review progress toward past professional goals and develop future goals to address career advancement.

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 Division of Neuroscience has worked with the ONPRC MRI facility to make key tools that contributed to the characterization of our unique non human primate (NHP) models. Key technological advances with Division of Neuroscience are:
Fetal brain imaging: Recent technological developments have enabled characterization of moving fetal brain, in utero, using MRI. Although this approach is being implemented in human clinical studies and medical practice, a multitude of unanswered questions exist regarding the dynamic image contrast changes and their relationship to specific biological transformations. Nonhuman primate studies are absolutely critical for histological validation of interpretations of fetal brain MRI, and for developing sensitive measurements to detect abnormal development. ONPRC investigators are currently funded to characterize fetal brain development in contexts of maternal intrauterine infection, fetal exposure to alcohol and anesthetic agents, and under varying conditions of malnourishment.
Innovative therapeutic strategies: With the use of MRI compatible stereotactic devices, as well as efforts to develop viral vectors for most efficient delivery of nucleic acid constructs, we are developing gene therapeutic strategies targeting specific brain nuclei. This work has been spearheaded with an initial focus on Huntington's disease, but now include pioneering work in alcohol addiction and targeting dopaminergic neurons in the ventral tegmental area.
MRI Technical Advances: In the past year helped developed tools that have significantly advanced our ability to identify and track how the brain adapts in normal development and disease states. These include: new informatic approaches, direct comparisons with human brain imaging results, novel applications of contrast agents, and optimal anesthetic conditions for measuring neurophysiological events.
Genomic and Epigenomic Bioinformatics Pipeline: Capitalizing on the ONPRC pedigreed populations. and MiSeq sequencers we produce genome, exon, transcriptome and methylome sequencing and a team of full-time, skilled bioinformaticists provide support for large-scale sequence analysis and gene mapping studies. A custom genetic database (PRIMeSeq) is underdevelopment to facilitate the storage and access of genomic data generated from members of the ONPRC macaque population. In the next year we will launch a systematic, genome sequencing effort, designed to establish colony-wide genotype data sets. These initiatives will establish an unparalleled nonhuman primate resource with comprehensive colony genomic data made available to all investigators. In addition to informing genotype-phenotype studies, researchers will be able to search for variants by chromosome position, by similarity to known human variants or by animal. In addition, research subjects can be selected based upon genotype or haplotype, enabling investigators to design studies based upon known or predicted functional genetic effects.

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: RPPR-Neuro_ResourceSharing.pdf

DIVISION OF NEUROSCIENCE: RESOURCE SHARING

A NIH-R24 (AA 013510) “Monkey Alcohol Tissue Research Resource” that has disseminated organ tissue and plasma samples to over 50 laboratories and is currently being used in 32 separate funded projects in Universities, Centers and Institutes across the country. We also have a unique aging resource of NHPs that is funded, in part, by the NIA and both facilitates research in the living NHP by outside investigators as well as provides tissue to study aspects of aging.

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?

Our program on macular degeneration [Excluded by Requester] PI) has advanced gene therapy of this disorder to human subject trials.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Division Chief	Institutional Base Salary	EFFORT			27,495.00	7,534.00	35,029.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **35,029.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
11	Division Staff	36.6			382,344.00	104,761.00	487,105.00
11	**Total Number Other Personnel**					**Total Other Personnel**	**487,105.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**522,134.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	375.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	375.00
Total Other Direct Costs	**750.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**522,884.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	522,884.00	146,408.00
		Total Indirect Costs	**146,408.00**

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)	**669,292.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Reproductive & Developmental Sciences

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

A better understanding of the processes and factors influencing human reproduction and development would greatly impact human health and quality of life. Currently it is estimated that 2 of 10 adult women are infertile, 4 of 10 pregnancies are "spontaneously" lost, and 1 of 10 children are born with a birth defect. It is also increasingly clear that environmental contaminants, lifestyle (e.g., the western-style diet), and clinical therapies (e.g., the chemo- and radiation therapy for cancer) can profoundly and negatively impact fertility, Conversely, 5 of 10 pregnancies are unintended and human population growth (to over 7 billion people) threatens our quality of life, if not life itself for many species, and threatens global resources. Thus, the rationale remains as great as ever to use advances in our knowledge of reproductive biology and fetal/neonatal development to better understand the causes of infertility and prevent its occurrence, as well as to develop the next generation of contraceptives to prevent fertility. Likewise, as our knowledge of gametes and early embryonic development expands, the use of these reproductive cells/tissues offers sources of pluripotent cells than have unparalleled potential for applications to regenerative medicine.

Nonhuman primates are a valuable model for research advances pertaining to human reproductive and fetal/neonatal health. It's been established that many of the factors and mechanisms controlling reproductive processes (notably within the hypothalamic-pituitary-gonadal axis, plus maternal recognition of pregnancy and term delivery) are more similar between monkeys, apes and man, than with typical laboratory rodent models. For logistical and ethical reasons, studies on humans and apes are very limited; consequently Old World monkeys (macaque species) are a preferred nonhuman primate (NHP) model for basic and applied studies on reproductive processes that portend translational applications to humans.

The Division of Reproductive & Developmental Sciences (DRDS) at ONPRC has a long and rich history in contributing significant advances in primate reproductive biology and its applications to women's health. Research and training activities span the continuum of reproductive processes from gamete (egg) and embryo development, to intrauterine pregnancy and maternal-fetal development, to delivery and neonatal health. A general theme of all laboratories is the use of NHP models for whole animal, cellular and molecular studies of direct relevance to women's reproductive and child health. The core, affiliate and visiting scientists embrace the objectives of the NPRC program in performing research on NHPs, developing NHP models of reproductive diseases, providing training opportunities in primatology, and disseminating our scientific advances. As such, our specific aims for the next 5-year grant interval are to:

Specific Aim 1: Promote research opportunities in existing fields of primate reproductive and developmental science.

Specific Aim 2: Expand opportunities in emerging fields of research.

Specific Aim 3: Ensure availability of primate resources for reproductive research.

Specific Aim 4: Promote efforts to train scientists that focus on primate and human reproductive health.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DRDS_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DRDS_Training.pdf

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

DRDS faculty were actively involved in outreach activities, which included sharing research expertise with U.S. and international scientists, as well as promoting and enhancing the understanding of research conducted in the division to members of the local community. National and international outreach activities included participation in a trainee-mentor luncheon at the annual Society for the Study of Reproduction meeting Excluded by a hands-on course demonstrating methods of ovarian tissue vitrification held at an Oncofertility Conference, Northwestern University Excluded by and a course at the International Society for Fertility Preservation in Brussels, Belgium, for clinicians interested in the field of cryopreservation and fertility preservation Excluded by Requester also organized a "Science Café" series that involved DRDS faculty Excluded by Requester Each session provided members of the local community an opportunity to learn of the research being conducted in the division and its relevance to reproductive health and disease. Through the efforts of Excluded by Requester ONPRC Outreach Coordinator, multiple programs for high school students

and high school teachers are held at the center and involved several division scientists. For example, nearly all division faculty served as panelists to provide advice to high school students seeking careers in science led a hands-on laboratory course on cryopreservation and tissue engineering for high school teachers at the 2014 Oregon Science Teacher Association conference as well as designed and pre-tested curricular materials for educators, information for website visitors, and to promote DRDS programs to the general public.

Excluded by Requester

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

There are no anticipated deviations from the stated specific aims for the DRDS over the coming year. Current faculty will continue to focus on their respective areas of research, service and training. The division will continue with stated plans to expand opportunities in emerging fields of reproductive research. Specifically, the focus will be on further developing collaborative relationships with other ONPRC divisions and clinical departments at OHSU. For example, division scientists are actively involved in the newly formed Center for Developmental Health headed by Excluded by Reques which is part of the Knight Cardiovascular Institute and the Department of Cardiology. The Center for Developmental Health aims to bring together researchers interested in dietary and environmental effects on embryogenesis and fetal development that subsequently lead to a greater propensity to develop disease after birth. It is anticipated that a concerted effort to bring together scientists interested in the developmental origins of health and disease will allow for the submission of individual investigator and multi-PI programmatic grant applications. Moreover, the division is poised to take advantage of its expertise in utilizing NHP models for studying women's health issues in applying for relevant NIH Funding Opportunity Announcements, including the recently announced NICHD Human Placenta Project initiative. Division scientists will continue being involved with training activities and plans for the coming year include resubmission of an institutional T32 training grant in reproductive biology (Co-PIs Excluded by Requester DRDS Physiology & Pharmacology, OHSU), with DRDS core scientists serving as mentors.

Excluded by Requester Pending Support

REPRODUCTIVE AND DEVELOPMENTAL SCIENCES: ACCOMPLISHMENTS

Specific Aim 1: Promote research opportunities in existing fields of primate reproductive and developmental science.

The DRDS continues to serve as a nationally and internationally recognized leader in reproductive sciences through the activities of its productive and collaborative scientific staff. The past year included changes in leadership to accommodate the retirement of Excluded by Requester as Division Head the beginning of June 2014, at which point Excluded by Requester was appointed as Interim Chair. Excluded by familiarity and more than 14 years of experience in the use of NHP models for studying reproductive physiology and issues related to reproductive health in women allowed for a smooth transition of leadership. Moreover, while Excluded by has stepped down as Division Head to focus on research endeavors full time, he is available to Excluded by for consultation regarding divisional matters. Through this reporting period, there were 11 core scientists with a primary appointment in DRDS Excluded by Requester or a joint appointment with other ONPRC divisions Excluded by Requester Diabetes, Obesity & Metabolism; Excluded by Requester Neuroscience; Excluded by Requester Neuroscience). There were also 10 affiliate scientists in the DRDS Excluded by Excluded by Requester. Due to loss of research support, Excluded by Requester (affiliate scientist) left the division January 2015.

Division faculty continued to make progress in research programs that are translational in nature and are of potential clinical significance in the following areas of reproductive biology:

Contraception: A main focus of studies performed in the division included the identification and development of novel female contraceptives that reversibly or irreversibly block gamete transport and fertilization. Support for these studies included continued funding through an NICHD U54 Contraceptive Research & Development Center grant Excluded by Requester, foundational grants Private Source Excluded by Requester Private Source Excluded by Requester and several pharmaceutical research contracts Private Source Private Source Excluded by Requester Private Source Excluded by Requester

Infertility & Oncofertility: Division faculty continued to maintain active research programs focused on understanding the underlying causes of infertility. For example, a collaborative effort involving DRDS scientists Excluded by Requester Excluded by Requester and faculty from within the Division of Diabetes, Obesity, & Metabolism supported by a P50 National Centers for Translational Research in Reproduction and Infertility (NCTRI) grant, aims to understand the role a Western style diet and hyperandrogenemia plays in the development of female infertility. Excluded by continued studies focused on advancing our understanding of ovarian follicle growth and survival in vitro as a means to achieve fertility preservation in those undergoing ovotoxic chemotherapy through grants from the Private Source Private Source and the Private Source Research conducted by Excluded by through the past year, supported by an NICHD R21 grant, focused on the development of a NHP model of endometriosis. Dr. Excluded by Requester conducted studies supported by the pharmaceutical company Gideon Richter PregLem SA to test novel therapies for treatment of female infertility.

Reproductive Aging: Through the use of the ONPRC Aging Resource Excluded by Requester and an R24 Resource Development grant Excluded by Postmenopausal Monkey Resource) studies are ongoing that serve to determine the effects of the aging process on reproductive function, primarily as related to alterations in neuroendocrine activities. The Aging Resource program allowed for the coordinated management and use of aging rhesus macaques for collaborative studies involving DRDS scientists Excluded by Requester and others at OHSU. Studies conducted as part of the R24 Postmenopausal Monkey Resource included comparisons of social behavior, cognitive function, brain structure, immune function, fat accumulation, indices of metabolism and bone density between estrogen depleted (i.e., ovariectomized) and estrogen supplemented rhesus macaques.

Development: Efforts in understanding primate development spanned the continuum of peri- or post-fertilization events through maternal-fetal pathologies that affect neonatal health. Excluded by continued to focus on the genetic and epigenetic mechanisms responsible for reprogramming of somatic cells to the totipotent and/or pluripotent state using somatic cell nuclear transfer (SCNT) and induced pluripotent stem cell technologies. Excluded by published in Nature this past year that human somatic cells are more faithfully reprogrammed to pluripotency by SCNT relative to what is achieved through iPS reprogramming. The support

for Excluded by Requester research included 3 NICHD R01 grants Excluded by Requester A new DRDS faculty, member began investigating the cellular and molecular mechanisms in primates that are responsible for the development of chromosomally abnormal embryos, which is associated with early pregnancy loss. Excluded by Requester research efforts were supported through the ONPRC P50 NCTRI grant and multiple foundation grants Private Source Private Source. Excluded by utilized recently developed non-invasive imaging techniques to better understand the development of the placental vasculature and circulation (supported by an NICHD R21 grant). Through an NICHD funded R01, Excluded by continued to study the effect of how premature birth initiated in response to infection results in lung disease and neurological impairment.

Specific Aim 2: Expand opportunities in emerging fields of research.
Opportunities to expand DRDS activities in emerging areas of reproductive science research included the development of multiple PI, center-based programs and the support of junior faculty that increase the breadth and expertise of the division. Regarding the former, Excluded by Requester submitted a proposal to the Private Source Private Source to establish the Oregon Center for Permanent Contraception (OPERM), which was funded January 2015. The mission of OPERM includes developing nonsurgical approaches for women that permanently prevents pregnancy and can be offered in areas with limited healthcare resources. Scientists from DRDS Excluded by Requester and other institutions (University of Washington) have individual research projects supported through OPERM that focus on novel, nonsurgical approaches leading to permanent occlusion of the oviduct. Through the support of ONPRC and OHSU administration, Excluded by Requester recently established the Center for Embryonic Cell & Gene Therapy, which focuses on the use of SCNT for the development of genetically matched stem cells and to prevent diseases arising from defective mitochondria transferred from the mother through the oocyte to offspring. The Embryonic Cell & Gene Therapy center, located on the OHSU South Waterfront campus, is a collaborative effort involving Excluded by Requester from DRDS and clinicians in the Department of Obstetrics & Gynecology's infertility group.

Progress was made expanding the division's research focus on maternal-fetal medicine and gamete/embryo biology over the past year. Based on the results of studies conducted through the support of an R21 and ONPRC pilot funding, Excluded by Requester developed novel, noninvasive imaging techniques that allow for real-time assessment of placental blood flow and nutrient transport. The results from his studies, which included increased understanding of how the placenta develops and adapts to adverse conditions, serve as the basis for Pending Support Excluded by Requester, a recently hired core scientist (September 2013), was successful in developing her research activities over the past year. Dr. Excluded by Requester brought new technologies and expertise to the division, including high-throughput microfluidic gene expression analysis and a real-time imaging system (in collaboration with the biotechnology company Auxogyn) that allows for noninvasive monitoring of embryonic growth and development. Excluded by Requester also established collaborations with Excluded by Requester in the Division of Neurosciences and bioinformaticists at OHSU to advance epigenetic and genetic research capabilities at ONPRC and OHSU. With Excluded by as the PI, this research team Pending Support Pending Support

Specific Aim 3: Ensure availability of primate resources for reproductive research.
It is imperative that the NHP needs for DRDS projects are effectively managed and balanced with those of the entire center. The need for adult female macaques by division scientists is in direct competition with the needs of the ONPRC Division of Comparative Medicine as this is the population that is required to sustain the center's breeding program. Thus, the division was involved in several activities that ensure sufficient availability of NHP resources for projects focusing on reproduction and development. As Division Head, Excluded by Requester is a member of the Animal Utilization Committee, which assesses all animal allocation requests for grant applications prior to their submission or activation. These requests are reviewed monthly for their feasibility based on animal availability and housing. Availability of animals for a given study is derived from a review of the current colony demographics and the effect removal of the requested cohort of animals would have on long-term colony stability. Division scientists also provided feedback and projections regarding their anticipated NHP needs. With the recent development of an electronic health record system and its implementation at ONPRC, division faculty now have access to the reproductive history of every animal at the center. This allowed investigators to assess ovarian cyclicity through daily menses reports and past fecundity, resulting in the selection of only those animals that are best suited for their studies. Lastly, utilization of the Timed Mated

Breeding (TMB) Resource and the Assisted Reproductive Technologies (ART) Core allow for the most efficient use of valuable NHP resources. The TMB provided [Excluded by Requester] pregnancies suitable for her studies, whereas the ART Core provided multiple investigators in the division with the necessary gametes and embryos for their research projects.

Specific Aim 4: Promote efforts to train scientists that focus on primate and human reproductive health. Training efforts within the DRDS is detailed below in the training section.

REPRODUCTIVE AND DEVELOPMENTAL SCIENCES: TRAINING AND PROFESSIONAL DEVELOPMENT

As stated in Specific Aim 4, a major goal of the Division of Reproductive & Developmental Sciences is to train the next generation of reproductive biologists. In terms of this divisional priority, its faculty are involved in the training of 2 Ph.D. students through the OHSU graduate Program in Molecular & Cellular Biosciences (PMCB). Both students, [Excluded by Requester] joined the laboratory of division scientist [Excluded by Requester]. Faculty within the division are also actively involved in the training of postdoctoral fellows. Through the past reporting period, DRDS faculty [Excluded by Requester] were involved in the mentoring of 5 postdoctoral Ph.D. trainees. Division faculty members are part of a T32 Reproductive Biology Training Grant, which in the past year provided support for 1 Ph.D. student and 1 eligible postdoctoral fellow. Postdoctoral fellows with the potential to develop independent research programs can be promoted to Staff Scientist, which in turn affords them the opportunity to seek their own research funding. [Excluded by Requester] worked with [Excluded by Requester] as a postdoctoral trainee to investigate the regulation of follicular development in primates. She was promoted from a postdoctoral fellow with [Excluded by] to a Staff Scientist 1 position and [Pending Support]. Through the close ties between the DRDS, Department of Obstetrics & Gynecology and Department of Pediatrics faculty, 3 M.D. fellows were involved in research projects overseen by division faculty. [Excluded by Requester] both Family Planning fellows from the Department of Obstetrics & Gynecology, are working with division scientists [Excluded by] [Excluded by Requester] on projects related to the development of novel contraceptives. [Excluded by Requester] is in Dr. [Excluded by Requester] laboratory, where she studied the effects of preterm birth on subsequent disease development. Support for the development of independent research careers is also available through an OHSU Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program. [Excluded by Requester], former postdoctoral trainee in DRDS, is currently serving as a second year BRCWH scholar where she investigates the mechanisms and regulation of ovarian folliculogenesis, as well as endocrine/paracrine pathways that influence follicular development and oocyte maturation in primates. Lastly, DRDS continues to train international students and scientists in the use of NHP for studying reproductive biology. The past year, [Excluded by Requester] from the Center for Uterine Cancer at the [Private Source] was a visiting scientist in Dr. [Excluded by Requester] Laboratory. [Excluded by Requester] completed and successfully defended her dissertation project, receiving her Ph.D. from the [Private Source]. Part of her dissertation research was performed under the mentorship of [Excluded by Requester] as a visiting Fogarty fellow. After completing her graduate studies, she received a faculty appointment in the Department of Research & Development [Private Source]. [Private Source] Additionally, a visiting Ph.D. student from Brazil [Excluded by Requester] joined Dr. [Excluded by Requester] laboratory for a one-year fellowship supported by her home institution [Private Source] to learn and optimize methods of NHP sperm cryopreservation, which will benefit assisted reproductive technologies (ART) in macaque species. [Excluded by Requester] a graduate student in the laboratory of an eminent reproductive scientist [Excluded by Requester] [Private Source] will work with [Excluded by Requester] [Excluded by] to learn procedures for studying monkey follicles and oocytes. She will perform experiments testing the effects of lipotoxicity and mitochondrial stress on oocyte quality.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

As previously stated, Excluded by Request brought new technologies and expertise to the division, including a Fluidigm™ high-throughput microfluidic gene expression analysis system and a real-time imaging system (Auxogyn) that allows for noninvasive monitoring of embryonic growth and development. The microfluidics system, which is overseen and managed by the ONPRC Molecular & Cellular Biology Support Core, allows for parallel RNA and DNA analyses from small samples (i.e., single cells to a few hundred cells). Through the use of a single-cell workflow, the system isolates, processes, and profiles individual/small numbers of cells for multiple genomics applications that include targeted gene expression, miRNA expression profiling, and whole exome/genome sequencing. The ability to perform detailed genomic studies with such sample sizes will expand the division's capacity to analyze critical molecular parameters in germ cells, embryos, and small biopsies/tissue samples. Proprietary Info

Proprietary Info

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

File uploaded: RPPR-DRDS_OtherProducts.pdf

C.5.b Resource sharing

File uploaded: RPPR-DRDS_ResourceSharing.pdf

REPRODUCTIVE AND DEVELOPMENTAL SCIENCES: OTHER PRODUCTS

The Endocrine Society completed a 5-minute film summarizing the NHP research performed in the DRDS, focusing on the projects being conducted as part of the ONPRC/OHSU P50 NCTRI grant. The Director of ONPRC [Excluded by] the Associate Director [Excluded by] the PI of the NCTRI Center [Excluded by Requester] and a postdoctoral fellow [Excluded by Request] provided interviews, combined with laboratory and animal footage, in support of the 5-year study investigating the effects of hyperandrogenemia and western-style (high fat/fructose) diet on the reproductive and metabolic systems in young adult monkeys and its relationship to the development of polycystic ovary syndrome in women.

REPRODUCTIVE AND DEVELOPMENTAL SCIENCES: TRAINING AND PROFESSIONAL DEVELOPMENT

Division scientists disseminate their research findings at regional, national, and international meetings, including the following:

Regional Conference

- Northwest Reproductive Sciences Symposium, hosted by Washington State University, Cle Elum WA, May 29-31, 2014. Participating DRDS faculty: Excluded by Requester

National Conferences

- The Annual Meeting of the Society for the Study of Reproduction, Grand Rapids MI, July 2014. Participating DRDS faculty: Excluded by Requester
- The Annual Meeting of the American Society of Reproductive Medicine. Honolulu HI, October 2014. Participating DRDS faculty: Excluded by Requester
- The 34th Annual Minisymposium on Reproductive Biology. Northwestern University, Chicago IL, January 2015. Participating DRDS faculty: Excluded by
- Research Focus Group Meeting of the National Centers for Translational Research on Reproduction and Infertility. Bethesda MD, May 2014. Participating DRDS faculty: Excluded by Requester
- NICHD Reproductive Center Directors Meeting. Bethesda MD, May 2014. Participating DRDS faculty: Dr. Excluded by Requester
- Annual Steering Committee Meeting for the NICHD Contraceptive Development & Research Centers. Bethesda MD, October 2014. Participating DRDS faculty: Excluded by Requester Excluded by Requester
- The Annual Meeting of the Society for Reproductive Investigation, San Francisco CA, March 2015. Participating DRDS faculty: Excluded by Requester
- The Annual Meeting of the Pediatric Academic Society, San Diego CA, April 2015. Participating DRDS faculty: Excluded by Requester

International Conferences

- European Workshop on Fetal and Neonatal Transition, Prato, Italy, August 2014. Participating DRDS faculty: Excluded by Requester
- The 41st Annual Meeting of the Fetal and Neonatal Physiological Society, St Vincent, Italy, August 2014. Participating DRDS faculty: Excluded by Requester
- International Conference on Nonsurgical Permanent Contraception. ONPRC, Beaverton OR, May 2014. Organized by DRDS scientist Excluded by Requester to convene a group of international experts to discuss research opportunities in the field.
- European Society of Human Reproduction and Embryology. Munich, Germany, June 2014. Participating DRDS faculty: Excluded by Requester
- Experts Meeting on Progestin-Releasing IUS. Private Source November 2014. Participating DRDS faculty: Excluded by Requester

Research results obtained by Division scientists are published in widely read reproductive sciences journals (see ONPRC publication list).

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Interim Division Chief	Institutional Base Salary	EFFORT			45,659.00	12,922.00	58,581.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **58,581.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
11	Division Staff	28.02			298,673.00	84,524.00	383,197.00
11	**Total Number Other Personnel**					**Total Other Personnel**	**383,197.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**441,778.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	270.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	428.00
Total Other Direct Costs	**698.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**442,476.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	442,476.00	123,893.00
		Total Indirect Costs	**123,893.00**

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)	**566,369.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Pathobiology & Immunology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The World Health Organization (WHO) estimates that infectious disease is responsible for 25% of all deaths worldwide and that this number is likely to be even larger if certain cancers, cardiovascular and respiratory/digestive deaths, which can also be attributed to infection are included. Interestingly, six diseases account for 90% of infectious disease deaths, and include acute respiratory infections (including pneumonia and influenza), AIDS and AIDS-associated disease, diarrheal diseases, tuberculosis, malaria and measles. To curb this growing global problem further elucidation of host-pathogen interactions is absolutely needed to better design therapeutics and vaccines to prevent morbidity and mortality from existing and newly emerging infectious agents. Commensurate with this need is the absolute requirement for an animal model that parallels and shares developmental, physiological and evolutionary relationships with humans, and are susceptible to the same or closely related infectious agents with similar, if not identical sequelae. Addressing this challenge is the goal for the scientists within the Division of Pathobiology and Immunology (DPI), which is home to a team of outstanding virologists, immunologists and pathologists, many of whom are also scientists within the Vaccine and Gene Therapy Institute (VGTI), who are imbued with a team ethic and a commitment to nonhuman primate (NHP) models. The fundamental theme is that progress in these areas of investigation requires high level expertise and experience in virology, immunology and pathology, a combination that is rarely found in a single investigator, but that would be provided by a close-knit collaborative environment in which scientists encompassing these disciplines could interact on a daily basis. Furthermore, it was felt that NHP models would be an essential element of any truly clinically relevant investigations in these areas.

Within the next 5 year funding cycle of the P51 the Division will focus on expanding its research portfolio by building upon our existing strengths to develop new NHP models of infectious and chronic disease, and simultaneously, train a new crop of scientists dedicated to the diligent use of NHP models to combat primate and human health concerns. Accomplishing these goals will be a challenge and we plan to tackle this by recruiting an established scientist, who utilizes NHPs for both infectious and chronic disease research to lead the Division within the next two years, and recruit immunologists (senior and junior investigators) to fill the gaps generated by the departure of Excluded by Requester within three years. The specific aims for the Division are:

Specific Aim 1: Promote and expand research opportunities in existing areas of NHP Immunology and Infectious Disease Science

Specific Aim 2: Develop new NHP models of emerging infectious and chronic disease

Specific Aim 3: Train a new era of scientists to expand NHP models of infectious disease

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Patho_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Patho_Training.pdf

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

Division scientists continue to present their cutting edge findings at national and international meetings, and at community outreach events the ONPRC hosts.

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

Division scientists will continue to attend and speak at national and international meetings, and publish their findings in scientific journals.

PATHOBIOLOGY & IMMUNOLOGY: ACCOMPLISHMENTS

We have been successful with these specific aims.

Specific Aim 1: Promote and expand research opportunities in existing areas of NHP Immunology and Infectious Disease. Two infectious disease programs were initiated or supported during this time period. First, *Mycobacterium tuberculosis* (Mtb) was evaluated in RM, and this was further expanded by vaccinating RM with a novel RhCMV vector encoding Mtb antigens. Vaccinated animals were characterized for their immune responses to the Mtb antigens and then challenged with Mtb. Remarkably, RhCMV/Mtb-vaccinated animals had significantly less disease compared to animals vaccinated with BCG vaccine or RhCMV vector alone. Dr. Picker and his collaborators intend to build upon these studies with modified RhCMV vectors in the coming year. The second new infectious disease program involved *Plasmodium falciparum*, the parasite responsible for malaria. Here, Excluded by Requester and his colleagues created recombinant RhCMV vectors encoding two P. falciparum antigens and vaccinated animal to characterize their immune response to the antigens. Afterwards, the animals were challenged with *P. falciparum* and monitored for disease. Although the animals developed robust T cell responses to the antigens, they were not protected from disease, suggesting that other P. falciparum antigens may need to be targeted. Excluded by Requester and his colleagues are creating other RhCMV vectors with different antigens and once these are made, they will be evaluated in animals.

Specific Aim 2: Develop new NHP models of emerging infectious and chronic disease. Our affiliate scientists, Excluded by Requester have continued to build upon their Chikungunya virus (CHIKV) program. Specifically, Excluded by Requester has an established collaboration with Excluded by Requester Private Source to evaluate recombinant antibodies targeting CHIKV in RM. These studies are scheduled to begin in 2015.

Excluded by Requester and his colleagues here at the ONPRC, Excluded by Requester are continuing to develop the Japanese macaque encephalomyelitis (JME) model of multiple sclerosis (MS)-like disease. Their group has evaluated cerebrospinal fluid (CSF) for biomarkers that are consistent with MS and have found that some animals with JME have oligoclonal bands, which are routinely used to aid in the diagnosis of MS. This finding and others further support the JME model as a valuable NHP model of MS.

Update on recruitment of Division Chief for Pathobiology and Immunology: We brought an experienced NHP immunologist in as a candidate for the Division Chief position. Unfortunately, this person was not considered further. For now, the search for a replacement has stopped and Excluded by Requester will continue in the interim position. We also are awaiting institutional support to replace the two immunologist positions (senior and junior) that we are hoping to fill.

Specific Aim 3: Train a new era of scientists to expand NHP models of infectious disease. We continue to pursue the goals described in this aim, which include working closely with the NHP Infectious Disease Unit (NHPID Unit) and Division of Comparative Medicine (DCM) for efficient use and management of NHP resources, participating on ONPRC committees that oversee NHP utilization and training the next generation of scientists to lead infectious disease research in NHPs.

PATHOBIOLOGY & IMMUNOLOGY: TRAINING AND PROFESSIONAL DEVELOPMENT

Many of the research grants supporting the Division's mission have funds to train post-doctoral fellows and graduate students. These trainees investigate the mechanisms that infectious pathogens utilize to gain a foothold in hosts and induce disease. Similarly, some of our trainees investigate the host response to pathogen infection to better understand how to eliminate the pathogens. These talented young scientists routinely discuss their research findings at a weekly seminar series. This provides trainees a forum to develop and improve their presentation skills for when they attend national and international scientific meetings. Our graduate students are in the Department of Molecular Microbiology and Immunology at OHSU where they are required to present their research at a departmental seminar and are required to meet with visiting seminar speakers. These settings provide students and post-doctoral fellows opportunities to network with others. Additionally, these trainees are actively involved in a journal club to present and discuss recent published work that has broad interest to the Division. Some of our more senior trainees participate in national meetings that offer workshops to assist or advise trainees in career development. Finally, OHSU offers courses for grant writing and an Office of Post-doctoral Affairs to respond to career and professional development needs.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

Several Division scientists are involved in the development of cytomegalovirus (CMV) vectors as therapeutic vaccines for HIV, Mtb, P. falciparum, Kaposi sarcoma-associated herpesvirus, Epstein Barr virus, hepatitis B virus, and prostate cancer. This involves the generation of human CMV vectors with defined modifications to eliminate potential unwanted affects. This includes the engineering of spread deficient viruses that are capable of infecting and expressing antigen(s) of interest, but are unable to replicate from the initial site of infection or draining lymph node.

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: RPPR-Patho_ResourceSharing.pdf

PATHOBIOLOGY & IMMUNOLOGY: RESOURCE SHARING

Recombinant rhesus CMV vectors, rhesus rhadinovirus reagents and other research reagents are routinely made available to requestors following the completion of institutional material transfer agreements executed by the OHSU Office of Technology Transfer & Business Development and the requestors' institutional official.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Interim Division Chief	Institutional Base Salary	EFFORT			45,825.00	12,373 00	58,198 00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **58,198.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
11	Division Staff	18.54			200,670.00	54,181.00	254,851.00
11	**Total Number Other Personnel**					**Total Other Personnel**	**254,851.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**313,049.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	355.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	713.00
Total Other Direct Costs	**1,068.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**314,117.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	314,117.00	87,953.00
		Total Indirect Costs	**87,953.00**

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)	**402,070.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Division of Diabetes, Obesity, & Metabolism

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

It is well publicized that obesity, diabetes and cardiovascular diseases (commonly referred to as metabolic diseases) have become the principal preventable cause of death in the United States. While there are many contributing factors to these diseases, it is recognized that sedentary life styles and the overconsumption of calorically dense and highly palatable foods are primary contributors of this world-wide health epidemic. More importantly, and more costly in regards to the long-term health of Americans, quality of life and for the economical impact on the health care system, is the devastating increase in childhood metabolic diseases. Over the past decade ONPRC has fostered the development of a small but internationally recognized and well-funded group of investigators focused on various aspects of metabolic diseases, including both adult and early onset obesity, diabetes and cardiovascular diseases. This group has developed several powerful nonhuman primate (NHP) models that uniquely mimic the complexities of the development and pathogenesis of metabolic diseases in humans. Using these models, and the unique tools available at ONPRC, this group has established strong and productive collaborations with renowned investigators at OHSU, throughout the United States and Internationally. In recognition of this evolving strength at ONPRC, the previous core grant renewal established a focused working group to continue to develop this area of expertise. The establishment of this working group was enthusiastically supported in the previous critique of the P51 grant and by the ONPRC Scientific Advisory Board. Over the past five years, ONPRC has invested in the establishment and expansion of the Obese NHP Resource, which supports the development and maintenance of these powerful animal models and research tools, and has made them available to the national research community. Because of the continued success of this research program and the recognized importance to improving human health, ONPRC has now formally established a new research division dedicated to the investigation of metabolic diseases, the Division of Diabetes, Obesity and Metabolism. Leading the development of this new division will be senior scientists 1) Excluded by Req ; Interim Division Head (formerly of the Division of Neuroscience); 2) Excluded by Requester ONPRC Associate Director for Research; 3) and Excluded by Request Formerly Director of ONPRC and member of the Division of Neuroscience) along with a talented group of young and affiliated scientists. Our scientists have set some fundamental goals for the coming five years that will be key for the continued development and long-term success of this division.

Specific Aim 1: To develop a fully integrated and collaborative Division focused on the understanding of the biology and pathophysiology of metabolic diseases, with a collective group of scientists focused on the diverse aspects of this health epidemic as a foundation. There will be a strong focus on increasing our understanding of the molecular and pathophysiological complications that develop during the progression of these diseases, as well as the investigation of therapeutics and interventions to prevent or reverse complications associated with these diseases.

Specific Aim 2: To recruit new investigators to provide new expertise and technical approaches to allow a more diverse and integrated approach to the investigation of these complex diseases. These diverse approaches and areas of expertise will allow a more efficient use of these valuable research models, as well as providing a rich intellectual environment. Currently the Division consists of 3 senior core scientists, two junior core scientists and 4 staff scientists. The goal over the next five years would be to expand the Division with the recruitment of two additional assistant core scientists in areas that complement our current faculty, but expand into areas where we lack expertise, like adipose biology, cardiology or immunology.

Specific Aim 3: To develop a supportive and constructive environment for training the next generation of scientists in the use of complex and highly translatable NHP models of metabolic diseases. The NHP model has been identified nationally as a critical translational research tool. This is especially important in the areas of metabolic diseases since the NHP model so closely mimics the human disease. However, only a small number of national investigators that regularly use this valuable model. Thus, it is key to provide a rich training environment and resources to expand this research community.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-DOM_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-DOM_Training.pdf

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

NOTHING TO REPORT

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

In light of significant changes in the senior faculty of the Division, we are considering a number of options to develop the Division in the future that reflect both a desire to maintain a strong academic home for the current divisional scientists as well as limitations on resources available for recruitments.

DIVISION OF DIABETES, OBESITY, AND METABOLISM: ACCOMPLISHMENTS

The Division has been very successful in maintaining a robust level of funding from a variety of sources, including the NIH, non-profit foundations, and industry. Two staff scientists Excluded by Requester who have been successful in obtaining independent grant support, have been promoted to the category of Assistant Scientist but without P51 core grant support. This is equivalent to a research assistant professor position, and was done to better reflect their success in developing an independent research program.

DIVISION OF DIABETES, OBESITY, AND METABOLISM: TRAINING & PROFESSIONAL DEVELOPMENT

The Division supports the training of postdoctoral and clinical fellows and also aims to provide opportunities for leadership for more junior members. For, example Excluded by has been promoted to Director of the Obese Resource, taking over the responsibilities of Excluded by Requester is being considered for management of the ONPRC microscopy core upon Excluded by Requester from ONPRC.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

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?

The principal impact of Divisional activities on technology transfer is represented by the Proprietary Info detail in section G below. This project will employ the NHP model of diet-induced obesity for discovery of targets for obesity and diabetes treatments, the rights to which will be licensed to Proprietary Inf by OHSU, with OHSU retaining IP rights to any targets not licensed to Proprietary Info leaving the option of establishing a new company to develop these targets.

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

The imminent retirement of [redacted] and the reduction in effort of [Excluded by] due to his recruitment to [Proprietary Info] will leave the current division significantly reduced in size and experience. The recruitment of additional core scientists in immunology and a joint recruitment with OHSU in cardiovascular research will replenish the faculty to some degree, but alternatives such as incorporation of core scientists who are now in other divisions as well as a closer relationship with the Division of Reproductive and Developmental Sciences are being considered to maintain a strong focus on metabolism at ONPRC.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Interim Division Chief	Institutional Base Salary		EFFORT		18,330.00	5,151.00	23,481.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **23,481.00**

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	Division Staff	3.14			29,401.00	8,262.00	37,663.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**37,663.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**61,144.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	225.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	375.00
Total Other Direct Costs	**600.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**61,744.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	61,744.00	17,288.00
		Total Indirect Costs	**17,288.00**

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)	**79,032.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Interdisciplinary Research Programs

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

In the previous P51 renewal, three Working Groups were established to foster areas that were not adequately represented by the existing Research Divisions. These included Biology of Aging, Metabolic Disease, and Stem Cells and Developmental Biology. The explicit goal of these was to establish interdisciplinary research programs that fostered interdivisional and inter- and intra-institutional collaborations. As expected, during the past funding period, each of these has evolved along different paths. As described below and in the research strategy section, the Biology of Aging Working Group has continued to mature and is now designated an IDRP at the Center. The Metabolic Disease Working Group has matured to become a new Research Division, as detailed in its designated section. The Stem Cell & Developmental Biology Working Group has been integrated into the original Division of Reproductive Sciences with its change in focus to the Division of Reproductive & Developmental Sciences. Two new Interdisciplinary Research Programs have been established based on recommendations from the 2011 Scientific Retreat. The Early Childhood Health & Development program represents the increasing interactions between the Center and the Departments of Ob-Gyn and Pediatrics at OHSU, and the Primate Genetics Program represents the growing importance of genetic and genomic aspects of the NHP model and the unique pedigreed NHP colonies at the Center. As with the Working Groups, these programs are supported minimally by the P51, to provide funds to enhance communication and interaction by supporting seminar speakers and symposia. The Specific Aims are:

Specific Aim 1: Biology of Aging. The Biology of Aging Program is a multi-disciplinary research program involving Core and Affiliate investigators from each of the four research Divisions, and it draws strength from the broad spectrum of scientific and technical expertise afforded by its members. Since nearly 20% of the US population will be 65+ years old by 2030, a universal goal is to find safe and effective ways of enhancing the health and quality of life in the elderly, and to find ways of reducing premature senescence. Unfortunately, the mechanisms that underlie normal and pathological human aging are still poorly understood, and this significantly hampers the development of effective therapies. NHPs are long-lived and show age-related physiological changes that more closely resemble those of humans. The associated Primate Aging Resource provides Center investigators an unique opportunity to study the etiology of normal and pathological human aging. The goals for the next funding period include: 1) strengthening existing NHP aging disease models and to developing new models; and 2) strengthen inter-disciplinary collaborations and increase their translational potential.

Specific Aim 2: Early Childhood Health & Development. The overall goal of the newly established Early Childhood Health & Development Program is to develop and utilize NHP models that encompass key developmental stages (i.e., prenatal and postnatal life) that have been demonstrated to strongly influence the risk of developing cardiovascular, pulmonary, metabolic and psychological disease during early childhood and throughout life. Specifically, program investigators collectively study events that occur during pregnancy (i.e., intra-amniotic infection, hypoxia, growth restriction, maternal nutrition, placental abnormalities and preterm birth), as well as broad aspects of human development (i.e., cardio-pulmonary physiology, neurodevelopment, immune function and vaccine development) as a means of understanding factors and/or events during prenatal and postnatal life that can have profound effect on the overall health of an individual and as an adult. The near-term goals of the program during the next funding period are to: 1) identify and develop key areas of research within the program to increase collaborative interactions and the scope of research in this area; 2) seek an array of funding opportunities to take advantage of the integrated interests of the program, in particular collaborative, team-science mechanisms; and 3) develop a strategic plan for longevity of the program.

Specific Aim 3: Primate Genetics Research. The goal of the Primate Genetics Program is to leverage the complementary genetics expertise of program investigators, unique ONPRC capabilities such as the Japanese Macaque Resource, and state-of-the-art technologies such as those available through the Molecular & Cellular Biology Research Support Core, to characterize the contribution of genetic and epigenetic variation to complex disease phenotypes in non-human primates, and to translate these findings to human disease. The goals of the program include :1) ongoing genetic studies in macular degereration and neuropsychiatric disorders, obesity, cardiovascular disease and obesity; 2) characterization of rhesus genome variation; 3) epigenetic studies in alcohol abuse and adiposity; and 4) NHP genomic analysis method development.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-IDRP_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-IDRP_Training.pdf

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

BIOLOGY OF AGING
The Biology of Aging program represents a corner stone of the OHSU Healthy Aging Alliance (HAA), and on 9/30/14 the HAA held a conference entitled "Harnessing Science and Communities for Healthy Brain Aging"; this was attended by >200 basic scientists, clinical scientists, health care providers and lay persons, and provided a platform for data sharing and networking.

PRIMATE GENETICS
Our publications were:

1 Excluded by Requester
Conserved syntenic clusters of protein coding genes are missing in birds. Genome Biology 2014 Dec 18; 15(12):565

2 Excluded by Requester
Excluded by Requester (2014) Ring chromosomes, breakpoint clusters and neocentromeres in sarcomas. Genes Chromosomes & Cancer 2014 Nov 25. doi: 10.1002/gcc.22228.

3. Excluded by Requester ¥and the International Consortium for the sequencing and annotation of the gibbon genome (2014) Gibbon genome and [illegible] karyotype evolution of small apes. Nature. 513(7517):195-201. PMID: 25209798. News & Views: Something to swing about.

4 Excluded by Requester Inference of transposable element ancestry. PLoS Genet. 2014 Aug 14;10(8):e1004482. doi: 10.1371. PMID: 25121584

5. Excluded by Requester
Excluded by Requester
Excluded by Requester Genomic organization and evolution of double minutes/homogeneously staining regions (dmin/hsr) with MYC amplification in human cancer. Nucleic Acids Res. 2014 Oct 1;42(14):9131-45. PMID: 25034695

6 Excluded by Requester
Excluded by R Development and validation of a SNP-based assay for inferring the genetic ancestry of rhesus macaques (Macaca mulatta). Am J Primatol. 2014 Nov;76(11):1105-13. doi: 10.1002/ajp.22290. Epub2014 Jun 2 PMID:24953496

7 Excluded by Requester
Excluded by Requester A new rhesus macaque assembly and annotation for next-generation sequencing analyses. Biol Direct. 2014 Oct 14;9(1):20. doi: 10.1186/1745-6150-9-20. PMID:25319552.

8 Excluded by Requester An empirical comparison of short tandem repeats (STRs) and single nucleotide polymorphisms (SNPs) for relatedness estimation in Chinese rhesus macaques (Macaca mulatta). Am J Primatol. 2014 Apr;76(4):313-24. doi: 10.1002/ajp.22235. Epub 2013 Nov 22. PMID:24273109

9. Excluded by Requester Genome typing of nonhuman primate models: implications for biomedical research. Trends Genet. 2014 Nov;30(11):482-7. doi: 10.1016/j.tig.2014.05.004. Epub 2014 Jun 18. PMID:24954183

10. Excluded by Requester "Drinking to Dependence Risk Factors in Nonhuman Primates," in Neurobiology of Alcohol Dependence, Noronha A, Cui C, Harris A, Crabbe JC, eds., San Diego: Academic Press, 2014, Chapter 20 pp. 408-420. ISBN: 9780124059412.

11. ACCEPTED
ACCEPTED

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

BIOLOGY OF AGING
There is growing awareness that nearly 50% of our genes have a circadian pattern of expression. Consequently, to better understand the etiology of normal and pathological aging it is imperative that we establish how these rhythms are established and how they change during aging. We intend to establish circadian gene expression profiles for target organ systems in the rhesus macaque, such as the prostate gland; we expect these studies to disclose pathological age-related changes and to shed new light on the development of safer and more effective therapies for the elderly.

To make more efficient use of the limited primate aging resource, we intend to coordinate some of the activities of the various interdisciplinary programs. In particular, we want to examine how genetics, hormones, and the circadian environment (including photoperiod and diet) contribute to the development of aging associated disorders, including cognitive decline, immune senescence, cardiovascular disease and diabetes.

EARLY CHILDHOOD HEALTH & DEVELOPMENT
Now that the ECHD program has strengthened, in part through the interdisciplinary interactions with the Center for Developmental Health, there is now a need for a broader strategic plan to continue building on our strengths, but also for the longevity of the program.

PRIMATE GENETICS
We plan to launch large-scale genomic sequencing and genotype analysis of ONPRC rhesus macaques Pending Support These data would be made available to other investigators through the creation of a genotype and phenotype searchable database, thus will immediately be of value for expanding interdisciplinary genetic research across all divisions.

We will continue to advance the genetic study of alcohol addiction, chromosome missegregation, healthy aging, cardiovascular disease biomarkers, and adiposity/obesity, through other funding mechanisms.

We will host three seminar speakers to present cutting edge research in the area of NHP genetic genomic research at the ONPRC. This effort is intended to expand interest in this topic at the ONPRC, as well as to establish new collaborative research opportunities using the ONPRC macaque population.

INTERDISCIPLINARY RESEARCH PROGRAMS: ACCOMPLISHMENTS

BIOLOGY OF AGING

The Biology of Aging program continues to emphasize interdisciplinary approaches to study causal relationships between diverse aging-related pathologies. For example, recent studies have shown that old animals with perturbed sleep-wake cycles have more pronounced cognitive impairment, as well as compromised immune function. Ongoing studies are examining the impact of high fat diet on the rate of development of these pathologies, and testing if various hormonal supplements have therapeutic potential. In addition, data from pilot studies has provided a foundation for grant proposals that utilize novel nonhuman primate models of human aging, including hot flashes, sarcopenia, and stroke.

EARLY CHILDHOOD HEALTH & DEVELOPMENT (ECHD)

In an effort to strengthen our collaborative interactions and expand the scope of research within our program, the ECHD group has combined efforts with the Center for Developmental Health at the Knight Cardiovascular Institute, OHSU. Lead by Excluded by Requester this interdisciplinary program has identified five major focus areas that overlap in many ways with the ECHD program (i.e., Behavioral health, brain & cognitive development; Maternal nutrition, obesity & metabolic disease; Placental function & development; Inflammation and immunology). Scientific and clinical Investigators from ONPRC and OHSU collectively meet monthly, alternating campuses. The ECHD group has facilitated video conferencing to enable maximum attendance, given the distance between each campus.

Through our collaborative efforts with the Center for Developmental Health, several new funding opportunities have emerged through pilot project funding from the KCVI. ONPRC investigators focused on placental development & function have already been successful in securing funding which will be use to generate preliminary data for a larger NIH application in the near future.

PRIMATE GENETICS

We focused on advancing NHP genomic analysis methods as a means to accelerate the use of NHPs as models of biomedical disease and precision medicine approaches. In the first 9 months of funding, we developed novel approaches to enable very low cost, whole genome analysis of rhesus macaques. Pending Support

Pending Support

One of our investigators Excluded by Requester completed and published the results of an international consortium study on the Genome gibbon.

INTERDISCIPLINARY RESEARCH PROGRAMS: TRAINING AND PROFESSIONAL DEVELOPMENT

BIOLOGY OF AGING

The Biology of Aging program also provided a fertile environment for the training of graduate students, summer interns, high-school teachers, as well as visiting scientists and students from the United Kingdom and from Chile.

PRIMATE GENETICS

Primate Genetics research programs included the training of two graduate students, one postdoctoral fellow and one junior faculty (staff scientist).

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: RPPR-IDRP_ResourceSharing.pdf

INTERDISCIPLINARY RESEARCH PROGRAMS: TRAINING AND PROFESSIONAL DEVELOPMENT

PRIMATE GENETICS

Genomic data is downloaded to public databases (dbSNP, SRA) for public access.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

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

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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. Interdisciplinary Program	3,000.00
Total Other Direct Costs	**3,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**3,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	3,000.00	840.00
		Total Indirect Costs	**840.00**

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)	**3,840.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Pilot Research Program

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The goal of the ONPRC Pilot Project program is to encourage new avenues of investigation using appropriate nonhuman primate (NHP) models through the provision of funds for generation of preliminary data that can serve as the foundation for follow-up support from the NIH and other agencies and sources. This will be achieved through pursuit of the following Specific Aims:

Specific Aim 1. Solicit proposals from a wide spectrum of potential applicants through effective outreach at the institutional, local, and national levels. Annual announcements are circulated through e-mail and the ONPRC website to Center, OHSU, and NPRC consortium members to attract a robust response from interested parties.

Specific Aim 2. Employ a strong, credible, and transparent review process to select the most meritorious proposals. Proposals are evaluated through a two-step process that includes an initial assessment of letters of intent by the ONPRC Research Advisory Committee (RAC), followed by a request for full proposals from the highest-ranked preliminary proposals. These are then reviewed in depth by the ONPRC RAC and external ad hoc reviewers chosen from the ONPRC National Scientific Advisory Board (NSAB) and other entities as necessary for appropriate expertise.

Specific Aim 3. Monitor progress and outcomes to determine return on investment of allocated funds. Productivity in terms of manuscripts and grants submitted and awarded based on Pilot Program support are assessed through final reports and follow-up monitoring by the Associate Director for Research.

The ONPRC Pilot Project program plays a critical role in allowing investigators to develop research projects using NHPs, and is especially important for new investigators recruited to the ONPRC who lack significant prior NHP research experience. The program also provides funds for established investigators to develop new NHP models and preliminary data that are absolutely essential if new external grant funding is to be obtained.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Pilot_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

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 solicitation for the current year pilot grant program has been sent out and proposals will be evaluated for funding that will start May 1, 2015.

PILOT RESEARCH PROGRAM: ACCOMPLISHMENTS

The pilot projects listed below were funded in the most recent budget period.

1. Excluded by Requester (OHSU, Ob/Gyn, Maternal Fetal Medicine) was awarded $25,728 for a project entitled "Use of advanced non-invasive imaging to understand altered placental hemodynamics and injury following prenatal alcohol exposure."
2. Excluded by Requester | Private Source was awarded $69,272 for a project entitled "Eliminating the latent SIV reservoir in rhesus macaques (RM) using Alemtuzumab."
3. Excluded by Requester (ONPRC, Division of Reproductive & Developmental Sciences) was awarded $55,000 for a project entitled "Anti-Müllerian Hormone (AMH) Actions during Primate Follicular Development."
4. Excluded by Requester (VGTI) was awarded $50,000 for a project entitled "Examining the roles of microRNAs (miRNAs) in Japanese macaque encephalomyelitis (JME), a model for Multiple Sclerosis (MS)."

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

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

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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 Program	200,000.00
Total Other Direct Costs	**200,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**200,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	200,000.00	56,000.00
		Total Indirect Costs	**56,000.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**256,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Improvement & Modernization

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Improvement and Modernization (I&M) funds are provided up to a maximum of [Proprietary Info] per year. These funds can be used to upgrade the physical plant (repairs and renovation of facilities) and to replace obsolete shared resources and equipment (FOA, IV. G.). At ONPRC, Facilities, the Division of Comparative Medicine (DCM), Information Systems (IS), and the Research Support Cores provide shared resources to support the NHP research mission of ONPRC. Items are requested by each of these areas, individually justified, and then a committee works with the requestors to prioritize the requests to insure the continued improvement and modernization of these shared resources and that the requests contribute to the fulfillment of the goals of the ONPRC. A distinction is made between routine maintenance items provided by Facilities and specialized improvement/maintenance programs aimed toward the long-term preservation of the integrity and functionality of our facilities. Routine maintenance is included in the Facilities operations budget; specialized improvement/maintenance is included in the I&M budget. The amount provided through this mechanism is an integral part of a larger effort to provide for the comprehensive upkeep and improvement of the ONPRC facilities and resources that are used for NHP research and support.

Through these funds I&M supports:
• Improvement and modernization of buildings and equipment used in support of the NHP resources and research through Facilities requests.
• Improvement and modernization of Research Support Core equipment used in support of NHP Research through requests from the individual Research Support Cores.
• Improvement and modernization of Information Systems specific to the NHP related work of the ONPRC such as the PRIMe system and NHP research related bioinformatics through requests from the ONPRC Information Systems.
• Improvement and modernization of the DCM resources that provide for the care of our NHP colony through requests from DCM.

Specific Aim 1: To appropriately identify, justify, and prioritize requests for the improvement and modernization of ONPRC resulting in improved equipment and facilities specifically related to NHP research and support.

Specific Aim 2: To provide for the timely implementation of the approved requests through skilled professionals resulting in efficient and effective use of the improved resources.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-IM_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

The center partners with the host institution's Design and Construction (DesCon) department for capital construction projects, both new construction as well as renovations. A decision tree is being developed to help determine when a project should be managed by DesCon or when it is appropriate to use the center's Facilities and Property Management group to be the project managers. Depending on the type of project, there are pros and cons for the two different groups. The host institution has a list of approved construction companies that is updated on a routine basis. The process is competitive to help insure high quality of service and reasonable pricing of services. The goal over the next reporting period is to finalize and implement the project management decision tree.

IMPROVEMENT & MODERNIZATION: ACCOMPLISHMENTS

The Improvements and Modernization (I&M) Committee developed a master list of all equipment and deferred maintenance needs for the center. The master list was then broken out by category with an estimated cost. The committee reviewed the list and ranked each item as high, medium or low priority and determines how current funds will be spent. This master list is a “living document” as the I&M committee meets every other month to review and update the list and priorities.

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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 ($)*	Funds Requested ($)*

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person

B. Other Personnel

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

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
1. General Equipment	500,000.00
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**500,000.00**

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*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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)	**500,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
		Total Indirect Costs	

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**500,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: Outreach & Community Engagement

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Support for biomedical research depends in great part on public awareness of the value of such research and an understanding of the process by which medical science discoveries are made. A number of studies indicate that science proficiency in the United States lags behind that in many other countries, creating a significant challenge for maintaining public support for research. Providing multiple opportunities for the general public to learn about biomedical research at the ONPRC and its value is, therefore, of critical importance to the long-term success and productivity of the research enabled by the core grant.

During the previous funding period, education outreach at the ONPRC involved a multi-faceted program that targeted a number of different populations using a variety of strategies. Thousands of students, teachers and members of the public participated in these programs. Our strategies included tours, classroom visits, an informal science program that is held weekly during the school year called Science Ambassadors, a docent program, courses for high school students, veterinary externships, and high school, undergraduate, and teacher apprenticeships and/or volunteer opportunities. Many students were exposed to hands-on learning opportunities thanks to the opening of a dedicated learning lab. A lecture series, the ONPRC Science Café, was launched. This provided an opportunity to inform the public (high school through mature adult) about research approaches to specific health issues as well as discussing the essential need for nonhuman primates in that research. The goal of each of these highly successful programs was to enhance science education and to provide unique experiences that strengthen public understanding of the value of biomedical research and the scientific process.

In the next funding period, we aim to continue and enhance these highly successful programs, and to expand their scope through additional outreach activities to the public and to state and federal legislators. Our specific aims are:

Specific Aim 1. To provide multiple outreach activities for the general public, teachers, and students. We will continue to offer the multiple successful programs developed at ONPRC to provide unique experiences that educate students and adults from multiple backgrounds. We will enhance existing programs and introduce additional new programs that will expand our outreach aims.

Specific Aim 2. To communicate the activities and discoveries of ONPRC personnel to the general public. In conjunction with our outreach activities, we will work closely with the Department of Strategic Communications at OHSU to highlight the exciting discoveries of Center scientists and other Center activities to the media and to state and federal legislators.

Specific Aim 3. To engage with the general public in a series of programs to foster discussions around science and the value of science. As one of our major initiatives in the next five years, we will seek funding to host Science Discussions in the Portland area, advised by a Community Advisory Board.

Specific Aim 4. To continue to represent ONPRC through participation in OHSU's public outreach events as appropriate. The ONPRC Outreach Porgram is an active participant in multiple OHSU-sponsored events. This affords multiple opportunities to educate the public about the role of the Center as an important component of OHSU's mission.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: RPPR-Outreach_Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: RPPR-Outreach_Training.pdf

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

NOTHING TO REPORT

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

- Identify community leaders to participate on the Community Advisory Board
- Identify additional sources of funding for programs in community/beyond
- Promote the "Partners in Science Program" to qualified teachers through presentations at Science Faculty meetings

• Assist in development/implementation of science fairs in the community
• Reach out to elected representatives at state and federal levels to invite them to learn more about the essential need for biomedical research leading to medical progress

OUTREACH & COMMUNITY ENGAGEMENT: ACCOMPLISHMENTS

Specific Aim 1: We hosted over 3500 visitors to our center during 2014, mostly through our popular tour program. To support our need to host visits from very large groups we continue to recruit and manage a group of volunteer docents. We have increased our efforts to engage underrepresented minorities and disadvantaged students in these programs. We provided a one day event (Science Saturday) for 24 – 5th graders in June of 2014, and a one day event (Camp Monkey) for middle school students in July. Working closely with our parent institution, OHSU, we are developing a one-week science summer camp that will host 24 students during the summer of 2015. Funding secured through yearly grant applications to a private donor allowed us to host over 20 students (high school and undergraduate) in apprenticeships during the summer of 2014.

Specific Aim 2: Highlights from 2014 news stories related to scientific discoveries at ONPRC include:

- International coverage of Ex cludedby Requester "Mitochondrial Manipulaitons" and FDA considerations (100+ stories featuring Excluded including:
  - **NY** http://www.nytimes.com/2014/03/18/science Ex cludedby Requester -mitochrondrial-manipulations.html?_r=1
  - **BBC**: http://www.bbc.com/news/health-26367220
  - **CNN**: http://www.cnn.com/2014/02/26/health/ivf-mitochondria/
  - **Slate**:http://www.slate.com/blogs/xx_factor/2014/02/26/_designer_babies_aren_t_on_their_way_hopefully_3_person_embryo_fertilization.html
  - Additional stories on: NBC, FOX, LA Times, WebMD, Daily Beast, Times of India, Reuters, BabyCenter, Bloomberg, CBS, USA Today, NPR Shots blog and various other blogs)
- A story run in the Portland Tribune, along with other Community newspapers, about Ex cluded by Requeste Excluded by Requester research on chromosomal rearrangements. (Portland Tribune Searching for Similarities: http://portlandtribune.com/ttt/89-news/240550-106967-searching-for-similarities)
  International coverage of Ex cludedby Requester research on Gibbon genome (over 150 stories for the second half of 2014)
- Online coverage that included ONPRC research on the effects of a high-fat diet in pregnant monkeys
- OregonLive coverage on Ex cludedby Requeste Ex cludedby Requeste HIV Vaccine research grant ("Oregon Health & Science University HIV vaccine research wins $25 million)
- Coverage from Portland Business Journal to Nature World News on Ex cludedby Requester work showing the effects of an omega-3 rish diet on brain development
- International coverage on Resveratrol supplements causing pancreatic problems in babies on zeenews.india.com

Specific Aim 3: Funding has been secured (through the NCTRI grant) to support a yearly spring Science Café series devoted to topics in female reproductive health; an additional series has been inaugurated during the fall (October) to showcase research in other ONPRC Divisions. These series (scheduled on 4-consecutive weeknights in April and October), featured various Center scientists discussing their work and the importance of the NHP model to that work.

Specific Aim 4: Outreach personnel and volunteers represented ONPRC at the annual meetings of the Oregon State Science Teachers' Association and the Washington State Science Teachers' Association; the OHSU/OMSI "Brain Fair;" the OHSU "Brain Awareness Lecture Series," and continue to participate as active members in OHSU's "SOAR" Committee (Science Outreach and Resources).
The Education & Outreach Office worked closely with OHSU's Government Relations Office to Arrange for several Oregon State representatives to visit the Center and meet with key personnel (Director, scientists, Outreach Coordinator).

OUTREACH & COMMUNITY ENGAGEMENT: TRAINING AND PROFESSIONAL DEVELOPMENT

Hands-on lab activities developed with the assistance of the ONPRC Office of Education & Outreach were piloted to educators at both the Oregon State Science Teachers Association and the Washington State Science Teachers' Association annual meetings during 2014. The Education and Outreach Coordinator actively recruits ONPRC scientist mentors and science teachers in nearby communities to participate in the Private Source "Partners in Science" summer apprenticeship program. Three science teachers were hosted at ONPRC during the summer of 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

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*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & 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				Unit Head	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
2	Unit Staff	1.98			14,543.00	3,869.00	18,412.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**18,412.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**18,412.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	300.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**300.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	450.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	375.00
Total Other Direct Costs	**825.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**19,537.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	19,537.00	5,470.00
		Total Indirect Costs	**5,470.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**25,007.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.

A. COMPONENT COVER PAGE

Project Title: NPRC Consortium-Based Activities

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

1. Behavioral Management (BMC). This group has the goal to strengthen communication and research collaboration to help to identify behavioral management best practices and promote psychological well-being for captive nonhuman primates (NHP). To this end, the BMC promotes resource sharing, standardization of terminology and assessment tools, and scientific collaboration among participants.
2. Breeding Colony Management (BCMC). This group enhances collaborations between NHP colony mangers of all national primate centers with regard to breeding management, herd health, regulatory compliance, SPF surveillance, facility management/design and resource sharing.
3. Clinical and Surgery Techniques (CAST). This group seeks to accelerate information transmission among NPRCs, to serve as a resource to develop best clinical and surgical practices among and within the NPRCs, and to facilitate networking among NPRCs and relevant institutes beyond NPRCs.
4. Computational Methods and Resources. The role of this group is to identify new and more productive synergies between people and computing technologies, to provide methods and software application resources to support other Consortium working groups, and to facilitate and make rigorous the sharing of data, practices and expertise between NPRCs.
5. Data Access Guidelines Group (DAGG). This group will develop and maintain processes to ensure all website content and related access permissions are reviewed and approved by DAGG representatives. They will educate working group participants on best practices to prevent unauthorized access or unnecessary exposure of shared information.
6. DNA Banking. This group will establish a National NHP DNA Bank to facilitate the distribution of NHP genomic resources for research use, establish a centralized web portal to enable direct access to DNA Bank content and distribution information and promote use of the National NHP DNA Bank through publications and targeted presentations.
7. Genetics and Genomics. This group has to goal of designing and developing a custom SNP- array for parentage analysis of rhesus macaques at all NPRCs, and an array for rhesus macaque ancestry analysis at all NPRCs. They plan to develop web-based analysis pipelines to facilitate parentage and ancestry genotype interpretation and to develop colony genetic management guidelines for optimizing the genetic health of NHP colonies across the NPRCs.
8. Integrity-Compliance. The purpose of this working group is to cultivate open discussions and critical thinking about matters related to compliance with federal regulations and NIH guidelines at the National Primate Research Centers (NPRCs). The first focus is the development of an on-line resource to provide information about IACUC protocol review and NPRC-specific attention to OLAW, USDA, and AAALAC regulations, guidelines and recommendations.
9. Occupational Health & Safety Working Group. This group plans to achieve a better understanding of the most updated information for those working with NHPs between the NPRCs, National B-virus lab and the Centers for Disease Control and well as to increase sharing of injury and exposure data between NPRCs to look for trends in data and share successful injury reduction strategies.
10. Outreach and Public Relations. The goal of this group is to share best practices with respect to handling issues that are unique to research involving animals, to identify opportunities to educate the public (both at public events, via the internet, and through the press), and to develop appropriate responses to persons who are opposed to biomedical research that involves animals. They will share activities and information via the web and will develop marketing/ outreach/teaching materials that can be used by all NPRCs locally and at a national level within NIH and with other governmental and non-governmental agencies.
11. Pathology. This group seeks to foster cooperation between the NPRC's to effect improved understanding of NHP pathology and to share best practices for greater efficiency. They have a goal to increase availability of the pathology resource (data, images, etc.) between and outside centers to better serve as a national resource for NHP Pathology.
12. Training. This group contributes to, and takes a leadership role in promoting, the exchange of clinical or operational case presentations of NHPs amongst NPRCs and other contributing institutions to foster a collegial and communicative environment amongst these institutions, and ultimately to promote best practices.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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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?

File uploaded: RPPR-NPRC_Training.pdf

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

1. Behavioral Management (BMC). Nothing to report

2. Breeding Colony Management (BCMC). Nothing to report.

3. Clinical and Surgery Techniques (CAST). Nothing to report.

4. Computational Methods and Resources. Installation of software tools at Tulane NPRC, and deployment via the NHPRC Consortium website. Poster presentation at AALAS and ASP conferences, presentations at monthly BCMC conference calls, and periodic briefings for Consortium working groups.

5. Data Access Guidelines Group (DAGG). Nothing to report.

6. DNA Banking. Nothing to report.

7. Genetics and Genomics.
• Excluded by Reque, Am J Primatol. 2014 Nov;76(11):1105-13.
• A white paper was completed that detailed recommended genetic management methods and goals for the genetic health of captive NHP colonies at the NPRCs.
• A workshop for NPRC colony managers and genetic staff from NPRCs was held at the ONPRC in Nov 2014, as previously described.

8. Integrity-Compliance. Nothing to report.

9. Occupational Health & Safety Working Group. Nothing to report.

10. Outreach. Nothing to report.

11. Pathology. We have contacted training group representatives for both laboratory animal medicine and veterinary pathology to disseminate information about the availability of the PPID resource.

12. Training. VGR participation is open to non-NPRC institutions that hold NIH-sponsored training grants. External institutions currently participating in the monthly sessions include:
• Private Source
• University of Missouri
• Colorado State University
• Private Source
• University of Michigan
• Private Source
• University of Illinois at Chicago
• UC Berkeley

It is estimated that, with full participation, approximately 100-150 veterinarians, students, pathologists, technicians and scientists are exposed to the activities and clinical work being performed at the NPRCs.

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

1. Behavioral Management (BMC). The BMC plans to use our newly developed record keeping system to collect data on social housing across NPRCs, as well as identify resource needs to reduce the use of single housing. We will also work on training staff to understand and identify the natural history and behavior, which is critical for improving primate welfare and fulfilling requirements in "The Guide."

2. Breeding Colony Management (BCMC).
The ONPRC will continue to actively participate in the monthly BCMC teleconferences. Actions anticipated during the next grant year include the following:

• TB: A survey will be developed to gather information. There are plans for a representative to meet with CNPRC and WiNPRC colleagues to discuss TB diagnostics. Proprietary Info
• Disaster recovery plan: Develop a more tailored survey based upon initial survey questions and discussion. Construct a template MOU for shared resources, and a cross-institutional staff liability waiver agreement that would allow transfer of personnel in the event of a crisis.
• BMC/BCMC Collaboration: Develop a survey to acquire further information for the BMC regulatory visit questions/concerns document.
• Regulatory: Facilitate attendance of USDA Regional Directors to Spring NPRC Director's meeting. Schedule an information-sharing meeting between BCMC and USDA VMO and Regional directors in 2015. Create a bibliography of publications related to NHP colony management from NPRC veterinarians/scientists to share with VMOs/Regional Directors.
• Nursery rearing: Develop a white paper on the need for nursery rearing for some studies.
• Viral testing: Successfully completed final versions of the SPF consortium's Virus Testing Best Practices (SIV, SRV, STLV, Herpes B) documents. All NPRC SPF sites are expected to adopt these best practices as laboratory protocols and use the standard procedures for follow-up testing when viral testing results are positive. The viral testing papers, written by BCMC members, will be consolidated into one manuscript to be submitted as a peer reviewed paper.
• Measles paper: Complete manuscript review and submit for publication.

• Necropsy survey: The Pathology Working Group is planning to develop a follow-on survey, but no additional action needed from BCMC at this time.
• Campylobacter study: No action needed from BCMC at this time; ONPRC will provide updates as the project moves forward.
Specific [redacted]
Private Wording: [redacted]: Demonstration of Colony Health Benchmarks Phase 2 to further identify potential cross-connections between NPRCs scheduled for March 2015. Continue population modeling prototype development; ONPRC currently using, TNPRC to collaborate and CNPRC has interest.
• Species diversity within NPRCs: Plan to develop 1-2 page summaries on all of the species available from the NPRC network for further discussion on Issues of supply and demand, less utilized species and availability of resource has a cost, projection of use in research versus cost to maintain, and loss of potential disease models and research opportunities.
• Extreme phenotypes: Identify a small group of NPRC personnel who will take on the responsibility for this program; begin by assessing the prevalence of the Extreme Phenotypes identified during the initial survey across all Centers; begin working with the appropriate NPRCs to collect and evaluate the pedigree information of the identified animals; develop an overall structure for the Extreme Phenotypes activities; develop a communication plan that with include identification of internal and external disease/phenotype experts; and develop a plan to advertise the availability of newly identified but currently unexploited primate models to the broader research community.

3. Clinical and Surgery Techniques (CAST). CAST will continue scheduled meetings that feature a specific topic presented on a rotational basis among the NPRCs. Additionally, members have shown interest in surveying the NPRCs to gather information about training requirements necessary to certify individuals as competent to perform certain procedures.

4. Computational Methods and Resources. We plan to deploy the population modeling application on the web, via the NHPRC Counsortium website, as well as locally at the other NPRCs. Once doing this we can federate the individual NPRC projections to yield a Consortium-wide projection tool. Phase II of the colony health benchmarking will be completed as an automated system, federating scheduled extracts from indivdual NPRCs to provide regular automatic updates on colony productivity.

5. Data Access Guidelines Group (DAGG). Nothing to report.

6. DNA Banking. Nothing to report.

7. Genetics and Genomics. Update the SNP parentage assay for use on the Fluidigm platform, which has lower assay cost and is currently well supported. Update PedSys software, in collaboration with Nylander et al., for use in colony genetic management.

8. Integrity-Compliance. Continue to share information and ideas on issues related to Integrity and compliance.

9. Occupational Health & Safety Working Group. Annual meeting of the OHSWG will be at WNPRC in May 2015. The OHSWG has proposed to better lines of communication with the Herpes B virus laboratory [Excluded by Requester] at HIV and Retro Virology Disease Branch of the CDC. OHSWG is proposing to establish industry standards for PPE with NHPs and risk assessments.

10. Outreach.
• Work with NPRC leadership to better define the role of this working group vis a vis the needs of both the NIH and the Center Directors.
• Represent NPRCs at outreach events (AALAS, 2015; Society for Neuroscience, 2015; 4th
Annual USA Science & Engineering Festival, 2016)
• Hold 4th Annual Outreach Working Group meeting, hosted by CNPRC
• Produce promotional marking materials, including digital media.
• Develop plans for a national effort to most effectively educate the public on the importance of NHP models in biomedical breakthroughs.

11. Pathology. Plans for the coming reporting period include the addition of more material to the PPID; ove[redacted] slides from the NEPRC archives are being scanned and curated, representing significant and difficult-to-obtain historical material held by NEPRC, and additional material from each of the primate centers pending adequate editing and curation resources. Content includes over [Propr] gross images from SWPRC from baboons, chimpanzees and cynomolgus macaques, over [redacted] gross images from Yerkes archives contribute by [redacted] and scans of SIV-related opportunistic infections from ONPRC, and case material presented at past NPRC Virtual Slide Conferences and Primate Pathology Workshops. Continued expansion of the PPID user community will be achieved through promotion to relevant professional groups. We are planning to expand the federated cross-center tissue inventory query to additional NPRCs, utilizing tools constructed for the NEPRC tissue archive transfer to the TNPRC. An expanded survey of pathology practices will be developed by the PWG. Results of these surveys will help refine best practices in pathology, including necropsy and histology services, clinical pathology, and research effort and support. A FY2015 Face-to-Face Meeting is proposed to be held at one of the Primate Centers (TBD) in order to advance the objectives of the cross-center tissue inventory query and development of best practices derived from the proposed survey of pathology practices.
Proprietary
Proprietary Info
Proprietary

12. Training. The ONPRC will continue to participate in the monthly Virtual Grand Rounds teleconferences. Other institutions have expressed an interest in participating in the VGR sessions. When institutions approach the consortium for participation in VGR presentations, an email will be sent querying the group members for objections to expansion. If no objections exist and the requesting program provides evidence of a robust veterinary training program and houses NHPs for biomedical

NPRC-BASED CONSORTIUM ACTIVITIES: ACCOMPLISHMENTS

1. **Behavioral Management (BMC).** The BMC made great progress in the past year. We standardized both the criteria for success and record keeping for social introductions and reasons for single housing of captive nonhuman primates. We also began to compare methodological differences across facilities to optimize social housing practices and identify necessary resources for reducing the use of single housing. We continued to work on a standardized method of assessing alopecia, and evaluated this system at the Yerkes NPRC during our 2014 face to face meeting. Finally, there was a high level of collaboration among BMC members, including 10 co-authored publications, 29 abstracts at national and international meetings, a joint workshop and a joint symposium at the American Society of Primatologists meeting. Several members are submitting papers for a special issue of the American Journal of Primatology co-sponsored by the BMC. Topics of focus for these collaborative efforts include pair housing, social management and productivity of breeding groups, and alopecia.

2. **Breeding Colony Management (BCMC).** The Breeding Colony Management Consortium (BCMC) is a very active group and continues to serve as a forum for cross-center exchange of colony management experiences on a broad array of pertinent subjects designed to improve Center approaches and enhancements to NPRC colony breeding and management programs, both individually and collectively. This past year was especially productive with significant ONPRC participation as the host institution for separate Genetics and Genomics Working Group and BCMC face-to-face meetings, as well as a joint GGWC-BCMC face-to-face meeting. The ONPRC has fully participated in all monthly online web meetings of the BCMC, and many Oregon Center members have an active role as the primary point-of-contact for BCMC topics and projects.

   The following BCMC initiatives were selected as priorities for 2014 and remain active:

   - TB: A review of TB occupational health program requirements for differences and potential approaches to standardize practices across all NPRCs.
   - Disaster recovery plan: This initiative seeks to define shared resources across NPRCs. A survey was conducted and discussed at the November F2F meeting at the ONPRC. Development of cross-center MOUs and staff liability waivers are ongoing to ensure 100% reimbursement for sharing of resources should the Government declare a Federal disaster area for a specific NPRC.
   - BMC/BCMC Collaboration: Discussion on possible collaborative projects between BMC and BCMC, endpoint policies for behavioral management, and prioritization of interactions and projects between BMC and BCMC.
   - Regulatory [Excluded by Requester] accomplished a first visit to USDA Western Regional Headquarters with [Excluded by Requester] to discuss potential partnership. Initial focus included information sharing and developing methods to track and address concerns.
   - Nursery rearing: Address recent NIH interest based on animals rights call-out of NICHD colony at NIHAC.
   - Viral testing: Successfully completed final versions of the SPF consortium's Virus Testing Best Practices (SIV, SRV, STLV, Herpes B) documents. All NPRC SPF sites are expected to adopt these best practices as laboratory protocols and use the standard procedures for follow-up testing when viral testing results are positive. The viral testing papers, written by BCMC members, will be consolidated into one manuscript to be submitted as a peer reviewed paper.
   - Measles paper: Measles vaccine experience and practices have been drafted into a manuscript for review by BCMC members.
   - Necropsy survey: A BCMC initiated survey on pathology practices across NPRCs was complted. The pathology working group will develop deeper survey based upon results.
   - Campylobacter study. [Excluded by] from the ONPRC is developing a vaccine project and will likely solicit participation from other NPRCs.
   - [Specific Private Vendor] projects: Colony Health Benchmarks is now transitioned to Phase 2 to further identify potential cross-connections between NPRCs. Population modeling prototype in development soon to be available to other NPRCs. Post approval monitoring toolset (Animal procedure reconciliation project, blood volume calculation tool refinement, and workflow integration and efficiency (surgery), will be available to all when completed.

Breeding Colony Management Consortium (BCMC) and the Genetics/Genomics Working Group (GGWG) Facie-to-Face Meeting. These two working groups met at the Oregon NPRC on November 9th covering a number of topics of importance to both groups. The meeting was comprised of structured presentations and open discussions concerning various topics, including strategies for managing and monitoring genetic variation in primate research colonies, recent technology improvements for genetic characterization of primates, developments in analytical tools and software, and others. As a result of the meeting, the following priorities were developed:

- Extreme phenotypes: The survey generated a list of potential disease models that have not, as yet, been catalogued across the NPRCs.
- Maintaining genetic diversity in NPRC NHP breeding colonies: Goal is to develop specific plans and procedures to manage nonhuman primate breeding to enhance genetic diversity. The ONPRC has developed a ranking process for breeding group formation to maintain genetic diversity.
- Species diversity within the NPRC program: Identified issues of supply and demand.
- Continuing refinement of SNPs for ancestry and parentage: Improving panels of SNPs, realizing more cost effective processes, developing and improving tools designed to analyze SNP data, and improving reliability and usefulness of the ancestry panel.
- MHC genetics: Issues still exist with availability of animals with requested haplotypes at some NPRCs. Recognition that requested number of animals with specific MHC haplotypes may interfere with preservation of genetic diversity if all requests are filled.
- NEPRC transfer of genetic information: Discussion on contract with regard to integrating NEPRC animals into other center's breeding colonies. NEPRC animals could be test case for developing a process to maintain genetic data on animals transferred between centers.

3. **Clinical and Surgery Techniques (CAST).**
During the reporting period, CAST hosted nine web conferences. The range of topics presented included craniotomy techniques, apheresis, neonatal anesthesia, and echocardiography. After each presentation, participants asked questions for clarification or additional information; an open forum for general discussion followed this question/answer session. The web conferences were well attended and usually had at least one representative from each of the NPRCs, with most NPRCs signing on as a group of practitioners gathered in a conference room. The featured presentations were posted to the CAST section of the NHPRC Consortium website after DAGG review. This website serves as a reference library of past presentations which may be accessed by members.

4. **Computational Methods and Resources.** We demonstrated federated colony-health benchmarking system, polling data from seven NPRCs to analyze and compare breeding strategies, identifying better practices in breeding colony management. This effort also established relationships and technical infrastructure to pursue broader data-sharing activities. We developed and deployed two post-approval-monitoring applications at Tulane NPRC using software tools developed at Oregon, saving 0.25 FTE at the Tulane NPRC, and allowing potential compliance irregularities to be detected well before any action is taken. We also developed portable population modeling application in collaboration with Tulane NPRC, validating it in use at Oregon NPRC; this tool is particularly easy to share with other NPRCs.

5. **Data Access Guidelines Group (DAGG).** The Data Access Guidelines Group completed its specific aims in the fall of 2013 and has not met for the past 18 months. Protocols and procedures were put into place for the working group chairs to handle most access requests. Potentially sensitive requests have the appropriate approvals secured through other channels. The full DAGG will be reconvened when necessary with a new chair and representatives from the centers to replace any vacancies caused by staff changes.

6. **DNA Banking.** DNA Bank inventories at the ONPRC were updated, and 56 samples requested were delivered.

7. **Genetics and Genomics.**
- We published a manuscript describing use of the 96 SNP ancestry array Excluded by Requester Am J Primatol. 2014 Nov;76(11):1105-13)

- We completed a white paper describing genetic management methods and metrics for use assessing genetic diversity at the NPRCs.
- A one-day workshop was held at the ONPRC to provide training for staff at each NPRC to learn how to implement the genetic management analysis tools. Excluded by Requester led this hands-on workshop, using the methods that she developed and are implemented at the ONPRC.
- Plans are underway to transition the SNP parentage assay from the current Illumina platform to the Fluidigm platform, since Illumina is discontinuing support for their platform. The assay will be adapted and tested by the ONPRC, CNPRC and YNPRC to ensure consistency during the transition.

8. **Integrity-Compliance.** This consortium has met on a quarterly basis by teleconference. Issue discussed include relationship with USDA and appeals related to citations, major vs. minor survival surgery, electronic IACUC systems, staff training to work with nonhuman primates.

9. **Occupational Health & Safety Working Group.** The Occupational Health & Safety Working Group (OHSWG) has phone meetings every 1-2 months to discuss updates for their respective NPRCs, issues of concern at their facilities, and injury reports. In April 2014, the ONPRC hosted an in-person two-day meeting of the OHSWG to more fully discuss injury reports, risk assessments, PPE use, and facilities concerns.

10. **Outreach.** During 2014, members of the NPRC Outreach Working Group (OWG) represented NPRC at the following meetings/events: Society for Neuroscience Annual Meeting (November 2014); the USA Science and Engineering Festival (April 2014); the NHP AIDS Conference (November 2014).

    As a group, the OWG collaboratively developed answers to questions about and/or responding to attacks on biomedical research involving animal subjects that came from a variety of directions (elected representatives, websites such as “Speaking of Research,” etc.).

    We are in the process of expanding the role of this group to include public relations for the consortium as a whole.

11. **Pathology.** The Pathology Working Group has continued to provide monthly Virtual Slide Conferences (VSC) featuring three to five NHP pathology cases from participating centers each month. The responsibility for digitally scanning the histologic material has been assumed by ONPRC for better integration with the Primate Pathology Image Database (PPID). The number of registered PPID users has expanded from 53 in 2013 to 164. Users now represent 52 institutions (in addition to NPRCs) in the U.S., Canada, Europe and Asia. The PPID now includes material from all eight NPRC’s. The number of edited and curated images has expanded to 1,406. Additional didactic material, including PowerPoint reviews of multiple disease entities and pertinent literature, has been added to many cases. A survey of pathology practices across centers was developed in conjunction with the BCMC.

12. **Training.** The Training Consortium continues to serve as a forum for cross-center exchange of clinical experiences, and provided both a speaking and education opportunity for ONPRC trainees and veterinary staff. During this past grant year, these Virtual Clinical Grand Round (VGR) sessions explored “best practices” and facilitated dissemination of clinical information to both new and seasoned members in the field. In general, VGR presentations also provided practice for residents and faculty alike in speaking to, and fielding questions from, a larger inter-institutional audience.

    Presentations, attendance, and participation in discussion are expectations of the residency programs at the ONPRC. In addition, faculty veterinarians are actively encouraged to present and often do. Excluded by Requester oversees scheduling of Center participation as the ONPRC representative for the VGR. The last ONPRC presentation, entitled "Abdominal Masses in Two Female Macaques", was provided by Excluded by Requester a second year resident in the Oregon LAM Consortium program on rotation at the ONPRC. The next ONPRC VGR presentation is scheduled for June of 2015.

    Other cases presented during the past 12 months included the following:
    - "Arteriovenous Fistulas: A case series at NEPRC"

- "Abdominal Masses in Male Rhesus Macaques"
- "Severe Nonregenerative Anemia in a SHIV-infected Pigtail Macaque"
- "Neoplasia in Related Caribbean Vervets"
- "Facial Excoriations in a Rhesus Macaque (Macaca mulatta)"
- "Ocular Herpes in a Chimpanzee "
- "Effects of Transplant Immune Suppression in Rhesus Macaques."
- "Cardiomyopathy and the Cardiac Assessment of Squirrel Monkeys (Saimiri spp.)".
- "Design and Validation of a Body Condition Scale in Squirrel Monkeys (Saimiri spp.)"
- "Ocular squamous cell carcinoma in a chimpanzee"
- "Cases of Granulomatous Inflammation"
- "What's your diagnosis? A rhesus macaque case"

NPRC-BASED CONSORTIUM ACTIVITIES: TRAINING AND PROFESSIONAL DEVELOPMENT

1. **Behavioral Management (BMC).** The BMC meets annually for a face to face meeting during the American Society of Primatologists meeting, which we all attend.

2. **Breeding Colony Management (BCMC).** Face-to-face meetings have fostered increased collaboration across all NPRCs. The BCMC has encouraged the NPRC Director's to continue this yearly forum between BCMC and other consortium groups.

3. **Clinical and Surgery Techniques (CAST).** CAST meeting presentations, discussions, and the CAST Presentations library serve to expand members' procedural proficiencies and repertoire, encourage the development of best practices at each center, and identify expertise among the NPRCs. Rotational topic presentations allow participants to practice and improve public speaking skills and ability to concisely communicate and orient others about a specific technique.

4. **Computational Methods and Resources.** Nothing to report.

5. **Data Access Guidelines Group (DAGG).** Nothing to report.

6. **DNA Banking.** Nothing to report.

7. **Genetics and Genomics.** A workshop was sponsored at the ONPRC in Nov 2014 and led by Excluded by Requester provided training for colony managers and geneticists from other NPRCs to learn genetic management analysis methods that were recommended in a GGWG white paper written this year.

8. **Integrity-Compliance.** The ability to interact with others in the same area provides for professional development. Members rotate in presenting a topic of interest to the group

9. **Occupational Health & Safety Working Group.** Meeting with OHSWG has provided exchanges of experience between members of the OHG and opportunities to review each other's processes and trainings.

10. **Outreach.** Nothing to report.

11. **Pathology.** The PPID is utilized extensively for basic training of laboratory animal medicine and veterinary pathology residents, including preparation for their respective certifying examinations. A majority of the new users in the past year represent these trainees and their mentors. Of the current users, approximately 40 serve as mentors to training programs, and over 120 are preparing for specialty boards in laboratory animal medicine and veterinary pathology. The VSC's provide excellent sources of continuing education and collaboration opportunities for all participants.

12. **Training.** See Accomplishments.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

BREEDING COLONY MANAGEMENT. Colony Health Benchmarks and Population Modeling projects utilize the [redacted] technical computing program using [redacted] Language. The program builds robust and efficient algorithms capable of handling these large-scale problems, integrating nearly 5,000 built-in functions covering all areas of technical computing.

Specific Private Vendor

Specific Private Vendor

GENETICS AND GENOMICS. Technologies all made freely available to other NPRCs and primate researchers.

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: RPPR-NPRC_ResourceSharing.pdf

NPRC-BASED CONSORTIUM ACTIVITIES: RESOURCE SHARING

GENETICS AND GENOMICS. Data developed is shared through the NHPRC consortium website, and through publications.

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

GENETICS AND GENOMICS. New assay for parentage and ancestry testing of macaques has been implemented and used at NPRCs.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

1. Behavioral Management (BMC). One challenge towards meeting our goals is decreased funding for face to face meetings. We will continue to have our monthly meetings via "GoToMeeting".

2. Breeding Colony Management (BCMC). Nothing to report.

3. Clinical and Surgery Techniques (CAST). Nothing to report.

4. Computational Methods and Resources. Nothing to report.

5. Data Access Guidelines Group (DAGG). Nothing to report.

6. DNA Banking. Nothing to report.

7. Genetics and Genomics. Nothing to report.

8. Integrity-Compliance. Nothing to report.

9. Occupational Health & Safety Working Group. Nothing to report.

10. Outreach. Nothing to report.

11. Pathology. Preparation and curation of material for inclusion in the PPID remains time consuming and labor intensive. The effort is frequently constrained by the limited time pathologists have available. Locally, we have attempted to mitigate this by efficient use of technicians to prepare material for inclusion, and regularly scheduled 1-2 hour curation sessions for each pathologist to achieve incremental expansion of content.

12. Training. Nothing to report.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 096997515

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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				Unit Head	Institutional Base Salary	EFFORT			0.00	0.00	0. 0

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Unit Staff	10.08			92,139.00	30,820.00	122,959.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**122,959.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**122,959.00**

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

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

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

Start Date*: 05-01-2015 **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)	10,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**10,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 096997515
Budget Type*: ● Project ● Subaward/Consortium
Enter name of Organization: OREGON HEALTH & SCIENCE UNIVERSITY

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

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	24,000.00
Total Other Direct Costs	**48,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**180,959.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	28.0	180,959.00	50,669.00
		Total Indirect Costs	**50,669.00**

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)	**231,628.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Program Director/Principal Investigator (Last, First, Middle): Robertson, Joseph E.

BUDGET JUSTIFICATION

No significant changes from previously recommended budget.