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

Federal Award Date: 09/05/2019

OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P51OD011106-58 REVISED
FAIN: P51OD011106

Principal Investigator(s):
Steven A. Ackerman

Project Title: Wisconsin National Primate Research Center Support

Brenda Egan
Managing Officer
University of Wisconsin - Madison
21 N. Park Street, Suite 6401
Madison, WI 537151218

Award e-mailed to: NIH@rsp.wisc.edu

Period Of Performance:
Budget Period: 05/01/2019 – 04/30/2020
Project Period: 06/10/1997 – 04/30/2022

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF WISCONSIN-MADISON 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 P51OD011106. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

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

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

Sincerely yours,

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

Additional information follows

SECTION I – AWARD DATA – 5P51OD011106-58 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$3,537,456
Fringe Benefits	$1,272,697
Personnel Costs (Subtotal)	$4,810,153
Consultant Services	$13,629
Equipment	$120,446
Materials & Supplies	$1,355,170
Travel	$61,270
Other	$675,858
Subawards/Consortium/Contractual Costs	$49,595
Publication Costs	$5,217
Federal Direct Costs	$7,091,338
Federal F&A Costs	$2,560,880
Approved Budget	$9,652,218
Total Amount of Federal Funds Obligated (Federal Share)	$9,652,218
TOTAL FEDERAL AWARD AMOUNT	$9,652,218
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
58	$9,652,218	$9,652,218
59	$9,652,218	$9,652,218
60	$9,652,218	$9,652,218

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:	1396006492A1
Document Number:	POD011106L
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021
OD	8014499	$9,652,218	$9,652,218	$9,652,218

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 09/04/2019
Award Processed: 09/05/2019 12:04:03 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD011106-58 REVISED

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

SECTION III – TERMS AND CONDITIONS – 5P51OD011106-58 REVISED

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

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as

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

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

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

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

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

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

This award has been assigned the Federal Award Identification Number (FAIN) P51OD011106. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

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

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

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

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 5P51OD011106-58 REVISED

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

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

CHANGE IN PI

This revision reflects ORIP approval of the change of principal investigator from Dr. Norman Drinkwater to Dr. Steven Ackerman, who will serve as the interim PI, in accordance with the grantee's request dated July 25, 2019.

All previous terms and conditions remain in effect.

SUBJECT FOA
This award is subject to the conditions set forth in PAR-14-226, "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: https://grants.nih.gov/grants/guide/pa-files/PAR-14-226.html

ORIP FUNDING PLAN FOR FY2019
This non-competing award reflects the NIH Fiscal Policy for Grant Awards for FY2019 (see NIH Guide Notice NOT-OD-19-031) and the implementation of the ORIP FY2019 grants funding policy: https://orip.nih.gov/funding/awards-funding-policy

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

Jon Levine

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

CONSORTIUM
This award includes funds awarded for subcontractual/consortium activity with Baylor University. Consortia are to be established and administered as described in the NIH Grants Policy Statement (NIH GPS). The referenced section of the NIH GPS, Part II Chapter 15 is available at: http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf.

DIRECT CHARGES OF F&A-TYPE COSTS
Funds have been requested for office supplies and postage. The allowability of charges to this project for this purpose is predicated on the grantee's compliance with the applicable cost principles.

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

MEALS
The charging of meal costs directly to a grant is an exceptional activity and contingent upon the following: the grantee institution having a written policy in place ensuring consistent treatment of

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

PRIOR APPROVAL REQUEST
Any prior approval request (e.g., changes to key personnel as noted on the award, changes in human and animal subjects requiring prior approval, carryover requests) must be submitted to the assigned Grants Management Specialist and Programmatic Official. Please refer to Part II Chapter 8 the NIH Grants Policy Statement for the activities and/or expenditures that require NIH approval at http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf

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 https://orip.nih.gov/

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: Debbie Chen
Email: chendeb@mail.nih.gov **Phone**: 301-594-9521 **Fax**: 301-451-5462

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

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011106-58 REVISED

INSTITUTION: UNIVERSITY OF WISCONSIN-MADISON

Budget	Year 58	Year 59	Year 60
Salaries and Wages	$3,537,456	$3,524,245	$3,522,888
Fringe Benefits	$1,272,697	$1,423,439	$1,422,891
Personnel Costs (Subtotal)	$4,810,153	$4,947,684	$4,945,779
Consultant Services	$13,629	$13,619	$13,613
Equipment	$120,446	$124,012	$127,684
Materials & Supplies	$1,355,170	$1,327,022	$1,326,511
Travel	$61,270	$54,965	$54,943
Other	$675,858	$575,417	$575,195
Subawards/Consortium/Contractual Costs	$49,595	$49,577	$49,558
Publication Costs	$5,217		
TOTAL FEDERAL DC	$7,091,338	$7,092,296	$7,093,283
TOTAL FEDERAL F&A	$2,560,880	$2,559,922	$2,558,935
TOTAL COST	$9,652,218	$9,652,218	$9,652,218

Facilities and Administrative Costs	Year 58	Year 59	Year 60
F&A Cost Rate 1	37%	37%	37%
F&A Cost Base 1	$6,921,297	$6,918,707	$6,916,041
F&A Costs 1	$2,560,880	$2,559,922	$2,558,935

A. OVERALL COVER PAGE

Project Title: Wisconsin National Primate Research Center Support	
Grant Number: 5P51OD011106-58	**Project/Grant Period:** 06/10/1997 - 04/30/2022
Reporting Period: 05/01/2018 - 04/30/2019	**Requested Budget Period:** 05/01/2019 - 04/30/2020
Report Term Frequency: Annual	**Date Submitted:** 03/01/2019
Program Director/Principal Investigator Information: NORMAN R DRINKWATER , BS PHD **Phone number:** (608) 262-7992 **Email:** drinkwater@oncology.wisc.edu	**Recipient Organization:** UNIVERSITY OF WISCONSIN-MADISON UNIVERSITY OF WISCONSIN MADISON 21 N PARK AVE, STE 6401 MADISON, WI 537151218 **DUNS:** 161202122 **EIN:** 1396006492A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: BRENDA EGAN 21 N Park St, Suite 6401 MADISON, WI 53715 **Phone number:** 6082623822 **Email:** baegan@rsp.wisc.edu	**Signing Official:** BRENDA EGAN 21 N Park St, Suite 6401 MADISON, WI 53715 **Phone number:** 6082623822 **Email:** baegan@rsp.wisc.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 Wisconsin National Primate Research Center (WNPRC) is an integral component of the national and international NHP research enterprise, serving as a critically important resource for basic and translational biomedical research. From its inception through the present funding period, the WNPRC has been responsive to the overall objective of the Nation Primate Research Center (NPRC) program “to provide the animals, facilities, and expertise needed to enable research using NHP.” The fundamental mission of the WNPRC is to increase our understanding of basic primate biology and to improve human health and quality of life through support of outstanding NHP research programs. To accomplish these objectives, the WNPRC focuses on these overarching Specific Aims:

Specific Aim 1: To generate new knowledge of primate biology, from the molecular to the organismal levels.

Specific Aim 2: To help discover treatments, preventions, and cures for human diseases.

Specific Aim 3: To facilitate research worldwide by providing the most advanced expertise, resources, and training to scientists around the globe.

Specific Aim 4: To meet the Specific Aims of all individual units and programs of the WNPRC.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

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

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
3P51OD011106-56S2	Supplement for AIDS-Related Renovation Funding	To perform several alterations and renovations to the second floor WNPRC Building 2 Annex to ensure SIV/SHIV experiments can continue unhindered at the WNPRC.	Work on the hallway ceiling project was completed before the end date of April 2018. Work on the final stage of this project, the installation of the new auxiliary heat exchanger for the cage washer located in the basement of the WNPRC Building 2 Annex is almost complete. The heat exchanger has been installed and the plumbing hook-up for the unit is in the process of being completed. Once the plumbing work is completed, a UW steamfitter will run a steam connection to the unit and it will be functional by March of 2019. Please see attached detailed progress report in the Overall Accomplishments section for more detail.
3P51OD011106-56S1	Antibody-Mediated Depletion of the Viral Reservoir in SIV-Infected Macaques	The aim of this project was to determine if Fc gamma R-mediated functions of the bNAb PGT145 can deplete viral reservoirs and prevent viral rebound after the cessation of antiretroviral therapy. Due to the slow pace of material transfer agreement negotiations with Gilead and ViiV Healthcare to obtain the antiretroviral drugs needed for the original study design, we decided to determine if	The objective of this project is to determine if PGT145, which directs the lysis of SIV-infected cells by ADCC, but does not neutralize SIV infectivity, can protect macaques against a mucosal SIV challenge. Results: Despite high concentrations of PGT145 (214-367 µg/ml) and potent ADCC activity (50% ADCC titers 1:181-1:313) in plasma on the day of challenge, all of the animals

		passive transfer of PGT145 to rhesus macaques prior to SIV challenge could protect against SIV infection–which is consistent with our overall objective to assess non-neutralizing, Fc gamma R-dependent antibody functions for the ability to eliminate virus-infected cells and contain SIV replication.	became infected. Moreover, viral RNA loads in plasma did not differ significantly between PGT145- and DEN3-treated animals during acute or chronic infection. Please see attached detailed progress report in Overall Accomplishments section for more details.
3P51OD011106-57S1	Nanoplatforms for targeted in vivo LRRK2 genomic editing in nonhuman primates	The specific aims for this supplement are to engineer NCs of preassembled Cas9-gRNA to truncate neuronal LRRK2, and to assess the feasibility of using our novel RNP NC delivery system for in vivo CRISPR/ Cas9 truncation of the LRRK2 gene in a common marmoset model.	During this reporting period (September to December 2018) our team focused on optimizing the nanocapsules (NCs), validating the kinase essay and habituating marmosets for behavioral data collection. Dr. Gong's team has produced 17 new batches of NCs. The NCs are being tested in primary neuronal cultures to assess their safety and efficacy. Cell pellets were collected from DAergic differentiated marmoset embryonic and iPSCs wild type and LRRK2 G2019S genomic edited. The pellets were sent to the Cookson lab where they were lysed and evaluated for LRRK2 kinase activity. Please see attached detailed progress report in Overall Accomplishments section for more detail.

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

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

NOTHING TO REPORT

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

We have continued to make excellent progress in the development of our services and resources, and WNPRC investigators in all four of our Working Groups remain engaged in cutting-edge, high-impact scientific studies utilizing non-human primates. In the coming budget year, we will be focused upon implementing plans for the expansion of our animal holding and procedure areas at the Wisconsin Institute for Medical Research. We are currently applying for funding to complete renovation of existing space for additional macaque holding and space for SIV/HIV research projects, and construction of a marmoset precision medicine core facility to support the new embryonic and cell genomic editing techniques for development of cell-based therapeutics, gene therapies, and animal models of human disease. With each of our Core-PIs funded to continue their individual and collaborative studies, we anticipate major progress in all of the high-impact studies described within this report. We anticipate that our Core and Affiliate investigators will continue to make major new advances in understanding and developing new treatments for Parkinson's disease, hematopoietic disorders, infertility, complications of pregnancy, and a variety of infectious diseases, including HIV/SIV and Zika. Equally important, the WNPRC will continue to host high-impact studies by major investigators located around the country, including studies to refine recently reported vaccine approaches for the prevention of HIV/SIV infection.

OVERALL

Accomplishments

Research Highlights

The WNPRC made major progress in the research conducted by members of each of our four working groups. Monthly "Work-in-Progress" meetings held by each group has facilitated scientific progress, fostered many new collaborative efforts, and increased both the number and success rate of new grant applications. A few highlights of progress in the four working groups are noted here. In the **Energy Metabolism and Chronic Disease (EMCD)** working group our investigators have continued to assess effects of adult-onset moderate CR in rhesus macaques to determine how effectively this paradigm is able to increase health-span and maximum lifespan in a primate species while also working to understand the mechanisms behind the known positive effects of CR. EMCD investigators showed that CR engages RNA processing of genes associated with a highly integrated reprogramming of hepatic metabolism. EMCD investigators have also been engaged in studies of food intake and digestion in common marmosets at the WNPRC and the SNPRC, in attempts to determine how variations in digestive abilities are linked to intestinal inflammation, leading to chronic diarrhea, weight loss, vitamin D deficiency, and eventually marmoset wasting syndrome and/or metabolic bone disease. They found poor digesters on all diets at both centers, with high fecal fat in poor digesters consistent with malabsorption syndrome which could lead to vitamin D deficiency. Additional studies have been examining metabolic effects of high fat feeding beginning in adolescence (~6 months of age) and continuing through adulthood (~24 months of age) in common marmosets. They have shown that 4 months of feeding a diet high in a healthy balance of fats to subadult male marmosets led to improved glucoregulatory function compared to normally fed individuals. In other marmoset studies, EMCD investigators assessed the effects of estrogen depletion in adult females, a condition that leads to bone loss in almost all mammals with frequent regular ovarian cycles. They found no differences in bone density following ovariectomy, indicating that this species may possess unique adaptations to avoid bone loss associated with estrogen deficiency. Progress is also reported in pre-clinical Parkinson's disease studies, including development of PET markers of neuroinflammation to assess responses of rhesus macaques to iPSC-derived midbrain dopaminergic cell grafts, and in the demonstration that pioglitazone may protect peripheral catecholamine synthetic enzymes following catecholamine cell toxin exposure.

Major advances have also been made by members of the **Neuroscience** working group, including the Levine and [Redacted by] laboratories, who have used a hypothalamic estrogen receptor alpha (ERα) gene silencing method to demonstrate for the first time in any primate that hypothalamic ERα is a critically important regulator of body weight and energy homeostasis. The [Redacted by agreement] group was successful in establishing consistent methods for the generation of gonadotropin-releasing hormone (GnRH) neurons from human embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC), paving the way for future cell transplantation methods to rescue fertility in certain reproductive developmental disorders. The [Redacted by agreement] group, as well as the Levine and [Redacted] laboratories, published new works further demonstrating the importance of brain estradiol in the regulation of reproductive hormone secretions and fertility. The [Redacted by] laboratory is determining how central deactivation of the thalamus influences cortico-cortical interactions and hence, arousal in male monkeys. They have demonstrated that stimulation of the central lateral thalamus at 50Hz (mimicking the spike rate of CL neurons during wakefulness) overrode effects of isoflurane and propofol anesthesia, leading to arousal of the anesthetized animals. The [Redacted by agreement] group investigates how neurons in the middle temporal cortex (area MT, a visual cortical area important for motion and depth processing), represent multiple visual stimuli moving in different directions and/or at different speeds. They found that neurons in area MT show a robust bias toward the near surface in response to two overlapping moving stimuli located at different depths. The [Redacted by agreement] and [Redacted] groups continue to investigate the etiology and potential avenues for treatment of glaucoma. Towards these ends they have developed custom-made catheters that cannulate Schlemm's Canal (SC) in a non-human model, they are examining whether feline immunodeficiency viral vector transfection efficiency can be improved by application of the proteasome inhibitor M132, using immortalized human trabecular meshwork cells and monkey organ-cultured anterior segments. The [Redacted] has laboratory has demonstrated the importance of iron for brain development during the first year of life, especially for the maturation of white matter tracts in the brain, using cutting-edge neuroimaging methods, MRI and diffusion tensor imaging scans. Investigators in the [Redacted by] Levine, and [Redacted] laboratories have also developed an

efficient non-viral CRISPR/Cas9 delivery system for *in vivo* genome editing. Their strategy requires the delivery of preassembled Cas9-gRNA ribonucleoproteins (RNPs) using nanocapsules (NCs) specifically engineered for delivering an RNP payload across the blood-brain barrier (BBB). As proof-of-principle, they will target the *leucine-rich repeat kinase 2 (LRRK2)* gene in common marmoset monkeys. The *LRRK2* mutation *G2019S* (glycine to serine) is the most common mutation associated with sporadic and familial Parkinson's disease (PD). Preliminary work in common marmoset-derived neural stem cells demonstrated that CRISPR/Cas 9 can be used for editing the *LRRK2* gene in marmosets. Currently, they are working in parallel, optimizing nanoparticles for IV delivery, while performing baseline evaluations in four common marmoset monkeys.

In **Reproductive and Regenerative Medicine (RRM)** working group members studies, several innovative NHP MHC-defined bone marrow transplantation models were established. These models include i) transplantation of autologous genetically modified CD34+ cells and ii) allogeneic transplantation of TCRα/β-depleted bone marrow cells. Allogeneic transplantation of TCRα/β-depleted bone marrow cells has been performed in five animals. Following optimization conditioning and post-transplant immunosuppression, successful HSC engraftment was achieved without a significant GVHD in MHC-matched and blood group identical Mauritian cynomolgus macaques (MCMs). In other studies, effects of allogeneic TCRα/β-depleted bone marrow transplantation on SHIV infected animals on retroviral therapy was evaluated, with the results of these studies demonstrating that the latent reservoir can persist in ART-treated macaques after profound lymphocyte depletion and allogeneic HSCT. During the past year, the WNPRC performed more than 22 successful HSC transplants in rhesus and Mauritian cynomolgus macaques (MCM) in autologous and allogeneic settings. Additionally, transfusion of iPSC-derived blood products was performed in setting of myeloablative bone marrow transplant in MCMs, and a novel protocol for generation of myeloid-derived suppressor cells from nonhuman primate iPSCs was established. In the current grant period, significant progress was made in deriving nonhuman primate transgene-free iPSC lines and optimizing conditions for their maintenance, including: NHP iPSCs from MCMs with the most common MHC homozygous genotypes were generated, protocols for reprogramming T cells into iPSCs and differentiating them back to "rejuvenated" T cells were established, SIV-resistant iPSC lines with homozygous CCR5 knockout were established, and safety of transfusion of iPSC-derived hematopoietic progenitors in NHP model was demonstrated. In addition, a novel method for induction blood cell production from NHP iPSCs using modified mRNA was established and published, as was derivation of marmoset iPSC and their differentiation to neural progenitors and neurons. Transdisciplinary collaborations were also established to develop postnatal assessment paradigms for rhesus offspring from maternal Zika infection; initial results from these new studies indicate potential brain white matter tract alterations in rhesus infants Zika-exposed in utero.

The WNPRC has been a leader in nonhuman primate models for HIV/AIDS for more than 20 years and currently supports a diverse research portfolio that encompasses each of the areas established as major NIH priorities in AIDS research. AIDS research remains the largest single focus area of **Global Infectious Disease** (GID) core researchers and affiliates, but in recent years GID investigators have also developed an internationally recognized program in Zika virus pathogenesis. Some highlights of work conducted by GID investigators in 2018 include a landmark study in which a novel AIDS vaccine candidate elicited effective neutralizing antibodies against the difficult-to-neutralize SIVmac239 strain. This vaccine used a macaque herpesvirus vector to deliver a "near-full-length" simian immunodeficiency virus (SIV) genome. Further studies of this promising candidate will be conducted in the coming year at WNPRC. WNPRC investigators also established a macaque model of HIV-tuberculosis co-infections; this is significant because tuberculosis is the leading cause of death among HIV-infected people in the developing world, but little is understood about how HIV and Mycobacterium tuberculosis might interact. WNPRC AIDS investigators received multiple new awards in 2018 to initiate new studies of HIV cure strategies in the primate model, ensuring that this program will continue to be robust in the coming years. The multidisciplinary consortium we call the Zika Experimental Science Team (ZEST) secured a new P01 grant to study Zika virus pathogenesis in pregnant macaques and their offspring. This new project will integrate comprehensive neurodevelopmental assessments of infants born to Zika-infected mothers into investigations of the mechanisms of Zika virus pathogenesis, further enhancing the translatability of results from macaque models to the human clinic. In studies completed in 2018, the team

showed that Zika virus infection during pregnancy significantly increases the risk of miscarriage and pregnancy loss, suggesting that these are underappreciated adverse outcomes of congenital Zika virus infection.

Administrative Highlights

During the current budget period, the WNPRC has continued to make major gains in efficiency, productivity, and optimization of resource utilization and management. The productivity and quality of administrative support has continued to improve with the renovation of office space and installation of new work stations in Building 2, accommodating the coalescence of staff in human resources. With respect to our infrastructure, we are nearing completion of new neuroscience and physiological recording facilities in Building one that will ultimately accommodate advanced optogenetics, chemogenetics, and optical imaging methodologies for our Neuroscience and EMCD investigators. The WNPRC has continued to construct caging and modified facilities at the Blue Mounds quarantine and holding unit to accommodate increased numbers of cynomolgus and rhesus macaques, as well as additional marmosets derived from the original marmoset colony at the New England Primate Research Center. In response to the demands of our increased research study portfolio, we have expanded our veterinary technical staff, as well as the number of research associates in our Scientific Protocol Implementation unit.

OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT

The University of Wisconsin-Madison requires that all graduate students and postdoctoral researchers supported by NIH funding utilize Individual Development Plans to set academic and career goals and facilitate conversations with their mentors. Additionally, the university recommends that all graduate students and postdoctoral researchers utilize IDPs, regardless of funding source.

The university offers a collection of resources and tools to support mentees, mentors, and PIs in implementing IDPs. These include a UW-Madison IDP template, workshops for mentees (both face-to- face and online videos), peer learning groups for mentees, as well as guidelines for mentors. More information can be found here: http://grad.wisc.edu/pd/idp.

IDP activity for NIH-funded graduate students and postdoctoral researchers is tracked in the university's IDP reporting system, a tool that maintains mentee privacy yet allows mentors and PIs to monitor IDP-related activity.

INVESTIGATORS TRAINED (5/1/2018 – 12/31/2018)

Type of Trainee	Number of Trainees
Post-doctoral	5
Graduate Student	16
Undergraduate Student	28
Veterinary Trainee	10
Other Trainee	132
Total:	**191**

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	Bimber BN, Evans DT. The killer-cell immunoglobulin-like receptors of macaques. Immunological reviews. 2015 September;267(1):246-58. PubMed PMID: 26284482; PubMed Central PMCID: PMC5903432.
Non-Compliant	Kumar A, D'Souza SS, Moskvin OV, Toh H, Wang B, Zhang J, Swanson S, Guo LW, Thomson JA, Slukvin II. Specification and Diversification of Pericytes and Smooth Muscle Cells from Mesenchymoangioblasts. Cell reports. 2017 May 30;19(9):1902-1916. PubMed PMID: 28564607.
Complete	Kraynak M, Flowers MT, Shapiro RA, Kapoor A, Levine JE, Abbott DH. Extraovarian gonadotropin negative feedback revealed by aromatase inhibition in female marmoset monkeys. American journal of physiology. Endocrinology and metabolism. 2017 November 1;313(5):E507-E514. PubMed PMID: 28679622; PubMed Central PMCID: PMC5792143.
Complete	Emborg ME. Nonhuman Primate Models of Neurodegenerative Disorders. ILAR journal. 2017 December 1;58(2):190-201. PubMed PMID: 28985333; PubMed Central PMCID: PMC5886328.
Complete	Kenealy BP, Keen KL, Garcia JP, Kohlenberg LK, Terasawa E. Obligatory role of hypothalamic neuroestradiol during the estrogen-induced LH surge in female ovariectomized rhesus monkeys. Proceedings of the National Academy of Sciences of the United States of America. 2017 December 26;114(52):13804-13809. PubMed PMID: 29229849; PubMed Central PMCID: PMC5748216.
Complete	Aktas Z, Rao H, Slauson SR, Gabelt BT, Larsen IV, Sheridan RTC, Herrnberger L, Tamm ER, Kaufman PL, Brandt CR. Proteasome Inhibition Increases the Efficiency of Lentiviral Vector-Mediated Transduction of Trabecular Meshwork. Investigative ophthalmology & visual science. 2018 January 1;59(1):298-310. PubMed PMID: 29340644; PubMed Central PMCID: PMC5961099.
Complete	Wu HL, Wiseman RW, Hughes CM, Webb GM, Abdulhaqq SA, Bimber BN, Hammond KB, Reed JS, Gao L, Burwitz BJ, Greene JM, Ferrer F, Legasse AW, Axthelm MK, Park BS, Brackenridge S, Maness NJ, McMichael AJ, Picker LJ, O'Connor DH, Hansen SG, Sacha JB. The Role of MHC-E in T Cell Immunity Is Conserved among Humans, Rhesus Macaques, and Cynomolgus Macaques. Journal of immunology (Baltimore, Md. : 1950). 2018 January 1;200(1):49-60. PubMed PMID: 29150562; PubMed Central PMCID: PMC5736429.
Complete	Eudailey JA, Dennis ML, Parker ME, Phillips BL, Huffman TN, Bay CP, Hudgens MG, Wiseman RW, Pollara JJ, Fouda GG, Ferrari G, Pickup DJ, Kozlowski PA, Van Rompay KKA, De Paris K, Permar SR. Maternal HIV-1 Env Vaccination for Systemic and Breast Milk Immunity To Prevent Oral SHIV Acquisition in Infant Macaques. mSphere. 2018 January 10;3(1). PubMed PMID: 29359183; PubMed Central PMCID: PMC5760748.
Complete	Mohr EL, Block LN, Newman CM, Stewart LM, Koenig M, Semler M, Breitbach ME, Teixeira LBC, Zeng X, Weiler AM, Barry GL, Thoong TH, Wiepz GJ, Dudley DM, Simmons HA, Mejia A, Morgan TK, Salamat MS, Kohn S, Antony KM, Aliota MT, Mohns MS, Hayes JM, Schultz-Darken N, Schotzko ML, Peterson E, Capuano S 3rd, Osorio JE, O'Connor SL, Friedrich TC, O'Connor DH, Golos TG. Ocular and uteroplacental pathology in a macaque pregnancy with congenital Zika virus infection. PloS one. 2018 January 30;13(1):e0190617. PubMed PMID: 29381706; PubMed Central PMCID: PMC5790226.
Complete	Bissel SJ, Gurnsey K, Jedema HP, Smith NF, Wang G, Bradberry CW, Wiley CA. Aged Chinese-origin rhesus macaques infected with SIV develop marked viremia in absence

	of clinical disease, inflammation or cognitive impairment. Retrovirology. 2018 February 1;15(1):17. PubMed PMID: 29391069; PubMed Central PMCID: PMC5796498.
Complete	Ellis-Connell AL, Balgeman AJ, Zarbock KR, Barry G, Weiler A, Egan JO, Jeng EK, Friedrich T, Miller JS, Haase AT, Schacker TW, Wong HC, Rakasz E, O'Connor SL. ALT-803 Transiently Reduces Simian Immunodeficiency Virus Replication in the Absence of Antiretroviral Treatment. Journal of virology. 2018 February 1;92(3). PubMed PMID: 29118125; PubMed Central PMCID: PMC5774892.
Complete	Seth N, Simmons HA, Masood F, Graham WA, Rosene DL, Westmoreland SV, Cummings SM, Gwardjan B, Sejdic E, Hoggatt AF, Schalk DR, Abdullah HA, Sledge JB, Nesathurai S. Model of Traumatic Spinal Cord Injury for Evaluating Pharmacologic Treatments in Cynomolgus Macaques (<i>Macaca fasicularis</i>). Comparative medicine. 2018 February 1;68(1):63-73. PubMed PMID: 29460723; PubMed Central PMCID: PMC5824141.
Complete	Großkopf AK, Ensser A, Neipel F, Jungnickl D, Schlagowski S, Desrosiers RC, Hahn AS. A conserved Eph family receptor-binding motif on the gH/gL complex of Kaposi's sarcoma-associated herpesvirus and rhesus monkey rhadinovirus. PLoS pathogens. 2018 February 12;14(2):e1006912. PubMed PMID: 29432452; PubMed Central PMCID: PMC5825162.
Complete	Kalin NH. Corticotropin-Releasing Hormone Binding Protein: Stress, Psychopathology, and Antidepressant Treatment Response. The American journal of psychiatry. 2018 March 1;175(3):204-206. PubMed PMID: 29490496; PubMed Central PMCID: PMC5873578.
Complete	Schouest B, Weiler AM, Janaka SK, Myers TA, Das A, Wilder SC, Furlott J, Baddoo M, Flemington EK, Rakasz EG, Evans DT, Friedrich TC, Maness NJ. Maintenance of AP-2-Dependent Functional Activities of Nef Restricts Pathways of Immune Escape from CD8 T Lymphocyte Responses. Journal of virology. 2018 March 1;92(5). PubMed PMID: 29237831; PubMed Central PMCID: PMC5809740.
Complete	Vermilyea SC, Emborg ME. The role of nonhuman primate models in the development of cell-based therapies for Parkinson's disease. Journal of neural transmission (Vienna, Austria : 1996). 2018 March;125(3):365-384. PubMed PMID: 28326445; PubMed Central PMCID: PMC5847191.
Complete	Yamada Y, Kemnitz JW, Weindruch R, Anderson RM, Schoeller DA, Colman RJ. Caloric Restriction and Healthy Life Span: Frail Phenotype of Nonhuman Primates in the Wisconsin National Primate Research Center Caloric Restriction Study. The journals of gerontology. Series A, Biological sciences and medical sciences. 2018 March 2;73(3):273-278. PubMed PMID: 28398464; PubMed Central PMCID: PMC5861888.
Complete	Rhoads TW, Burhans MS, Chen VB, Hutchins PD, Rush MJP, Clark JP, Stark JL, McIlwain SJ, Eghbalnia HR, Pavelec DM, Ong IM, Denu JM, Markley JL, Coon JJ, Colman RJ, Anderson RM. Caloric Restriction Engages Hepatic RNA Processing Mechanisms in Rhesus Monkeys. Cell metabolism. 2018 March 6;27(3):677-688.e5. PubMed PMID: 29514073; PubMed Central PMCID: PMC5844481.
Complete	Chang TA, Bondarenko GI, Gerami-Naini B, Drenzek JG, Durning M, Garthwaite MA, Schmidt JK, Golos TG. Trophoblast differentiation, invasion and hormone secretion in a three-dimensional in vitro implantation model with rhesus monkey embryos. Reproductive biology and endocrinology : RB&E. 2018 March 16;16(1):24. PubMed PMID: 29548332; PubMed Central PMCID: PMC5857108.
Complete	Haran KP, Hajduczki A, Pampusch MS, Mwakalundwa G, Vargas-Inchaustegui DA, Rakasz EG, Connick E, Berger EA, Skinner PJ. Simian Immunodeficiency Virus (SIV)-Specific Chimeric Antigen Receptor-T Cells Engineered to Target B Cell Follicles and Suppress SIV Replication. Frontiers in immunology. 2018 March 20;9:492. PubMed PMID: 29616024; PubMed Central PMCID: PMC5869724.
Complete	Richard J, Prévost J, Baxter AE, von Bredow B, Ding S, Medjahed H, Delgado GG, Brassard N, Stürzel CM, Kirchhoff F, Hahn BH, Parsons MS, Kaufmann DE, Evans DT, Finzi A. Uninfected Bystander Cells Impact the Measurement of HIV-Specific Antibody-Dependent Cellular Cytotoxicity Responses. mBio. 2018 March 20;9(2). PubMed PMID: 29559570; PubMed Central PMCID: PMC5874913.
Complete	Aliota MT, Dudley DM, Newman CM, Weger-Lucarelli J, Stewart LM, Koenig MR, Breitbach ME, Weiler AM, Semler MR, Barry GL, Zarbock KR, Haj AK, Moriarty RV,

	Mohns MS, Mohr EL, Venturi V, Schultz-Darken N, Peterson E, Newton W, Schotzko ML, Simmons HA, Mejia A, Hayes JM, Capuano S 3rd, Davenport MP, Friedrich TC, Ebel GD, O'Connor SL, O'Connor DH. Molecularly barcoded Zika virus libraries to probe in vivo evolutionary dynamics. PLoS pathogens. 2018 March 28;14(3):e1006964. PubMed PMID: 29590202; PubMed Central PMCID: PMC5891079.
Complete	Jones CA, Duffy MK, Hoffman SA, Schultz-Darken NJ, Braun KM, Ciucci MR, Emborg ME. Vocalization development in common marmosets for neurodegenerative translational modeling. Neurological research. 2018 April;40(4):303-311. PubMed PMID: 29457539; PubMed Central PMCID: PMC6083835.
Complete	Kempton SJ, Israel JS, Capuano S III, Poore SO. Repair of a Large Ventral Hernia in a Rhesus Macaque (<i>Macaca mulatta</i>) by Using an Abdominal Component Separation Technique. Comparative medicine. 2018 April 2;68(2):177-181. PubMed PMID: 29663944; PubMed Central PMCID: PMC5897975.
Complete	Terasawa E, Garcia JP, Seminara SB, Keen KL. Role of Kisspeptin and Neurokinin B in Puberty in Female Non-Human Primates. Frontiers in endocrinology. 2018 April 6;9:148. PubMed PMID: 29681889; PubMed Central PMCID: PMC5897421.
Complete	D'Souza SS, Kumar A, Slukvin II. Functional Heterogeneity of Endothelial Cells Derived from Human Pluripotent Stem Cells. Stem cells and development. 2018 April 15;27(8):524-533. PubMed PMID: 29583085; PubMed Central PMCID: PMC5910050.
Complete	Riesche L, Tardif SD, Ross CN, deMartelly VA, Ziegler T, Rutherford JN. The common marmoset monkey: avenues for exploring the prenatal, placental, and postnatal mechanisms in developmental programming of pediatric obesity. American journal of physiology. Regulatory, integrative and comparative physiology. 2018 May 1;314(5):R684-R692. PubMed PMID: 29412686; PubMed Central PMCID: PMC6008109.
Complete	Schmidt JK, Block LN, Golos TG. Defining the rhesus macaque placental miRNAome: Conservation of expression of placental miRNA clusters between the macaque and human. Placenta. 2018 May;65:55-64. PubMed PMID: 29908642; PubMed Central PMCID: PMC6007866.
Complete	Uenishi GI, Jung HS, Kumar A, Park MA, Hadland BK, McLeod E, Raymond M, Moskvin O, Zimmerman CE, Theisen DJ, Swanson S, J Tamplin O, Zon LI, Thomson JA, Bernstein ID, Slukvin II. NOTCH signaling specifies arterial-type definitive hemogenic endothelium from human pluripotent stem cells. Nature communications. 2018 May 8;9(1):1828. PubMed PMID: 29739946; PubMed Central PMCID: PMC5940870.
Complete	Shin YC, Bischof GF, Lauer WA, Gonzalez-Nieto L, Rakasz EG, Hendricks GM, Watkins DI, Martins MA, Desrosiers RC. A recombinant herpesviral vector containing a near-full-length SIVmac239 genome produces SIV particles and elicits immune responses to all nine SIV gene products. PLoS pathogens. 2018 June 18;14(6):e1007143. PubMed PMID: 29912986; PubMed Central PMCID: PMC6023237.
Complete	Weger-Lucarelli J, Garcia SM, Rückert C, Byas A, O'Connor SL, Aliota MT, Friedrich TC, O'Connor DH, Ebel GD. Using barcoded Zika virus to assess virus population structure in vitro and in Aedes aegypti mosquitoes. Virology. 2018 June 20;521:138-148. PubMed PMID: 29935423; PubMed Central PMCID: PMC6309320.
Complete	Imai H, Dinis JM, Zhong G, Moncla LH, Lopes TJS, McBride R, Thompson AJ, Peng W, Le MTQ, Hanson A, Lauck M, Sakai-Tagawa Y, Yamada S, Eggenberger J, O'Connor DH, Suzuki Y, Hatta M, Paulson JC, Neumann G, Friedrich TC, Kawaoka Y. Diversity of Influenza A(H5N1) Viruses in Infected Humans, Northern Vietnam, 2004-2010. Emerging infectious diseases. 2018 July;24(7):1128-1238. PubMed PMID: 29912683; PubMed Central PMCID: PMC6038741.
Complete	Kang H, Mesquitta WT, Jung HS, Moskvin OV, Thomson JA, Slukvin II. GATA2 Is Dispensable for Specification of Hemogenic Endothelium but Promotes Endothelial-to-Hematopoietic Transition. Stem cell reports. 2018 July 10;11(1):197-211. PubMed PMID: 29861167; PubMed Central PMCID: PMC6066910.
Complete	Slukvin II, Kumar A. The mesenchymoangioblast, mesodermal precursor for mesenchymal and endothelial cells. Cellular and molecular life sciences : CMLS. 2018 July 10. PubMed PMID: 29992471; PubMed Central PMCID: PMC6328351.
Complete	Metzger JM, Moore CF, Boettcher CA, Brunner KG, Fleddermann RA, Matsoff HN,

	Resnikoff HA, Bondarenko V, Kamp TJ, Hacker TA, Barnhart TE, Lao PJ, Christian BT, Nickles RJ, Gallagher CL, Holden JE, Emborg ME. In vivo imaging of inflammation and oxidative stress in a nonhuman primate model of cardiac sympathetic neurodegeneration. NPJ Parkinson's disease. 2018 July 13;4:22. PubMed PMID: 30038956; PubMed Central PMCID: PMC6045637.
Complete	Vermilyea SC, Emborg ME. In Vitro Modeling of Leucine-Rich Repeat Kinase 2 G2019S-Mediated Parkinson's Disease Pathology. Stem cells and development. 2018 July 15;27(14):960-967. PubMed PMID: 29402177; PubMed Central PMCID: PMC6044417.
Complete	Zhao G, Liu F, Oler JA, Meyerand ME, Kalin NH, Birn RM. Bayesian convolutional neural network based MRI brain extraction on nonhuman primates. NeuroImage. 2018 July 15;175:32-44. PubMed PMID: 29604454; PubMed Central PMCID: PMC6095475.
Complete	Dudley DM, Van Rompay KK, Coffey LL, Ardeshir A, Keesler RI, Bliss-Moreau E, Grigsby PL, Steinbach RJ, Hirsch AJ, MacAllister RP, Pecoraro HL, Colgin LM, Hodge T, Streblow DN, Tardif S, Patterson JL, Tamhankar M, Seferovic M, Aagaard KM, Martín CS, Chiu CY, Panganiban AT, Veazey RS, Wang X, Maness NJ, Gilbert MH, Bohm RP, Adams Waldorf KM, Gale M Jr, Rajagopal L, Hotchkiss CE, Mohr EL, Capuano SV 3rd, Simmons HA, Mejia A, Friedrich TC, Golos TG, O'Connor DH. Miscarriage and stillbirth following maternal Zika virus infection in nonhuman primates. Nature medicine. 2018 August;24(8):1104-1107. PubMed PMID: 29967348; PubMed Central PMCID: PMC6082723.
PMC Journal - In process	Garcia JP, Keen KL, Kenealy BP, Seminara SB, Terasawa E. Role of Kisspeptin and Neurokinin B Signaling in Male Rhesus Monkey Puberty. Endocrinology. 2018 August 1;159(8):3048-3060. PubMed PMID: 29982393.
Complete	Suknuntha K, Tao L, Brok-Volchanskaya V, D'Souza SS, Kumar A, Slukvin I. Optimization of Synthetic mRNA for Highly Efficient Translation and its Application in the Generation of Endothelial and Hematopoietic Cells from Human and Primate Pluripotent Stem Cells. Stem cell reviews. 2018 August;14(4):525-534. PubMed PMID: 29520567; PubMed Central PMCID: PMC6014909.
Complete	Martins MA, Tully DC, Pedreño-Lopez N, von Bredow B, Pauthner MG, Shin YC, Yuan M, Lima NS, Bean DJ, Gonzalez-Nieto L, Domingues A, Gutman MJ, Maxwell HS, Magnani DM, Ricciardi MJ, Bailey VK, Altman JD, Burton DR, Ejima K, Allison DB, Evans DT, Rakasz EG, Parks CL, Bonaldo MC, Capuano S 3rd, Lifson JD, Desrosiers RC, Allen TM, Watkins DI. <i>Mamu-B*17</i>⁺ Rhesus Macaques Vaccinated with <i>env</i>, <i>vif</i>, and <i>nef</i> Manifest Early Control of SIVmac239 Replication. Journal of virology. 2018 August 15;92(16). PubMed PMID: 29875239; PubMed Central PMCID: PMC6069176.
Complete	Li H, Hai Y, Lim SY, Toledo N, Crecente-Campo J, Schalk D, Li L, Omange RW, Dacoba TG, Liu LR, Kashem MA, Wan Y, Liang B, Li Q, Rakasz E, Schultz-Darken N, Alonso MJ, Plummer FA, Whitney JB, Luo M. Mucosal antibody responses to vaccines targeting SIV protease cleavage sites or full-length Gag and Env proteins in Mauritian cynomolgus macaques. PloS one. 2018 August 28;13(8):e0202997. PubMed PMID: 30153293; PubMed Central PMCID: PMC6112674.
Complete	Fox AS, Oler JA, Birn RM, Shackman AJ, Alexander AL, Kalin NH. Functional Connectivity within the Primate Extended Amygdala Is Heritable and Associated with Early-Life Anxious Temperament. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2018 August 29;38(35):7611-7621. PubMed PMID: 30061190; PubMed Central PMCID: PMC6113902.
Complete	Colman RJ. Non-human primates as a model for aging. Biochimica et biophysica acta. Molecular basis of disease. 2018 September;1864(9 Pt A):2733-2741. PubMed PMID: 28729086; PubMed Central PMCID: PMC5772001.
Complete	Kapoor A, Schultz-Darken N, Ziegler TE. Radiolabel validation of cortisol in the hair of rhesus monkeys. Psychoneuroendocrinology. 2018 November;97:190-195. PubMed PMID: 30053699; PubMed Central PMCID: PMC6138524.
Complete	Park MA, Jung HS, Slukvin I. Genetic Engineering of Human Pluripotent Stem Cells Using PiggyBac Transposon System. Current protocols in stem cell biology. 2018 November;47(1):e63. PubMed PMID: 30281932; PubMed Central PMCID: PMC6212322.

Complete	Sutton MS, Ellis-Connell A, Moriarty RV, Balgeman AJ, Gellerup D, Barry G, Weiler AM, Friedrich TC, O'Connor SL. Acute-Phase CD4⁺ T Cell Responses Targeting Invariant Viral Regions Are Associated with Control of Live Attenuated Simian Immunodeficiency Virus. Journal of virology. 2018 November 1;92(21). PubMed PMID: 30111562; PubMed Central PMCID: PMC6189504.
Complete	Janaka SK, Tavakoli-Tameh A, Neidermyer WJ Jr, Serra-Moreno R, Hoxie JA, Desrosiers RC, Johnson RP, Lifson JD, Wolinsky SM, Evans DT. Polymorphisms in Rhesus Macaque Tetherin Are Associated with Differences in Acute Viremia in Simian Immunodeficiency Virus Δ<i>nef</i>-Infected Animals. Journal of virology. 2018 November 15;92(22). PubMed PMID: 30135127; PubMed Central PMCID: PMC6206476.
Complete	Heffron AS, Mohr EL, Baker D, Haj AK, Buechler CR, Bailey A, Dudley DM, Newman CM, Mohns MS, Koenig M, Breitbach ME, Rasheed M, Stewart LM, Eickhoff J, Pinapati RS, Beckman E, Li H, Patel J, Tan JC, O'Connor DH. Antibody responses to Zika virus proteins in pregnant and non-pregnant macaques. PLoS neglected tropical diseases. 2018 November 27;12(11):e0006903. PubMed PMID: 30481182; PubMed Central PMCID: PMC6286021.
In Process at NIHMS	Slukvin II, Uenishi GI. Arterial identity of hemogenic endothelium: a key to unlock definitive hematopoietic commitment in hPSC cultures. Experimental hematology. 2018 November 28. PubMed PMID: 30500414.
Complete	Rodgers MA, Ameel C, Ellis-Connell AL, Balgeman AJ, Maiello P, Barry GL, Friedrich TC, Klein E, O'Connor SL, Scanga CA. Preexisting Simian Immunodeficiency Virus Infection Increases Susceptibility to Tuberculosis in Mauritian Cynomolgus Macaques. Infection and immunity. 2018 December;86(12). PubMed PMID: 30224552; PubMed Central PMCID: PMC6246917.
Complete	Ziegler TE, Kapoor A, Binkley NC, Rice KS, Rogers J, Jolly CJ, Phillips-Conroy JE. Comparison of vitamin D metabolites in wild and captive baboons. American journal of primatology. 2018 December;80(12):e22935. PubMed PMID: 30537386; PubMed Central PMCID: PMC6390488.
Complete	Buechler C, Semler M, Baker DA, Newman C, Cornish JP, Chavez D, Guerra B, Lanford R, Brasky K, Kuhn JH, Johnson RF, O'Connor DH, Bailey AL. Subclinical Infection of Macaques and Baboons with A Baboon Simarterivirus. Viruses. 2018 December 10;10(12). PubMed PMID: 30544677; PubMed Central PMCID: PMC6316555.
Complete	Haj AK, Arbanas JM, Yamniuk AP, Karl JA, Bussan HE, Drinkwater KY, Graham ME, Ericsen AJ, Prall TM, Moore K, Cheng L, Gao M, Graziano RF, Loffredo JT, Wiseman RW, O'Connor DH. Characterization of Mauritian Cynomolgus Macaque FcγR Alleles Using Long-Read Sequencing. Journal of immunology (Baltimore, Md. : 1950). 2019 January 1;202(1):151-159. PubMed PMID: 30530595; PubMed Central PMCID: PMC6314804.
In Process at NIHMS	Weisgrau KL, Vosler LJ, Pomplun NL, Hayes JM, Simmons HA, Friedrichs KR, Rakasz EG. Neutrophil progenitor populations of rhesus macaques. Journal of leukocyte biology. 2019 January;105(1):113-121. PubMed PMID: 30395351.
In Process at NIHMS	Metzger JM, Emborg ME. Autonomic dysfunction in Parkinson disease and animal models. Clinical autonomic research : official journal of the Clinical Autonomic Research Society. 2019 January 2. PubMed PMID: 30604165.
Complete	Pauthner MG, Nkolola JP, Havenar-Daughton C, Murrell B, Reiss SM, Bastidas R, Prévost J, Nedellec R, von Bredow B, Abbink P, Cottrell CA, Kulp DW, Tokatlian T, Nogal B, Bianchi M, Li H, Lee JH, Butera ST, Evans DT, Hangartner L, Finzi A, Wilson IA, Wyatt RT, Irvine DJ, Schief WR, Ward AB, Sanders RW, Crotty S, Shaw GM, Barouch DH, Burton DR. Vaccine-Induced Protection from Homologous Tier 2 SHIV Challenge in Nonhuman Primates Depends on Serum-Neutralizing Antibody Titers. Immunity. 2019 January 15;50(1):241-252.e6. PubMed PMID: 30552025; PubMed Central PMCID: PMC6335502.
Complete	Kumar A, Lee JH, Suknuntha K, D'Souza SS, Thakur AS, Slukvin II. NOTCH Activation at the Hematovascular Mesoderm Stage Facilitates Efficient Generation of T Cells with High Proliferation Potential from Human Pluripotent Stem Cells. Journal of immunology (Baltimore, Md. : 1950). 2019 February 1;202(3):770-776. PubMed PMID: 30578305; PubMed Central PMCID: PMC6344284.

Complete	Macdonald JA, Corrado PA, Nguyen SM, Johnson KM, Francois CJ, Magness RR, Shah DM, Golos TG, Wieben O. Uteroplacental and Fetal 4D Flow MRI in the Pregnant Rhesus Macaque. Journal of magnetic resonance imaging : JMRI. 2019 February;49(2):534-545. PubMed PMID: 30102431; PubMed Central PMCID: PMC6330144.
Complete	Kovner R, Fox AS, French DA, Roseboom PH, Oler JA, Fudge JL, Kalin NH. Somatostatin Gene and Protein Expression in the Non-human Primate Central Extended Amygdala. Neuroscience. 2019 February 21;400:157-168. PubMed PMID: 30610938; PubMed Central PMCID: PMC6361692.
PMC Journal - In process	Martins MA, Gonzalez-Nieto L, Shin YC, Domingues A, Gutman MJ, Maxwell HS, Magnani DM, Ricciardi MJ, Pedreño-Lopez N, Bailey VK, Altman JD, Parks CL, Allison DB, Ejima K, Rakasz EG, Capuano S 3rd, Desrosiers RC, Lifson JD, Watkins DI. The Frequency of Vaccine-Induced T-Cell Responses Does Not Predict the Rate of Acquisition after Repeated Intrarectal SIVmac239 Challenges in <i>Mamu-B*08⁺</i> Rhesus Macaques. Journal of virology. 2019 March 1;93(5). PubMed PMID: 30541854.

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

Nothing to report

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

Nothing to report

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Component(s)	Country	SS
eRA Commons User Name	Y	Drinkwater, Norman R.	BS,PHD	PD/PI	EFFORT						NA
	N	Redacted by agreement		Undergraduate Student					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Undergraduate Student					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Undergraduate Student					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Undergraduate Student					Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			Undergraduate Student					Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			Undergraduate Student					Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			Undergraduate Student					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N		BS	Non-Student Research Assistant					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N		BS,DVM	Undergraduate Student					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N		DVM,BA	Graduate					Other-5900		NA

		Redacted by agreement		Student (research assistant)					(WNPRC Veterinary Services …esources-007))		
eRA Commons User Name	N			Undergraduate Student	EFFORT				Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			Undergraduate Student					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N		BS	Undergraduate Student					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Undergraduate Student					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Undergraduate Student					Other-5897 (WNPRC Compliance and Train…esources-004))		NA
	N			Graduate Student (research assistant)					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Associate Research Specialist					Other-5895 (WNPRC Behavioral Services …esources-002))		NA
	N			Associate Research Specialist					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Data Entry Assistant					Other-5896 (WNPRC Colony Management Un…esources-		

									003))		
	N	Redacted by agreement		Senior Media Specialist	EFFORT				Admin Core-5892 (WNPRC Information Technolo…tems Services)		NA
	N			Veterinary Technician 2					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Unit Head, Compliance and Training					Other-5897 (WNPRC Compliance and Train…esources-004))		NA
	N			Senior Research Specialist					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Lab Technician Support Supervisor					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist					Other-5898 (WNPRC Pathology Services (…esources-005))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist					Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Human Resources Assistant Advanced					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			IS Network Support					Admin Core-5892 (WNPRC		NA

				Technician					Information Technolo…tem s Services)		
	N	Redacted by agreement		Animal Research Technician	EFFORT				Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Assistant Scientist					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Executive Assistant					Admin Core-5884 (WNPRC Director's Office)		NA
	N			Grants Manager					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Grants Assistant					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N		DVM	Associate Research Animal Veterinarian					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Laboratory Mgr I					Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			University Services Program Associate					Other-5897 (WNPRC Compliance and Train…esourc es-004))		NA
	N			Animal Research Technician Advanced					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Senior Research					Other-5899 (WNPRC		

				Specialist					Scientific Protocol …esources-006))		
	N	Redacted by agreement	DVM	Assistant Research Animal Veterinarian	EFFORT				Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Clinical Veterinarian					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Veterinary Technician 2					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N		DVM	Clinical Veterinarian					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Grants and Purchasing Administrative Assistant					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Grants Coordinator					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Unit Head, Colony Management					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician Advanced					Other-5896 (WNPRC Colony Management Un…esources-003))		NA

	N	Redacted by agreement		Associate Research Specialist	EFFORT		Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Senior Research Specialist			Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist			Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Associate Research Specialist			Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N		DVM	Research Animal Veterinarian			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Associate Information Process Consultant - EHR Developer			Other-5909 (WNPRC Informatics and Data…ic-Units-003))		NA
	N			Research Specialist			Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			Associate Scientist			Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N			Animal Research Technician Advanced			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony		NA

									Management Un…esources-003))		
	N	Redacted by agreement		Animal Research Technician	EFFORT				Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N		DVM	Research Animal Veterinarian					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Training Coordinator					Other-5897 (WNPRC Compliance and Train…esources-004))		NA
	N			Animal Research Technician Senior					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Research Program Manager I					Other-5898 (WNPRC Pathology Services (…esources-005))		NA
	N			Animal Research Technician Objective					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			University Services Program Associate					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist					Other-5898 (WNPRC Pathology		NA

									Services (…esources-005))		
	N	Redacted by agreement		Animal Research Technician Senior	EFFORT				Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Veterinary Technician 1					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Mechanician - Journey					Admin Core-5889 (WNPRC Facilities and Improvement)		NA
	N			Assistant Director, Administrative Services					Admin Core-5890 (WNPRC Operational Services Division)		NA
	N			Animal Research Technician Objective					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			University Services Program Associate					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA

	N	Redacted by agreement		Animal Research Technician	EFFORT		Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Veterinary Technician I			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Assistant Researcher			Other-5905 (WNPRC Non-Human Primate Pr…-Res-Pro-001))		NA
	N			Assistant Scientist			Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Veterinary Technician 3			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician Objective			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N		DVM	Associate Research Animal Veterinarian			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Purchasing Associate			Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Lab Technician Support Supervisor			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Senior Editor			Admin Core-5884 (WNPRC Director's		NA

									Office)		
	N	Redacted by agreement		LAB SA CO & REC TEC O	EFFORT				Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Unit Head, IT Services					Admin Core-5892 (WNPRC Information Technolo…tems Services)		NA
	N			Associate Research Specialst					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Research Program Manager I					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Assistant Scientist					Other-5905 (WNPRC Non-Human Primate Pr…-Res-Pro-001))		NA
	N			Veterinary Technician 2					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Human Resources Assistant					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Research Assistant					Other-5905 (WNPRC Non-		NA

		Redacted by agreement							Human Primate Pr…-Res-Pro-001))		
	N			Animal Research Technician	EFFORT				Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Veterinary Technician 3					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Associate Research Specialist					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Human Resources Assistant Advanced					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Assoc Admin Prgm Spec					Other-5897 (WNPRC Compliance and Train…esources-004))		NA
	N			Veterinary Technician I					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Unit Head, Facilities Management and Shop Services					Admin Core-5889 (WNPRC Facilities and Improvement)		NA

	N	Redacted by agreement		Animal Research Technician	EFFORT		Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist			Other-5906 (WNPRC Stem Cell Resources …-Res-Pro-002))		NA
	N			Associate Research Specialist			Other-5895 (WNPRC Behavioral Services …esources-002))		NA
	N			Senior Research Specialist			Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Research Specialist			Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N			Associate Research Specialist			Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Research Services Administrative Assistant			Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Research Specialist			Other-5905 (WNPRC Non-Human Primate Pr…-		NA

									Res-Pro-001))		
	N	Redacted by agreement		Animal Research Technician Objective	EFFORT				Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Pathology Associate Research Specialist					Other-5898 (WNPRC Pathology Services (…esources-005))		NA
	N			Veterinary Technician 3					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Veterinary Technician 3					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Research Specialist					Other-5895 (WNPRC Behavioral Services …esources-002))		NA
	N			Research Program Specialist					Other-5912 (WNPRC Virology Services Un…ic-Units-006))		NA
	N			Veterinary Technician 2					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Associate Research Specialist					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N			Mechanician - Journey					Admin Core-5889 (WNPRC Facilities and Improvement)		NA
	N			Senior Research Specialist					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA

	N	Redacted by agreement		EHR Developer	EFFORT		Other-5909 (WNPRC Informatics and Data…ic-Units-003))		NA
	N			Veterinary Technician 1			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Senior Research Specialist			Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Veterinary Technician 2			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Veterinary Technician I			Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Senior Research Specialist			Other-5895 (WNPRC Behavioral Services …esources-002))		NA
	N			Research Program Manager I			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Research			Other-5896		NA

		Redacted by agreement		Program Manager I	EFFORT		(WNPRC Colony Management Un…esources-003))		
	N			Animal Research Technician Senior			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			University Services Program Associate			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician Senior			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Animal Research Technician			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Assistant Trainer			Other-5897 (WNPRC Compliance and Train…esources-004))		NA
	N			Animal Research Technician Senior			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			SR INFORM PROC CONSLT			Admin Core-5892 (WNPRC Information Technolo…tems Services)		NA
	N			Lab Technician Support Supervisor			Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Associate Research Specialist			Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N			University Services Program			Other-5896 (WNPRC Colony		NA

				Associate					Management Un…esources-003))		
	N	Redacted by agreement		Senior Research Specialist	EFFORT				Other-5912 (WNPRC Virology Services Un…ic-Units-006))		NA
	N			Senior Research Specialist					Other-5911 (WNPRC Immunology Services …ic-Units-005))		NA
	N			Grants Assistant					Admin Core-5891 (WNPRC Administrative Services Unit)		NA
	N			Senior Scientist					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N			Animal Research Technician Objective					Other-5896 (WNPRC Colony Management Un…esources-003))		NA
	N			Veterinary Technician I					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
eRA Commons User Name	N		BS	Undergraduate Student					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N		PHD,BS	Assistant Scientist					Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N		DVM,MS, OTH	Pathologist					Other-5898 (WNPRC Pathology Services (…esources-005))		NA
	N			Graduate Student (Research Assistant)					Other-5900 (WNPRC Veterinary Services …esources-007))		NA

eRA Commons User Name	N	Redacted by agreement		Undergraduate Student	EFFORT			Admin Core-5891 (WNPRC Administrative Services Unit)	NA
	N		PHD	Core-PI				Other-5895 (WNPRC Behavioral Services …esources-002))	NA
	N		BS,PHD	Unit Head, Genetic Services				Other-5910 (WNPRC Genetics Services Un…ic-Units-004))	NA
	N			Research Associate				Other-5905 (WNPRC Non-Human Primate Pr…-Res-Pro-001))	NA
	N		BS,PHD	Associate Director of Research Services				Other-5911 (WNPRC Immunology Services …ic-Units-005))	NA
	N		MD,PHD	Core-PI				Other-5898 (WNPRC Pathology Services (…esources-005))	NA
	N		PHD	Unit Head, Immunology Services				Other-5911 (WNPRC Immunology Services …ic-Units-005))	NA
	N		PHD	Core-PI				Other-5908 (WNPRC Assay Services Unit …ic-Units-002))	NA
	N		PHD	Unit Head, EHR Services				Other-5909 (WNPRC Informatics and Data…ic-Units-003))	NA
	N		PHD,MS, BS	Core-PI				Other-5905 (WNPRC Non-Human Primate Pr…-Res-Pro-001))	NA
	N			Associate Research Specialist				Other-5911 (WNPRC Immunology Services …ic-Units-005))	NA
	N			Unit Head,				Other-5898	NA

eRA Commons User Name		Redacted by agreement		Pathology Services					(WNPRC Pathology Services (…esources-005))		
	N		PHD,MD	Unit Head, Precision Medicine Core - Therapies	EFFORT				Other-5905 (WNPRC Non-Human Primate Pr…-Res-Pro-001))		NA
	N		PHD,BS	Assistant Scientist					Other-5905 (WNPRC Non-Human Primate Pr…-Res-Pro-001))		NA
	N		BA,PHD	Director					Admin Core-5884 (WNPRC Director's Office)		NA
	N		DVM	Co-Unit Head, SPI					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N		OTH	Associate Research Specialist					Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA
	N		PHD	Co-Unit Head, SPI					Other-5899 (WNPRC Scientific Protocol …esources-006))		NA
	N		PHD,BS	Unit Head, Behavior Management & Enrichment					Other-5895 (WNPRC Behavioral Services …esources-002))		NA
	N		DVM	Associate Director,Animal Srvcs; Unit Head, Veterinary Srvcs					Other-5900 (WNPRC Veterinary Services …esources-007))		NA
	N		BS,PHD	Core-PI					Other-5910 (WNPRC Genetics Services Un…ic-Units-004))		NA
	N		PHD	Unit Head, Virology Services					Other-5912 (WNPRC Virology Services Un…ic-Units-		NA

									006))		
eRA Commons User Name	N	Redacted by agreement	PHD	Unit Head, Assay Services	EFFORT				Other-5908 (WNPRC Assay Services Unit …ic-Units-002))		NA

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

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

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

No

D.2.b New Senior/Key Personnel

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

No

D.2.c Changes in Other Support

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

Yes

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D.2.d New Other Significant Contributors

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

No

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

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

NA

OTHER SUPPORT

Redacted by agreement

ACTIVE

(THIS AWARD)
5P51 OD011106-57 (Drinkwater) 07/21/17 – 04/30/22
NIH/OD $7,198,609
Director's Office
These funds support the Director's Office of the Wisconsin Primate Research Center.
Role: Director, WNPRC

EFFORT

3P50 HD044405-15S1 (Dunaif) 07/01/13 – 06/30/19
NIH/NICHD $177,431
Genes, Androgens and Intrauterine Environment in PCOS
Project IV: Effects of Androgens on Female Reproduction
This grant supports a Specialized Center of Research entitled "Genes, Androgens, and Intrauterine Environment in PCOS." The projects are designed to investigate the genetic and developmental basis of the pathogenesis of polycystic ovarian syndrome. Project III includes experiments that test the hypothesis that excess intrauterine androgen exposure leads to the programming of pancreatic and brain tissue to exhibit symptoms of PCOS in adulthood. The hypothesis specifically holds that the pathogenesis of PCOS arises from a disruption of the expression and functional activity of ATP-sensitive potassium channels in neurons and pancreatic beta cells.
Role: Center Co-Director and Principal Investigator of Project III

EFFORT

P50 HD028934-24 (Marshall) *(formerly U54)* 04/01/14 – 03/31/19
NIH/NICHD $208,541
Clinical and Basic Studies in Polycystic Ovarian Syndrome (RFA-HD-14-017)
Project II: Hypothalamic Steroid Receptors and the Pathogenesis of PCOS
Studies related to this project will make use of viral vector-mediated gene silencing and a validated nonhuman primate model of androgen induced reproductive PCOS phenotypes to address these major gaps in our understanding of the mechanisms that mediate the pathogenesis of PCOS.
Role: P.I., Project II

EFFORT

(NEW)
P50 HD028934-24 (Marshall) *(formerly U54)* 12/01/17 – 03/30/19
NIH/NICHD $50,000
Clinical and Basic Studies in Polycystic Ovarian Syndrome (RFA-HD-14-017)
Pilot Project: *In vivo* Imaging of Brain Aromatase in Pubertal Rhesus Monkeys
To quantitate aromatase expression in the juvenile monkey brain, and begin testing the hypothesis that pubertal onset is associated with a reduction of neuroestradiol synthesis resulting from diminished hypothalamic aromatase expression.
Role: P.I.

EFFORT

5R21HD084992-02 (Levine) 04/01/16 – 03/31/19
NIH $275,000 total direct
Neuroestrogen restraint of GnRH in juvenile female primates
The proposed studies are designed to test the novel hypothesis that neuroestrogens mediate the prepubertal restraint of GnRH release during the juvenile period of development in female primates.
Role: P.I.

(NEW)
1UG3NS111688-01, Gong (PI) 09/30/18 – 07/31/21 EFFORT
NIH $500,000
Enabling Nanoplatforms for Targeted In Vivo Delivery of CRISPR/Cas9 Ribonucleoproteins in the Brain
The primary goal of this project is to develop efficient, non-viral delivery vehicles for safe and efficient *in vivo* CRISPR genome editing. The unique nanocapsules we plan to develop will ultimately enable high efficiency neuron-targeted genome editing in the brain, thereby offering new hope to treat devastating neurodegenerative diseases.
Role: Co-PI

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

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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: The Board of Regents of the University of Wisconsin System	161202122	WI-002	Suite 6401 21 N Park St Madison WI 537151218

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)
7389687	Income from fees for services & research projects performed

G.12 F&A COSTS

Not Applicable

Wisconsin NPRC
Information Requested in P51 RPPR Instructions

1.A. Nonhuman primates (NHPs) housed at NPRC supported partially, or in whole, by the P51 grant[1].

Census Date: 2/15/2019

Genus/Species	Breeding Colony[2]				Animals Not in Breeding Colony[3]				Total Colony Census
	M	F	U[4]	Total	M	F	U[4]	Total	
Macaque mulatta (Indian)	162	332	1	495	96	73		169	664
Macaque fascicularus	16	46		62	15	12		27	89
Callithrix jacchus	21	22	2	45	79	104		183	228
Total	**199**	**400**	**3**	**602**	**190**	**189**		**379**	**981**

[1]This entry does not include animals supported by a U24 or U42 SPF grant.

[2]Total number of animals in breeding colony including adult breeding animals and designated juvenile replacements at time of report.

[3]Animals on protocol or otherwise not in the breeding colony at the time of report.

[4]Sex undetermined.

1.B. Nonhuman primates housed at NPRC - supported by U24 or U42 or other sources[1].

Census Date: 2/15/2019

Genus/Species	Breeding Colony[2]				Animals Not in Breeding Colony[3]				Total Colony Census
	M	F	U[4]	Total	M	F	U[4]	Total	
Macaque mulatta (Indian)					231	182		413	413
Macaque fascicularus					51	72		123	123
Callithrix jacchus					5	9		14	14
Total					**287**	**263**		**550**	**550**

[1]This entry does not include animals supported by a U24 or U42 SPF grant.

[2]Total number of animals in breeding colony including adult breeding animals and designated juvenile replacements at time of report.

[3]Animals on protocol or otherwise not in the breeding colony at the time of report.

[4]Sex undetermined.

1.C. Total Nonhuman primates housed at NPRC, irrespective of source of support.

Genus/Species	Total Number of Animals
Callithrix jacchus	242
Macaque fascicularus	212
Macaque mulatta (Indian)	1,077
Total	**1,531**

2. Tissue Distribution Program Information. It is not necessary to report samples broken down by

species.

Dates covered by the report: 1/1/2018 – 12/31/2018

Sample Type	Number of Samples Distributed
Tissue	6,259
Genetic	12
Cells	61
Other	49,100
Total	**55,432**

3. Types of project. Include all projects performed in whole, or in part, during the reporting period.

Project Type	Number of Projects
Research	177
Management	12
Pilot	27
Total	**216**

4. Percentage of AIDS-related P51 grant dollars.

AIDS - related P51 %: 49

Description: The UW-Madison fiscal year runs July 1 to June 30. Therefore, we collected FY 2018 data for grant/award projects with active budget periods between 7/01/2017 - 6/30/2018. Projects involving SIV/HIV research were specifically labeled in the data collected. The WNPRC generated $9,284,608 total direct costs in FY18, of which $4,571,504 (or 49%) was AIDS-related.

5. Information regarding the number of investigators by type.

Type of Investigator	Number
Core	64
Affiliate	133
Visiting	4
Other	57
Total	**258**

6. The number of peer reviewed publications directly attributed to P51 activity. Explain how this number was derived; e.g., publications that directly cite the P51 grant, or other types of citation or information.

Source	Number
Articles	56
Book Chapters	2
Reviews	3
Total	**61**

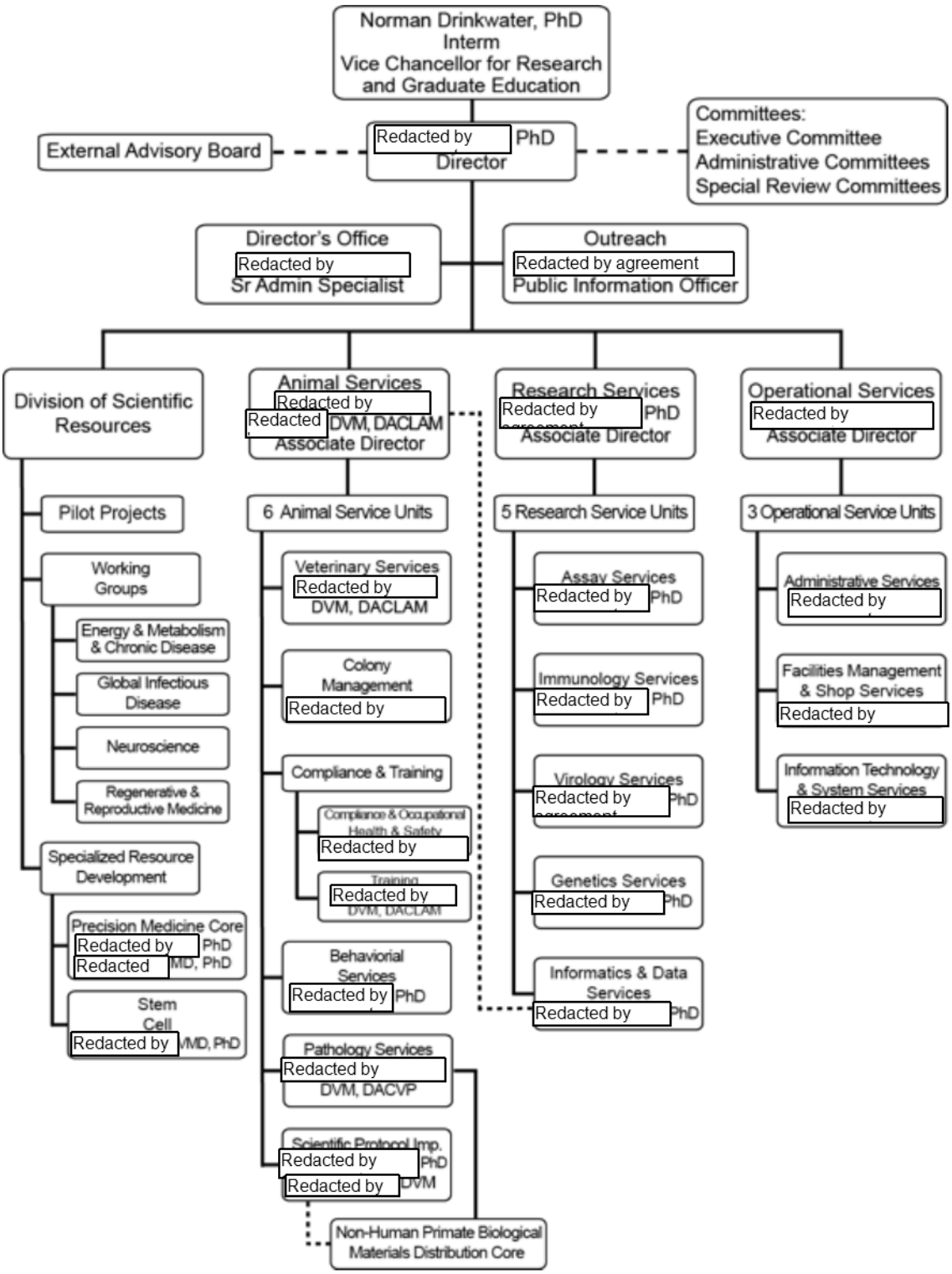
7. The number of individuals trained during the reporting period by type.

Type of Trainee	Number of Trainees
Post-doctoral	5
Graduate student	16
Undergraduate student	28
Veterinary trainee	10
Other trainee	132
Total	**191**

Description: N/A

8. Organizational chart that show the relationship of the NPRC to the Institution and the major organizational divisions within the NPRC.

See Next Page



9. Individual projects performed during the reporting period.

See Next Page

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: ANTIBODY EFFECTOR FUNCTION IN PROTECTION AGAINST HIV-1

SPID#: 1201

UNIT/DIVISION: Immunology/Research Services

TYPE: Research

START DATE: 1/1/2018

END DATE: 12/31/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R37AI055332

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	The Scripps Research Institutute/Department of Immunology and Microbial Sciences
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

We wish to test that antibody effector function is critical to protection against HIV challenge. We can dissect the crucial functions important in vivo and we can use this knowledge to improve in vitro assays to predict the types of antibody responses that will provide optimal benefit against HIV exposure. We use the recombinant Simian Human Immunodeficiency Virus (SHIV) infected-Rhesus macaque model to understand the role of two different functions (ADCC and phagocytosis) of the protective antibodies against HIV infection in humans.

PROGRESS REPORT:

In 2018 we determined the efficacy of broadly neutralizing PGT121 LALAP antibody lacking Fc-domain-mediated effector functions against mucosal challenge with 300TCID50 SHIV162P3.

We treated a group of three Rhesus macaques with 0.2 mg/kg wild type PGT121, a group of 15 animals with 0.2 mg/kg LALAP mutant PGT121 lacking effector functions and a group of five animals with 0.2mg/kg DEN3 specific irrelevant antibody. We compared the viremia in the three groups of animals and found that the absence of Fc-domain mediated effector functions did not impair the protective effect of PGT121 antibody.

PUBLICATIONS:

PMID	Title

None

FUNDING SOURCES:

Redacted by agreement Ph.D., funded by NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: THE FUNCTIONAL SIGNIFICANCE OF CTL ESCAPE

SPID#: 1203

UNIT/DIVISION: Immunology/Research Services

TYPE: Research

START DATE: 1/1/2018

END DATE: 12/31/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R37AI052056

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Miami Miller Medical School/Department of Pathology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

Our hypothesis is that a vaccine eliciting both virus neutralizing antibodies and effective CTL in Mamu B*08 or –B*17 positive macaques will increase the number of elite controllers. In a previous study, we were able to show that Mamu B*08 positive macaques vaccinated with certain proteins found in the SIV virus known as Nef and Vif increased the number of elite controller animals as compared to the control animals. In this study, we investigated whether adding a viral protein called Env to this vaccine strategy would further increase the number of elite controller animals.

PROGRESS REPORT:

Immunology Services (IS) of the Wisconsin National Primate Research Center (WNPRC) has shipped samples to Redacted by agreement of the University of Miami Miller School of Medicine.

PUBLICATIONS:

PMID	Title
30541854	Vaccine-induced T-cell responses do not predict the rate of acquisition after repeated intrarectal SIVmac239 challenges in <i>Mamu-B*08+</i> rhesus macaques.
6023237	A new clinical and experimental concept on fat embolism.

FUNDING SOURCES:

NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: MECHANISMS UNDERLYING PERSISTENT LENTIVIRUS REPLICATION

SPID#: 1207

UNIT/DIVISION: Immunology/Research Services

TYPE: Research

START DATE: 1/1/2018

END DATE: 11/30/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R01AI096966

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Arizona/Department of Medicine
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
		University of Minnesota/Veterinary & Biomedical Sciences
Other Core and Affil.		

PROJECT DESCRIPTION:

HIV-1 is highly concentrated in follicular CD4+ T cells, which are 30 to 40 times more likely to be productively infected than extrafollicular CD4+ T cells. T follicular helper cells (TFH) are a specialized subset of antigen-specific cells that migrate into B cell follicles. Whether the follicular cells that are preferentially infected by HIV-1 are TFH is unknown. The specific aims of this proposal are:
to determine susceptibility of human and rhesus macaque lymphoid tissue follicular CD4+ T cells to productive HIV/SIV infection in vitro; to determine the frequency, distribution, and phenotype of T cells that propagate lentiviruses in lymphoid tissues during acute and chronic infection in vivo; and to determine whether follicular lentivirus-specific CTL are deficient in number and/or function compared to extrafollicular CTL in vitro and in vivo.

PROGRESS REPORT:

In 2018 we have determined the cell-associated viral burden in several T cell populations in collaboration with the Virology Unit of the Primate Center. We have used lymph node samples from seven SIVmac239-infected animals. We sorted out T helper and T regulatory cells from the follicular and the extrafollicolar region of the lymph nodes.

PUBLICATIONS:

PMID	Title

Haran, P., Hajduczki, A., Pampusch, M.S., Mwakalundwa, G., Bolivar-Wagers, S., Vargas-Inchaustegui, D.A.,

Rakasz, E.G., Fife, B.T., Connick, E., Berger, E.A., Skinner, P.J. SIV-specific CAR-T cells engineered to target B cell follicles and suppress SIV replication. Frontiers in Immunol. 2018. 9:492.

FUNDING SOURCES:

NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: WOMB TO WOMB: PROGRAMMING REPRODUCTIVE DEVELOPMENT IN THE FEMALE

SPID#: 1302

UNIT/DIVISION: Assay/Research Services

TYPE: Research

START DATE: 6/1/2013

END DATE: 5/30/2018

GENERAL CATEGORY: Reproductive

SUB-CATEGORY: Development

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R01HD076018

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Illinois
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

This is a subcontract of this funded grant to study 1) the birth status and energetic status during pregnancy in the common marmoset and how it predicts pregnancy success; 2) to examine the daughters of these pregnancies on how their mother's physical parameters during pregnancy will influence their pregnancy; and 3) we will determine if females who experienced intrauterine restriction will exhibit impaired adult metabolic and reproductive function.

PROGRESS REPORT:

This is the final year and a Pending Support Under the subcontract, the reproductive and metabolic hormones have been measured in the F0 females and the F1 daughters.

PUBLICATIONS:

PMID	Title
29412686	The common marmoset monkey: avenues for exploring the prenatal, placental, and postnatal mechanisms in developmental programming of pediatric obesity.

FUNDING SOURCES:

NICHD

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: CAN VACCINE-INDUCED CD8 T CELLS PREVENT CHRONIC PHASE AIDS VIRUS REPLICATION?

SPID#: 1401

UNIT/DIVISION: Immunology Services/Research Services

TYPE: Research

START DATE: 1/1/2018

END DATE: 12/31/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R01AI108421

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Miami Miller Medical School/Department of Pathology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

Vaccines developed between 2000 and 2010 and tested in the macaque-SIV (Simian Immunodeficiency Virus) model reduced virus replication, but did not achieve reduction of virus replication below detection level. New results using several new vaccine vectors suggest that suppressing SIV proliferation below detection level may be possible. The mentioned vaccinations used a large portion of the SIV virus proteins to elicit immune responses. The construction of a vaccine, containing multiple, large virus proteins is extremely expensive. Therefore in this project we wish to test whether suppression of SIV proliferation below detection level is possible with a novel vaccine regimen that contains only a small fraction of the AIDS virus.

PROGRESS REPORT:

Immunology Services (IS) of the Wisconsin National Primate Research Center (WNPRC) performed plasmablast analysis, and has shipped processed blood samples to Redacted by agreement of the University of Miami Miller School of Medicine.

PUBLICATIONS:

PMID	Title
6023237	A new clinical and experimental concept on fat embolism.

FUNDING SOURCES:
NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: A NOVEL HIV-1 VACCINE TARGETING THE 12 PROTEASE CLEAVAGE

SPID#: 1404

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 6/13/2014

END DATE: 5/31/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R01AI111805

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Manitoba/Department of Medical Microbiology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin Nation Primate Research Center
Other Core and Affil.		University of Manitoba/Department of Medical Microbiology
		CIMUS Research Institute
		University of Santiago de Compostela, Spain/Center for Virology and Vaccine Research
		Beth Israel Deaconess Medical Center/Harvard Medical School

PROJECT DESCRIPTION:

The great genetic diversity and rapid mutation of human immunodeficiency virus (HIV-1), popularly known as AIDS, and the dual roles of lymphocytes (white blood cells) in the disease as both the immune defense cells as well as the target cells in HIV-1 infection have posed enormous challenges for developing an effective preventative HIV vaccine. Because a key difference between HIV-1 and other infectious viruses is that the target cells are also the hosts initial defense cells, the strategy for a vaccine for HIV-1 should not be the same as the ones dealing with other viruses that target non-immune cells. By learning from natural immunity observed in HIV resistant Kenyan sex workers, we hypothesized that an effective HIV vaccine should target specific key sites within the HIV virus instead of targeting only the traditional full HIV proteins presented to the lymphocytes. We have identified these key places as the protease cleavage sites (PCS) where HIV generates infectious viral particles from its full virus. The PCS are important because the enzyme that cuts proteins for the HIV virus, the protease, is responsible for producing HIV particles that can infect people. The protease has to bind 12 specific places in the HIV virus and conduct 12 separate cutting reactions to generate an infectious virus. If it can't bind to these places, the virus generated cannot infect the specific lymphocytes called CD4 T cells. A vaccine that targets the 12 PCS could generate immune responses to force the virus to change itself, which would change these special cutting sites to result in a virus that may not be infectious to people.

PROGRESS REPORT:

All work with the animals is finished. We are still shipping samples to collaborators, finalizing data, and working on various manuscripts.

PUBLICATIONS:

PMID	Title

Li H, Hai Y, Lim SY, Toledo N, Crecente-Campo J, Schalk D, Li L, Omange RW, Dacoba TG, Liu LR, Kashem MA, Wan Y, Liang B, Li Q, Rakasz E, Schultz-Darken N, Alonso MJ, Plummer FA, Whitney JB, Luo M. Mucosal antibody responses to vaccines targeting SIV protease cleavage sites or full-length Gag and Env proteins in Mauritian cynomolgus macaques. PLoS One. 2018 Aug 28;13(8):e0202997. doi: 10.1371/journal.pone.0202997. PMCID: PMC6112674

FUNDING SOURCES:

DHHS, PHS, NIH, NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: GAMMA-2 HERPES VIRUSES AS VACCINE VECTORS FOR AIDS

SPID#: 1407

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 3/15/2005

END DATE: 11/30/2022

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R37AI063928

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Miami Miller School of Medicine/Department of Microbiology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		University of Miami Miller School of Medicine
		University of Miami Miller School of Medicine

PROJECT DESCRIPTION:

Persistent, recombinant herpes viruses are being used in monkeys to try to match the degree of protection that can be achieved with live attenuated strains of SIV. The proposed experiments with replication-competent rhesus macaque rhadinovirus (RRV) vectors will overcome this deficiency and allow full testing of the promise of this approach. The proposed experiments will allow a greater appreciation of the potential for recombinant herpesviruses in particular, and persistent vectors in general, for their capacity to provide protection against AIDS virus exposure. If shown to be significantly better than other vaccine approaches, it will shape the emphasis for ongoing preclinical vaccine discovery research.

An effective vaccine against HIV/AIDS remains the greatest public health challenge of our time. Unfortunately, there are good reasons for believing that development of an effective vaccine against HIV/AIDS is going to be extremely difficult to achieve. These predicted difficulties have more-or-less been borne out by vaccine trials in monkeys and in people. The problem is HIV itself. Once HIV gets its foot in the door, it has an uncanny ability to replicate continuously, without relent, in spite of apparently strong immune responses by the host. Many feel that immunologic memory such as that induced by traditional vaccines that are quickly cleared by the immune system will not be enough to provide sustained protection against HIV. New long-lasting or permanent vaccines are sorely needed.

Eight distinct human herpesviruses have been defined. These are further grouped into three subclasses, alpha, beta and gamma. Most adults in the United States are infected with four or more herpesviruses. These infections are life-long and immune responses to these herpesviruses persist for the life of the infected host. We are exploring using a gamma-2 herpesvirus as a novel, experimental approach to an AIDS vaccine. For example, a live herpesvirus (capable of replicating itself and infecting cells) of a strain of the varicella-zoster virus has been put into millions of people as the vaccine to prevent chicken pox in children and its recurrence as shingles in

adults. Our vision is to create a type of live herpesvirus that will induce immunity to HIV that can be given to children 10-12 years of age to provide life-long vaccine protection against HIV/AIDS.

Once the results of the initial vaccine trial are obtained, additional trials may be planned to build upon and improve upon the initial results. If vaccine protection is hugely successful, we will need to perform additional experiments to determine what component of the vaccine contributes most importantly to protection. We will also need to investigate in this event the ability to protect against SIV that is not exactly matched in sequence. If vaccine protection is not very successful in the initial trial, experiments expressing more of the SIV genes and different routes of vaccine administration will need to be tested. We also feel that we can achieve higher levels of anti-SIV antibody responses with improvements to RRV vector design. In addition to RRV vector design, we will also try boosts to the RRV vector vaccine regimen. This will allow for better immunogenicity to create a more efficacious result when the animals are eventually challenged with SIV or SHIV. Also, because RRV shedding is commonly detected in saliva, oral delivery of these RRV vectors might be tried to better approximate natural transmission and possibly increase their immunogenicity to generate higher antibody titers. This will ultimately allow us to determine if oral rRRV/SIV vaccination results in better immunogenicity than IV vaccination. If the results are favorable, we will use this as preliminary data for a grant submission to establish this as a possible route of vaccination for AIDS.

PROGRESS REPORT:

Macaques vaccinated with rRRV/SIV vectors in previous experiments developed lower than expected levels of SIV-specific T-cell responses. Subsequent boosting with rRRV via the i.v. and oral route did not enhance immune responses considerably. While the cause of this low immunogenicity is not clear, we tried three different approaches to enhance the T-cell responses in the past year.

First, we postulated that circumventing existing vector immunity against rRRV by a DNA-based approach can yield substantially improved immune responses. Therefore, the rRRV-vaccinated monkeys were boosted with a recombinant (r) DNA plasmid encoding a replication-incompetent, near-full-length SIVmac239 (SIVnfl) genome. The backbone of this rDNA plasmid (pCMVkan) was provided by Redacted by agreement at the University of Pennsylvania (Rosati et al., J Virol 2005). The rDNA/SIVnfl constructs were delivered by intramuscular (IM) electroporation (EP). Results from this experiment will be published in early 2019.

Secondly, a common factor in previous experiments has been the initial delivery of the rRRV/SIV constructs via the intravenous (IV) route. Since RRV is highly prevalent among captive bred rhesus macaques and natural transmission is thought to occur through exposure to bodily secretions, including saliva, we orally vaccinated two macaques with a mixture of five rRRV/SIV vectors. We used the same constructs and dose that were delivered intravenously in the ongoing Experiment 1 to subsequently monitor cellular and humoral SIV-specific immune responses in these animals, allowing direct comparison of the immunogenicity of oral versus IV rRRV/SIV vaccination. Data collection is in progress.

Finally, a major challenge in HIV vaccine development is our lack of knowledge on eliciting protective immune responses against this virus. It is not clear, for instance, the extent to which regulatory pathways (termed “immune checkpoints”) can dampen desirable immune responses elicited by vaccination. Given the clinical success of immune checkpoint inhibitors in enhancing tumor immunity, blocking immunomodulatory pathways may facilitate the induction of effective immune responses against HIV. Redacted by agreement (with additional K01 funding) began experiments using ipilimumab, a cancer drug that blocks the CTLA-4 regulatory pathway. CTLA-4 is a co-inhibitory receptor that is upregulated on T-cells shortly after T-cell activation. CTLA-4 suppresses immune responses primarily by interfering with CD28 signaling–a key step for optimal T-cell activation. It is well established that preventing CTLA-4 activity can augment T-cell responses. In the current study we test the hypothesis that blocking CTLA-4 during vaccination will result in a more effective vaccine. We have three groups of eight rhesus macaques. Two groups of rhesus macaques are vaccinated against SIVmac239, one group will receive mock vaccination. We will prime immune responses with electroporated DNA (EP DNA) and enhance the immunogenicity of electroporated DNA with the co-administration of an IL-12 expressing plasmid. (IL-12 is a naturally occurring T cell-stimulating factor, produced by macrophages and dendritic cells, and it possesses a well-known immune response augmenting activity). We follow the electroporation regimen with a boost using a persistent herpesviral vector (the rhesus monkey rhadinovirus (RRV)). Group 1 and 3 will be treated with Ipilimumab (anti-CTLA-4 monoclonal antibody) at the time of the EP DNA vaccination (EP DNA+Ipilimumab/RRV) whereas Group 2 will be primed with EP DNA in the absence of Ipilimumab (EP DNA/RRV). We are in the vaccination process at the time of this report. We plan to challenge all goups with repeated low dose intrarectal inoculations of SIVmac239. We will evaluate vaccine efficacy based on the rate of SIV acquisition and post-infection viral loads. We will collect blood, lymph node, and colon/rectal biopsy samples before and after vaccination, and before and after viral challenges to monitor virus proliferation, and antigen-specific immune responses. We will monitor these animals for up to 2 years after infection, depending on the control of viral proliferation they will exhibit. After concluding the study, the animals will be either euthanized, or reassigned to another AIDS-related project.

PUBLICATIONS:

PMID	Title
29912986	A recombinant herpesviral vector containing a near-full-length SIVmac239 genome produces SIV particles and elicits immune responses to all nine SIV gene products.
29432452	A conserved Eph family receptor-binding motif on the gH/gL complex of Kaposi's sarcoma-associated herpesvirus and rhesus monkey rhadinovirus.
29875239	<i>Mamu-B*17</i>⁺ Rhesus Macaques Vaccinated with <i>env</i>, <i>vif</i>, and <i>nef</i> Manifest Early Control of SIVmac239 Replication.

FUNDING SOURCES:

Redacted by Redacted by funded by NIAID; Redacted by funded by Office of Director (K01OD023032, subaward to Redacted by

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: IMMUNOGLOBULINS DELIVERED BY AAV VECTOR FOR THE PREVENTION OF SIV INFECTION

SPID#: 1408

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 7/18/2012

END DATE: 11/30/2021

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: R01AI098446

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Miami Miller School of Medicine/Department of Microbiology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
		University of Wisconsin-Madison/Wisconsin National Primate Research Cetner
Other Core and Affil.		University of Miami/Miller School of Medicine

PROJECT DESCRIPTION:

In the classical approach to immunization against viral diseases, viral proteins are delivered or expressed in the vaccine recipient and it is hoped that the resultant immune responses are protective. For a variety of reasons, such a classic approach faces severe obstacles to success against HIV-1. The Redacted by laboratory has been investigating a nonclassical approach by which a viral vector, adeno-associated virus (AAV), is used to achieve very long-term delivery of anti-HIV monoclonal antibodies (mAbs) with potent neutralizing activity against a broad spectrum of HIV-1 isolates. AAV vectors have proven safe in human testing and are currently the vector of choice for correction of hereditary enzyme/metabolism deficiencies. When delivered intramuscularly, transgene expression can continue for years, decades, probably for life, as long as the transgene product is not viewed as foreign. The vision is that a single inoculation of AAV vector making a cocktail of potent broadly-neutralizing antibodies will provide sterilizing immunity for the rest of the individual's life. Although an antibody may be viewed as a “self” protein, studies in monkeys have revealed that a host antibody response may occur to the delivered mAb and this may severely limit the concentration of mAb that can be achieved. The Redacted by agreement laboratory will continue its progress toward minimizing the anti-anti problem and achieving consistent delivery of desirable antibodies using rhesus monkey models. These studies are directly targeted to facilitating development of this concept for use in humans. AAV vector has recently been used to deliver single chain Fv immunoadhesin (scFVI) versions of rhesus monkey antibodies with neutralizing activity against SIV. Two different approaches are compared for AAV vector delivery of the authentic IgG version of these scFVIs. We will determine whether

delivery of authentic IgG decreases the frequency with which anti-anti responses are observed. We will determine whether AAV vector can be used to deliver dimeric secretory IgA and whether secretory IgA provides a more effective barrier to SIV infection by the mucosal route. Finally, we will determine whether antibody-dependent cellular cytotoxicity is important for the protective effects of the IgG versions of 4L6 and 5L7. Results from these experiments in rhesus monkeys will inform and guide development of analogous vectors for the prevention of HIV-1 infection in humans.

PROGRESS REPORT:

We followed up on ways to consistently deliver high levels of human anti-HIV broadly neutralizing antibodies to SHIV infected monkeys as an approach to therapy. The experiment included the modifications and improvements that have provided the best results to date: a) Inclusion of micro RNA de-targeting sequences to prevent the antibody expression in antigen presenting cells; b) Use of recombinant AAV8, with a recombinant AAV1 boost if necessary; c) Removal of the WPRE (woodchuck hepatitis virus posttranscriptional regulatory element, generally used to enhance expression) to avoid potential immune responses; d) Use of the LS mutation in the Fc portion of the antibodies to increase their half-life; e) Use of a two-antibody combination (3BNC117 and 10-1074) that has completely suppressed SHIV replication in one monkey (r2438) to below the limit of detection for more than a year. We then added a boost phase to this plan with booster inoculation of AAV1 expressing the 3BNC117-IgG1-LS and 10-1074-IgG1-LS antibodies with a CMV promoter and micro RNA binding sites via the IM route, with a dose for each antibody of 0.1 x 10^13 vector genome copies per kg of body weight (GC/kg).

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

DHHS, PHS, NIH, NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: TOWARDS KSHV VLP-BASED VACCINE DEVELOPMENT

SPID#: 1509

UNIT/DIVISION: SPI/Animal Services

TYPE: Pilot

START DATE: 1/1/2015

END DATE: 4/30/2019

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: P51OD011106

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	Beckman Research Institute of City of Hope
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

Kaposi's sarcoma-associated herpesvirus (KSHV) is an emerging pathogen particularly in African and Mediterranean countries where KSHV is endemic and prevalence is rapidly increasing in the general population. KSHV is the causative agent of three human malignancies, Kaposi's sarcoma (KS), primary effusion lymphoma, and multicentric Castleman's disease. KS is the most common cancer among persons with AIDS and is often incurable with current treatment options. Prophylactic vaccines to KSHV are lacking. Although several KSHV-host interactions in cell culture systems have been identified, it is not clear which virus envelope glycoproteins are essential for virus entry in vivo, a rational target for vaccine development. The overall goal of this is to define the role of KSHV glycoprotein (gp)K8.1 in mediating virus entry in vivo, a prerequisite step in designing vaccines that stimulate humoral immunity and evoke potent T-cell responses, thereby preventing infection. We hypothesize that immunization of marmosets, a recently developed NHP model susceptible to KSHV infection and disease with KSHV gpK8.1 incorporated into virus-like particles (VLPs), will be the ideal candidate for preventing KSHV infection.

PROGRESS REPORT:

In this year we inoculated 2 marmosets with KSHV I.V. and repeated inoculation 4 months later. We are monitoring the animals for evidence of virus.

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

DHHS, PHS, NIH, Office of Director P51OD011106 and NCI for K01CA184388

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: A RADIOMETABOLISM STUDY OF HAIR HORMONES IN RHESUS MACAQUES

SPID#: 1512

UNIT/DIVISION: Assay Services/Research Services

TYPE: Pilot

START DATE: 1/1/2015

END DATE: 4/30/2019

GENERAL CATEGORY: Assay

SUB-CATEGORY: Radiolabel

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: P51OD011106

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Wisconsin-Madison/Wisconsin National Primate Research Center
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

The aims of the study were to determine when, how much and in what form radiolabeled steroids were incorporated into hair.

PROGRESS REPORT:

We have completed all radiolabeled experiments with two for cortisol, 2 for testosterone and 1 for progesterone. The cortisol paper has been written and published and the testosterone and progesterone manuscripts are in progress. There was also an expected finding with the cortisol as it was also incorporated into the hair as an unknown metabolite. Further work to identify this metabolite are underway with the UW-Madison Biotechnology Center and the Small Molecule Screening Center.

PUBLICATIONS:

PMID	Title

Radiolabel validation of cortisol in the hair of rhesus monkeys. Kapoor A, Schultz-Darken N, Ziegler TE. Psychoneuroendocrinology, 2018 Nov; 97:190-195.

FUNDING SOURCES:

DHHS, PHS, NIH, WNPRC Pilot Program P51OD011106

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: PREVENTING HIV-1 TRANSMISSION WITH ECD4-IG

SPID#: 1602

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 6/1/2016

END DATE: 5/31/2019

GENERAL CATEGORY: Immunology

SUB-CATEGORY: AIDS

NIH GRANT: ☐ Yes ☒ No

GRANT NUMBER: OPP1132169

SUPPORTING ORGANIZATION: Private Source

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	Scripps Research Institute, Florida
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		Scripps Research Institute, Florida

PROJECT DESCRIPTION:

Current HIV-1 therapy options include large cocktails of drugs with significant side effects and poor patient compliance. Our experimental approach will determine whether current anti-HIV-1 therapies can be supplemented or replaced with a cocktail of antibody or antibody-like entry inhibitors delivered by recombinant adeno-associated virus (AAV) vectors. Our experimental approach will determine whether current anti-HIV-1 therapies can be supplemented or replaced with a cocktail of antibody or antibody-like entry inhibitors delivered by recombinant adeno-associated virus (AAV) vectors. An AAV-based therapy can be administered with a one-time injection and produce high titers of therapeutics that can last for several years. This approach significantly decreases cost and toxicities associated with current therapies, increases patient compliance and could serve as salvage therapy following drug breakthrough. AAV vectors include no viral genes and have repeatedly been demonstrated as safe in humans and rhesus macaques, therefore providing a promising avenue for long-term therapeutics.

PROGRESS REPORT:

Four SHIV-infected animals treated with AAV have either no or very low (<15) viral loads for almost 1.5 years after lifting ART treatment. We have plans to treat an additional 4 animals with AAV in 2019. We are waiting on another group that is currently under triple ART therapy. In addition we now have one animal expressing >100Ug/ml of eCD4-Ig. First one since the original Nature paper in 2016.

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

Private Source

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: IPILIMUMAB AS AN ADJUVANT FOR HIV VACCINES

SPID#: 1603

UNIT/DIVISION: Immunology/Research Services

TYPE: Research

START DATE: 1/1/2018

END DATE: 12/31/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: K01OD023032

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Miami/Miller Medical School/Department of Pathology
Prin. NPRC Core Sci.		University of Wisconsin- Madison/Wisconsin National Primate Research Center
Other Core and Affil.		

PROJECT DESCRIPTION:

CTLA-4 has been shown to regulate the breadth of T-cell responses. Indeed, a new study has shown that Ipilimumab therapy broadens tumor-specific CD8+ T-cell responses in melanoma patients. Since this enhanced T-cell priming activity could be especially useful for eliciting T-cell immunity against HIV, we will determine the breadth of vaccine-induced, SIV-specific T-cell responses in EP DNA/RRV-SIVnfl vaccinated rhesus macaques treated with Ipilimumab monoclonal antibody and compare it to vaccinated and non-vaccinated animals that will not receive monoclonal antibody treatment.

PROGRESS REPORT:

Immunology Services Unit (IS) of the Wisconsin National Primate Research Center (WNPRC) organized the blood and tissue sampling of 16 animals. IS also processed blood samples, and shipped them to Redacted by agreement Redacted by at Leidos, Frederick, MD for viral load quantification.

PUBLICATIONS:

PMID	Title

None.

FUNDING SOURCES:

NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: VIRAL ESCAPE FROM AAV EXPRESSED TRANSGENES

SPID#: 1604

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 4/1/2016

END DATE: 3/31/2018

GENERAL CATEGORY: Infectious Disease

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: P01AI100263

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	Scripps Research Institute, Florida
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		Scripps Research Institute, Florida

PROJECT DESCRIPTION:

Recombinant adeno-associated virus (AAV) vectors can safely deliver long-term (>2 years), high-titers (>200 µg/ml) of antibody-like inhibitors to rhesus macaques. These titers are well above the IC90s of several broadly neutralizing HIV-1 antibodies. AAV vectors have an established safety record in humans, and risks associated with their use are modest, arguably lower than those associated with current antiviral regimens. Our immediate goal is to stably suppress an ongoing SHIV-infection in rhesus macaques, using specific combinations of antiviral proteins delivered by AAV vectors. To do so, we will address directly the key challenges of safety, efficacy, viral escape, and immune clearance of expressed transgenes. We first focus on the common goal of establishing of a system in which viral loads in SHIV-infected animals can be reproducibly suppressed. These studies will establish principles and protocols directly applicable to subsequent human clinical trials.

PROGRESS REPORT:

We compared AAV-expressed broadly neutralizing antibodies (bNAbs) and eCD4-Ig bearing rhesus IgG1 and IgG2 Fc domains. Macaques expressing IgG2 bNAbs had significantly higher peak titers than those with IgG1. All bNAbs elicited strong anti-drug antibody (ADA) responses, but greater protection was observed with IgG2-isotyped bNAbs. Similarly, rh-eCD4-IgG2 expressed more efficiently, and elicited fewer ADA, than did rh-eCD4-IgG1. Moreover, only rh-eCD4-IgG2 afforded robust protection from multiple SIVmac239 challenges, demonstrating its exceptional breadth in vivo. Our data also show that the rhesus IgG1 Fc domain more consistently elicits ADA than IgG2, and suggest that the greater effector functions of IgG1 are not necessary when neutralizing activity is efficient.

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

NIAID

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: BELIEVE: BENCH TO BED ENHANCED LYMPHOCYTE INFUSIONS TO ENGINEER VIRAL ERADICATION

SPID#: 1605

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 8/1/2018

END DATE: 6/30/2019

GENERAL CATEGORY: Immunology

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: UM1AI126617

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	Harvard University/ Beth Israel Deaconess Medical Center, Center for Virology and Vaccine Research
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		Weill Cornell Medical College Devision of Infectious Diseases

PROJECT DESCRIPTION:

Human immunodeficiency virus (HIV) infection is still one of the world's most significant infectious diseases, with around 37 million people living with HIV at the end of 2014 with 2.6 million being children (UNAIDS 2015 World AIDS Day report). Clearly, the need for a cure for HIV/AIDS remains compelling. Currently, most cure efforts focus on targeting the latent (dormant) reservoir of virus, believed to be the major obstacle for eradicating HIV. The underlying principle of the cure strategy involves reactivation of ""sleeping"" infected cells so the immune system can eliminate them.

Although HIV-1 can be effectively suppressed with antiretroviral therapy, it is not eradicated from the body. The majority of HIV-1 infected persons who cease therapy have resurgent viremia due to the presence of long-lived HIV-1 reservoirs. The mechanism(s) by which these reservoirs are seeded, maintained, and are subject to sustained virologic remission or rebound upon antiretrovial therapy cessation is not understood. A detailed understanding of HIV reservoir genesis, and the factors that dictate viral control or rebound, in the absence of antiretroviral therapy, is critical to develop approaches to therapeutically foster HIV-1 remission in patients on long-term antiretroviral therapy.

The goals of the experiments outlined in this protocol are as follows:

1) To characterize the lymphoid reservoirs of virus in Simian Immunodeficiency Virus (SIV or SHIV) infected adult and infant rhesus macaques (Macaca mulatta) that have been treated with antiretroviral therapy (ART) to evaluate the hypotheses that specific lymphoid tissue in the animal harbors significant amounts of virus.

2) To compare the ability of two very specific immune cells (cells honed to kill SIV or SHIV) to clear these reservoirs in laboratory grown, SIV or SHIV-infected cells.

3) To develop and evaluate a novel strategy to reduce virus in SIV or SHIV infected macaques by targeting the two specific immune cells to the animal's lymphoid tissue by introducing a molecule that improves the ability of the immune cells to enter the lymphoid cells.
4) To test the ability of the optimal immune cell identified in Goal 3 combined with an agent designed to wake up sleeping SIV or SHIV-infected cells to reduce reservoirs of these cells in ART-treated rhesus macaques.

PROGRESS REPORT:

We currently have 3 groups of 20 monkeys infected with SHIV, ART therapy that we are testing for aims 3 and 4 listed above.

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

NHP Core - Delaney Cure Grant funded by NIAID,NIDA, and NINDS

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: VACCINE TO INDUCE AB PRODUCTION IN CERVICOVAGINAL MUCOSA

SPID#: 1705

UNIT/DIVISION: SPI/Animal Services

TYPE: Pilot

START DATE: 9/1/2017

END DATE: 4/30/2018

GENERAL CATEGORY: Immunology

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: P51OD011106

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Minnesota/Department of Microbiology and Immunology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Resae
Other Core and Affil.		Massachusetts Institute of Technology/Departments of Biological Engineering, and Materials Science and Engineering

PROJECT DESCRIPTION:

Each year more than 2 million people are newly infected with HIV, mostly through sexual contact, and women comprise 60% of these new infections. Thus, an effective HIV vaccine, particularly for preventing HIV-1 sexual transmission to women, is urgently needed. To that end, studies using the simian immunodeficiency virus (SIV) intravaginal infection in rhesus monkeys (SIV-RM model) provide an excellent model of HIV sexual transmission to women and are undertaken to discover effective vaccination strategies to achieve prevention. In particular, studies of live attenuated SIVmac239Dnef (SIVDnef) vaccination in the SIV-RM model have revealed that a SIVDnef-induced local system of immunoglobulin G antibody (IgG Ab) production and concentration in the cervicovaginal mucosa can effectively target two viral vulnerabilities in early infection, resulting in robust protection from high-dose vaginal challenge of pathogenic SIV. First, local production of IgG Ab sustains high levels of virus-specific Ab that would have the most favorable odds by preventing or containing a small founder population of infected cells at the portal of entry soon after vaginal exposure to virus. Antibody is further concentrated by an IgG receptor in the cervicovaginal epithelium to form immune complexes with the SIV virus that then binds to an inhibitory IgG receptor in the epithelium. This effectively blocks early epithelium activation and subsequent recruitment of target cells (CD4 T cells) in the mucosa. This second opportunity for containment slows down local expansion and systemic dissemination of the founder population of infected cells. These study results provide us with a novel vaccine design principle to emulate – to develop non-replicating immunogens/adjuvants and immunization strategies that can reproduce this local system of IgG Ab production and concentration in the cervicovaginal mucosa, but circumvent the well-known safety issues associated with persistent replication of live attenuated SIV virus. We plan to test the central hypothesis that combining persistent systemic antigen exposure (using the SIV envelope peptide gp41t) with persistent mucosal antigen exposure will establish a local system of IgG Ab production and concentration in the cervicovaginal mucosa.

PROGRESS REPORT:

Several pilots were done on terminal animals to refine the vaginal antigen application. The silk microneedles did not adhere well to vaginal epithelium and various injection plans were tried until a bent needle for direct injection into the vaginal tissue appears to be working. We plan to begin live animal experiments in 2019.

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

DHHS, PHS, NIH, NIAID P51OD011106

Wisconsin National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: BELIEVE: BENCH TO BED ENHANCED LYMPHOCYTE INFUSIONS TO ENGINEER VIRAL ERADICATION

SPID#: 1801

UNIT/DIVISION: SPI/Animal Services

TYPE: Research

START DATE: 8/1/2018

END DATE: 6/30/2019

GENERAL CATEGORY: Immunology

SUB-CATEGORY: AIDS

NIH GRANT: ☒ Yes ☐ No

GRANT NUMBER: UM1AI126617

SUPPORTING ORGANIZATION: NIH

SPECIFIC INFORMATION:

INVESTIGATORS:

	Name	Dept
Principal Investigator	Redacted by agreement	University of Minnesota/Department of Veterinary and Biomedical Sciences Microbiology, Immunology and Cancer Biology
Prin. NPRC Core Sci.		University of Wisconsin-Madison/Wisconsin National Primate Research Center
Other Core and Affil.		Weill Cornell Medical College Division of Infectious Diseases

PROJECT DESCRIPTION:

Virus-specific CD8 T cells exert potent antiviral activity against HIV-1 and SIV both in vitro and in vivo. Despite abundant CD8 T cell responses in HIV-1-infected humans and SIV-infected macaques, they are unable to fully suppress virus replication. This is likely due to the majority of HIV-1 and SIV replication occurring in CD4+ T cells concentrated within B-cell follicles in secondary lymphoid tissues; where virus-specific CD8 T cells are relatively few in number. In fact, we found that in vivo effector virus-specific CD8 T cell to target SIV RNA+ cell ratios (E:T) were over 40-fold lower inside compared to outside of B cell follicles in lymphoid tissues during SIV infection in rhesus macaques. These findings indicate that B cell follicles are an immune privileged site in which low levels of virus-specific CD8 T cells permit ongoing viral replication. Furthermore, we found that the majority of virus-specific CD8 T cells fail to express the follicular homing molecule CXCR5, likely explaining low levels of virus-specific CD8 T cells localizing to and surveilling B cell follicles. Taken together these data suggest that the inability of HIV- and SIV-specific CD8 T cells to fully suppress virus replication may be due to a deficiency of virus-specific CD8 T cells in B-cell follicles. These findings have led us to our central hypothesis that targeting HIV-specific T cells to B cell follicles will lead to durable remission of HIV infection. In support of this hypothesis we have shown, in SIV-infected rhesus macaques, that increased levels of virus-specific CD8 T cells in B cell follicles is associated with lower viral loads. To test this hypothesis, we propose to evaluate a T cell immunotherapy product that targets virus-specific CD8 T cells to B cell follicles. We are calling this product CD4-MBL-CAR/CXCR5 T cell immunotherapy. Our long-term goal is to develop an intervention that will lead to durable remission of HIV infection.

PROGRESS REPORT:

Initiated a pilot experiment with 9 SIVmac251-infected monkeys; 6 treated CD4-MBL-CAR/CXCR5 T cell immunotherapy vs 3 controls. Finishing up animals experiments in early 2019. Early evidence points to immunotherapy delaying rebound after release of ART regimen.

PUBLICATIONS:

PMID	Title

FUNDING SOURCES:

IRF3 Redacted by agreement Cure Grant funded by NIAID,NIDA, and NINDS

10. Outreach. Provide a brief statement describing outreach activities including how the research community is informed about the capabilities of the NPRC, as well as other items related to outreach (e.g., community relations).

Description: The WNPRC publicizes its capabilities on a global level by reaching out to potential collaborators and affiliates through its website, scientific meetings, awards programs, and through a strong public outreach program that includes facebook and twitter pages.

The WNPRC has a strong local community and statewide outreach program to educate the public about the importance of biomedical research at the WNPRC, our human animal care program, and the critical link between animal research and improvements in human health. Near weekly outreach visits, presentations, science fairs with hands-on activities, and other events reach teachers, students and families from preschool age through lifelong learners/senior citizens.

Comments: Comments: Please see RPPR Component ID Other-5903, entitled "WNPRC Outreach," for detailed Outreach
reporting information from 12/1/2018 through 12/31/2018.

11. Comments. Provide information showing (in dollars) how the Resource was supported during the reporting period, broken down by: 1) Direct Costs of the ORIP grant, 2) Program Income, 3) Other Sources of support, including cost sharing by the grantee Institution and contribution of F&A costs from the ORIP grant or other grants. If program income is reported, the amount in this table must be the same as the amount reported in Section G.11, “Program Income” of the RPPR. Do not include support (e.g., individual R01 grants) for the PIs or other investigators that does not contribute directly to the NPRC. Describe any limitations of this information.

Direct Costs of the ORIP Grant	Program Income	Other Sources of Support	Total Support for the Resource
$7,198,609	$7,389,687	$1,602,794	$16,191,090

Description: Animal Services Division:
Veterinary Services* $424,961.24
Pathology Services** $474,648.16
Colony Management*** $4,375,840.49
Scientific Protocol Implementation $700,220.23
Division Total Income $5,975,670.12
*Includes charges from Veterinary and Surgical Units
**Includes charges from Pathology and Clinical Pathology Units
***Includes charges related to animal per diems, blood draws and replacement costs

Research Services Division:
Assay Services $414,115.85
Immunology Services $330,460.94
Virology Services $233,595.14
Genetics Services $396,453.94
Division Total Income $1,374,625.87

Operational Services Division
Facilities Management & Shop Services $39,391.28
Division Total Income $39,391.28

Income generated by the chargeback system is managed in a single account allocated at the end of the fiscal year and distributed based on priority need. Remaining income is allocated for equipment and other core needs of the Center.

The Associate Director of Operational Services works with the Grants & Financial Team to analyze income and expenses on a monthly basis and generate reports to Senior Management and Unit Heads in order to evaluate

charges for service, manage funds, and develop budgets.

Other Sources of Support:
The WNPRC received a total amount of $1,602,794 in State and Indirect Return for the UW-Madison FY19 fiscal year (7/1/18-6/30/19).

12. Feedback from Users. Provide a brief statement discussing how feedback is solicited and the topics that are covered (e.g. quality of: the web site, the ordering process, service delivered, etc.). If feedback has been solicited, include a brief summary of the most significant results, lessons learned and changes made in response to feedback.

- N/A

13. Infrastructure Improvements. Provide a list of major infrastructure improvements and capital equipment (as defined by the Institution) purchased during the reporting period. For NIH sources of support, report the Institute or Center from which support was derived.

Type of Improvement	Source of support
Sable Systems Respirometry Analysis System, Serial #FX2C-1701-07 ($23,279) - Shared Faculty Labs	P51-Base Grant support
Body Composition Analyzer, Serial #E26-305-R ($81,500) - Shared Faculty Labs	P51-Base Grant support
Micromanipulator, Hydraulic, Serial #17009 ($25,500) - Precision Medicine Core	P51-Base Grant support
Nikon TS-2R Eclipse Microscope, Serial #151017 ($26,507) - Precision Medicine Core	P51-Base Grant support
Transfection System, Neon (Invitrogen), Serial # MP924661 ($7,173) - Shared Faculty Labs	P51-Base Grant support
Cryostat, Serial #7065 ($46,592) - Shared Faculty Labs	P51-Base Grant support
Nikon Microscope, Eclipse Ti2-E, Serial #548680 ($145,760) - Shared Faculty Labs	P51-Base Grant support
Motorized Tug, Serial #WI-1087 ($7,588) - Colony Managment	P51-Base Grant support
Film Processor, Serial #5382 ($5,100) - Shared Faculty Labs	P51-Base Grant support
Centrifuge, Sorvall Legend ($6,998) - Shared Faculty Labs	P51-Base Grant support
Nucleic Acid Purification System, Serial #20000064 ($122,620) - Shared Faculty Labs	P51-Base Grant support
Gait Anaylsis System, Catwalk, Serial #170356.002 ($49,996) - Shared Faculty Labs	P51-Base Grant support
Portable Ultrasound, Serial #637571WX0 ($37,187) - Veterinary Services Unit	P51-Base Grant support
Particle Tracking Analyzer ($40,951) - Shared Faculty Labs	P51-Base Grant support
Anesthesia Workstation ($5,984) - Veterinary Services Unit	P51-Base Grant support
CO2 Incubator ($5,909) - Precision Medicine Core	P51-Base Grant support
Centrifuge, Serial #5811GI181154 ($9,949) - Shared Faculty Labs	P51-Base Grant support
Freezer, TSX Series Ultra-Low, Serial #175AT0501A ($15,986) - Assay Services Unit	P51-Base Grant support
ABR System, Serial #NV2009-1A ($29,866) - Veterinary Services Unit	P51-Base Grant support
ABAXIS, Handheld Analyzer, i-STAT 1 Serial#707855 ($6,108) - Veterinary Services Unit	P51-Base Grant support

Type of Improvement	Source of support
ABAXIS, Handheld Analyzer, i-STAT 1 Serial#708059 ($6,108) - Veterinary Services Unit	P51-Base Grant support
Freezer, TSX Series Ultra-Low, Serial #TLE60086A ($11,692) - Pathology Services Unit	P51-Base Grant support
Digital Camera, ORCA-FLASH 4.0 ($26,271) - Shared Faculty Labs	P51-Base Grant support
Repair of auxiliary heat exchanger on Building 2 cagewasher ($19,834.82) - Colony Management	P51-Base Grant support (-56S2)
Installation of 2nd floor ceiling tile in Building 2 ($38,691) - Colony Management	P51-Base Grant support (-56S2)

Description: Above is a list of infrastructure improvements and capital equipment (UW-Madison defines capital equipment as any individual item costing $5,000 or more and having a useful life of at least one year) purchased during 1/1/2018 - 12/31/2018. All improvements and capital equipment were supported by the WNPRC P51 base operating grant.

Composite Application Budget Summary

Categories	Budget Period
Salary, Wages and Fringe Benefits	4,810,153
Equipment	120,446
Travel	61,270
Participant/Trainee Support Costs	0
Other Direct Costs (excluding Consortium)	2,049,875
Consortium Costs	49,595
Direct Costs	7,091,339
Indirect Costs	2,560,879
Total Direct and Indirect Costs	9,652,218

Component Budget Summary

Components	Categories	Budget Period
5888-001 (Admin Core)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	3,783
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	946
	Consortium Costs	0
	Direct Costs	4,729
	Indirect Costs	1,750
TOTALS	Total Direct and Indirect Costs	6,479
5889-002 (Admin Core)	Salary, Wages and Fringe Benefits	0
	Equipment	120,446
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	120,446
	Indirect Costs	0
TOTALS	Total Direct and Indirect Costs	120,446
5886-003 (Admin Core)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	3,783

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	946
	Consortium Costs	0
	Direct Costs	4,729
	Indirect Costs	1,750
TOTALS	Total Direct and Indirect Costs	6,479
5887-004 (Admin Core)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	3,783
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	946
	Consortium Costs	0
	Direct Costs	4,729
	Indirect Costs	1,750
TOTALS	Total Direct and Indirect Costs	6,479
5884-005 (Admin Core)	Salary, Wages and Fringe Benefits	264,612
	Equipment	0
	Travel	7,572
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	16,182
	Consortium Costs	0
	Direct Costs	288,366
	Indirect Costs	106,695
TOTALS	Total Direct and Indirect Costs	395,061

5885-006 (Admin Core)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	3,783
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	946
	Consortium Costs	0
	Direct Costs	4,729
	Indirect Costs	1,750
TOTALS	Total Direct and Indirect Costs	6,479
5892-007 (Admin Core)	Salary, Wages and Fringe Benefits	272,835
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	23,514
	Consortium Costs	0
	Direct Costs	296,349
	Indirect Costs	109,649
TOTALS	Total Direct and Indirect Costs	405,998
5893-008 (Admin Core)	Salary, Wages and Fringe Benefits	199,074
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	243,710
	Consortium Costs	0

	Direct Costs	442,784
	Indirect Costs	163,830
TOTALS	Total Direct and Indirect Costs	606,614
5890-009 (Admin Core)	Salary, Wages and Fringe Benefits	19,186
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	19,186
	Indirect Costs	7,099
TOTALS	Total Direct and Indirect Costs	26,285
5891-010 (Admin Core)	Salary, Wages and Fringe Benefits	400,919
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	105,163
	Consortium Costs	0
	Direct Costs	506,082
	Indirect Costs	187,250
TOTALS	Total Direct and Indirect Costs	693,332
5901-001 (Core)	Salary, Wages and Fringe Benefits	3,485
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	3,485
	Indirect Costs	1,289
TOTALS	Total Direct and Indirect Costs	4,774
5896-001 (Other)	Salary, Wages and Fringe Benefits	992,779
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	625,767
	Consortium Costs	0
	Direct Costs	1,618,546
	Indirect Costs	598,862
TOTALS	Total Direct and Indirect Costs	2,217,408
5897-002 (Other)	Salary, Wages and Fringe Benefits	170,750
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	9,489
	Consortium Costs	0
	Direct Costs	180,239
	Indirect Costs	66,688
TOTALS	Total Direct and Indirect Costs	246,927

5894-003 (Other)	Salary, Wages and Fringe Benefits	102,791
	Equipment	0
	Travel	15,680
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	118,471
	Indirect Costs	43,834
TOTALS	Total Direct and Indirect Costs	162,305
5895-004 (Other)	Salary, Wages and Fringe Benefits	167,494
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	116,545
	Consortium Costs	0
	Direct Costs	284,039
	Indirect Costs	105,094
TOTALS	Total Direct and Indirect Costs	389,133
5904-005 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	211,785
	Consortium Costs	0

	Direct Costs	211,785
	Indirect Costs	78,360
TOTALS	Total Direct and Indirect Costs	290,145
5905-006 (Other)	Salary, Wages and Fringe Benefits	221,306
	Equipment	0
	Travel	2,943
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	211,780
	Consortium Costs	0
	Direct Costs	436,029
	Indirect Costs	161,331
TOTALS	Total Direct and Indirect Costs	597,360
5902-007 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	7,679
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	7,679
	Indirect Costs	2,841
TOTALS	Total Direct and Indirect Costs	10,520
5903-008 (Other)	Salary, Wages and Fringe Benefits	51,643
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	1,025
	Consortium Costs	0
	Direct Costs	52,668
	Indirect Costs	19,487
TOTALS	Total Direct and Indirect Costs	72,155
5900-009 (Other)	Salary, Wages and Fringe Benefits	543,837
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	16,795
	Consortium Costs	0
	Direct Costs	560,632
	Indirect Costs	207,434
TOTALS	Total Direct and Indirect Costs	768,066
5898-010 (Other)	Salary, Wages and Fringe Benefits	239,512
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	45,085
	Consortium Costs	0
	Direct Costs	284,597
	Indirect Costs	105,301
TOTALS	Total Direct and Indirect Costs	389,898

5899-011 (Other)	Salary, Wages and Fringe Benefits	304,577
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	7,798
	Consortium Costs	0
	Direct Costs	312,375
	Indirect Costs	115,579
TOTALS	Total Direct and Indirect Costs	427,954
5912-012 (Other)	Salary, Wages and Fringe Benefits	57,721
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	78,158
	Consortium Costs	0
	Direct Costs	135,879
	Indirect Costs	50,275
TOTALS	Total Direct and Indirect Costs	186,154
5910-013 (Other)	Salary, Wages and Fringe Benefits	124,821
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	57,014
	Consortium Costs	49,595

	Direct Costs	231,430
	Indirect Costs	67,279
TOTALS	Total Direct and Indirect Costs	298,709
5911-014 (Other)	Salary, Wages and Fringe Benefits	182,359
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	65,093
	Consortium Costs	0
	Direct Costs	247,452
	Indirect Costs	91,557
TOTALS	Total Direct and Indirect Costs	339,009
5908-015 (Other)	Salary, Wages and Fringe Benefits	228,010
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	37,642
	Consortium Costs	0
	Direct Costs	265,652
	Indirect Costs	98,291
TOTALS	Total Direct and Indirect Costs	363,943
5909-016 (Other)	Salary, Wages and Fringe Benefits	136,283
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	85,402
	Consortium Costs	0
	Direct Costs	221,685
	Indirect Costs	82,024
TOTALS	Total Direct and Indirect Costs	303,709
5906-017 (Other)	Salary, Wages and Fringe Benefits	113,562
	Equipment	0
	Travel	1,892
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	88,144
	Consortium Costs	0
	Direct Costs	203,598
	Indirect Costs	75,331
TOTALS	Total Direct and Indirect Costs	278,929
5907-018 (Other)	Salary, Wages and Fringe Benefits	12,597
	Equipment	0
	Travel	10,372
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	22,969
	Indirect Costs	8,499
TOTALS	Total Direct and Indirect Costs	31,468

TOTALS		**9,652,218**

Categories Budget Summary

Categories	Components	Budget Period
R&R Budget - Senior/Key Person Funds Requested	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	128,895
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	118,973
	5893-008 (Admin Core)	96,247
	5890-009 (Admin Core)	19,186
	5891-010 (Admin Core)	0
	5901-001 (Core)	3,485
	5896-001 (Other)	49,564
	5897-002 (Other)	71,149
	5894-003 (Other)	0
	5895-004 (Other)	101,753
	5904-005 (Other)	0
	5905-006 (Other)	41,306
	5902-007 (Other)	0
	5903-008 (Other)	51,643
	5900-009 (Other)	61,038
	5898-010 (Other)	82,751

	5899-011 (Other)	110,967
	5912-012 (Other)	19,281
	5910-013 (Other)	35,185
	5911-014 (Other)	81,562
	5908-015 (Other)	91,887
	5909-016 (Other)	62,043
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		1,226,915
R&R Budget - Other Personnel Funds Requested	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	135,717
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	153,862
	5893-008 (Admin Core)	102,827
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	400,919
	5901-001 (Core)	0
	5896-001 (Other)	943,215
	5897-002 (Other)	99,601
	5894-003 (Other)	102,791
	5895-004 (Other)	65,741

	5904-005 (Other)	0
	5905-006 (Other)	180,000
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	482,799
	5898-010 (Other)	156,761
	5899-011 (Other)	193,610
	5912-012 (Other)	38,440
	5910-013 (Other)	89,636
	5911-014 (Other)	100,797
	5908-015 (Other)	136,123
	5909-016 (Other)	74,240
	5906-017 (Other)	113,562
	5907-018 (Other)	12,597
TOTALS		3,583,238
R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	264,612
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	272,835
	5893-008 (Admin Core)	199,074
	5890-009 (Admin Core)	19,186

	5891-010 (Admin Core)	400,919
	5901-001 (Core)	3,485
	5896-001 (Other)	992,779
	5897-002 (Other)	170,750
	5894-003 (Other)	102,791
	5895-004 (Other)	167,494
	5904-005 (Other)	0
	5905-006 (Other)	221,306
	5902-007 (Other)	0
	5903-008 (Other)	51,643
	5900-009 (Other)	543,837
	5898-010 (Other)	239,512
	5899-011 (Other)	304,577
	5912-012 (Other)	57,721
	5910-013 (Other)	124,821
	5911-014 (Other)	182,359
	5908-015 (Other)	228,010
	5909-016 (Other)	136,283
	5906-017 (Other)	113,562
	5907-018 (Other)	12,597
TOTALS		4,810,153
R&R Budget - Section C. Total Equipment	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	120,446
	5886-003 (Admin Core)	0

	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0

	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		120,446
R&R Budget - Domestic Travel	5888-001 (Admin Core)	3,783
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	3,783
	5887-004 (Admin Core)	3,783
	5884-005 (Admin Core)	7,572
	5885-006 (Admin Core)	3,783
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	15,680
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	2,943
	5902-007 (Other)	7,679
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0

	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	1,892
	5907-018 (Other)	10,372
TOTALS		61,270
R&R Budget - Foreign Travel	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0

	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Section D. Total Travel	5888-001 (Admin Core)	3,783
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	3,783
	5887-004 (Admin Core)	3,783
	5884-005 (Admin Core)	7,572
	5885-006 (Admin Core)	3,783
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0

	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	15,680
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	2,943
	5902-007 (Other)	7,679
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	1,892
	5907-018 (Other)	10,372
TOTALS		61,270
R&R Budget - Tuition/Fees/Health Insurance	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0

	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0

	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Stipends	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0

	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Trainee Travel	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0

	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Subsistence	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0

	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Other Participants/Trainee Support Costs	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0

	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0

	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Section E. Total Participants/Trainee Support Costs	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0

	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Materials and Supplies	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	2,553
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	15,814
	5893-008 (Admin Core)	166,710
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	11,351
	5901-001 (Core)	0
	5896-001 (Other)	625,767
	5897-002 (Other)	8,809
	5894-003 (Other)	0
	5895-004 (Other)	116,545

	5904-005 (Other)	0
	5905-006 (Other)	46,083
	5902-007 (Other)	0
	5903-008 (Other)	1,025
	5900-009 (Other)	16,795
	5898-010 (Other)	21,823
	5899-011 (Other)	7,798
	5912-012 (Other)	78,158
	5910-013 (Other)	49,994
	5911-014 (Other)	62,767
	5908-015 (Other)	37,642
	5909-016 (Other)	1,892
	5906-017 (Other)	83,644
	5907-018 (Other)	0
TOTALS		1,355,170
R&R Budget - Publication Costs	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0

	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	1,000
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	1,892
	5911-014 (Other)	2,326
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		5,218
R&R Budget - Consultant Services	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0

	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	13,629
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0

	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		13,629
R&R Budget - ADP/Computer Services	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0

	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	5,128
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		5,128
R&R Budget - Subawards/Consortium/Contractual Costs	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0

	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	49,595
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		49,595
R&R Budget - Equipment or Facility Rental User Fees	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0

	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Alterations and Renovations	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0

	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0

	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Other Direct Cost 1	5888-001 (Admin Core)	946
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	946
	5887-004 (Admin Core)	946
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	946
	5892-007 (Admin Core)	7,700
	5893-008 (Admin Core)	77,000
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	93,812
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	680
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	211,785
	5905-006 (Other)	164,697
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	23,262

	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	83,510
	5906-017 (Other)	4,500
	5907-018 (Other)	0
TOTALS		670,730
R&R Budget - Other Direct Cost 2	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0

	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Other Direct Cost 3	5888-001 (Admin Core)	0
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	0
	5887-004 (Admin Core)	0
	5884-005 (Admin Core)	0
	5885-006 (Admin Core)	0
	5892-007 (Admin Core)	0
	5893-008 (Admin Core)	0
	5890-009 (Admin Core)	0

	5891-010 (Admin Core)	0
	5901-001 (Core)	0
	5896-001 (Other)	0
	5897-002 (Other)	0
	5894-003 (Other)	0
	5895-004 (Other)	0
	5904-005 (Other)	0
	5905-006 (Other)	0
	5902-007 (Other)	0
	5903-008 (Other)	0
	5900-009 (Other)	0
	5898-010 (Other)	0
	5899-011 (Other)	0
	5912-012 (Other)	0
	5910-013 (Other)	0
	5911-014 (Other)	0
	5908-015 (Other)	0
	5909-016 (Other)	0
	5906-017 (Other)	0
	5907-018 (Other)	0
TOTALS		0
R&R Budget - Section F. Total Other Direct Cost	5888-001 (Admin Core)	946
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	946

	5887-004 (Admin Core)	946
	5884-005 (Admin Core)	16,182
	5885-006 (Admin Core)	946
	5892-007 (Admin Core)	23,514
	5893-008 (Admin Core)	243,710
	5890-009 (Admin Core)	0
	5891-010 (Admin Core)	105,163
	5901-001 (Core)	0
	5896-001 (Other)	625,767
	5897-002 (Other)	9,489
	5894-003 (Other)	0
	5895-004 (Other)	116,545
	5904-005 (Other)	211,785
	5905-006 (Other)	211,780
	5902-007 (Other)	0
	5903-008 (Other)	1,025
	5900-009 (Other)	16,795
	5898-010 (Other)	45,085
	5899-011 (Other)	7,798
	5912-012 (Other)	78,158
	5910-013 (Other)	106,609
	5911-014 (Other)	65,093
	5908-015 (Other)	37,642
	5909-016 (Other)	85,402

	5906-017 (Other)	88,144
	5907-018 (Other)	0
TOTALS		2,099,470
R&R Budget - Section G. Total Direct Cost (A thru F)	5888-001 (Admin Core)	4,729
	5889-002 (Admin Core)	120,446
	5886-003 (Admin Core)	4,729
	5887-004 (Admin Core)	4,729
	5884-005 (Admin Core)	288,366
	5885-006 (Admin Core)	4,729
	5892-007 (Admin Core)	296,349
	5893-008 (Admin Core)	442,784
	5890-009 (Admin Core)	19,186
	5891-010 (Admin Core)	506,082
	5901-001 (Core)	3,485
	5896-001 (Other)	1,618,546
	5897-002 (Other)	180,239
	5894-003 (Other)	118,471
	5895-004 (Other)	284,039
	5904-005 (Other)	211,785
	5905-006 (Other)	436,029
	5902-007 (Other)	7,679
	5903-008 (Other)	52,668
	5900-009 (Other)	560,632
	5898-010 (Other)	284,597

	5899-011 (Other)	312,375
	5912-012 (Other)	135,879
	5910-013 (Other)	231,430
	5911-014 (Other)	247,452
	5908-015 (Other)	265,652
	5909-016 (Other)	221,685
	5906-017 (Other)	203,598
	5907-018 (Other)	22,969
TOTALS		7,091,339
R&R Budget - Section H. Indirect Costs	5888-001 (Admin Core)	1,750
	5889-002 (Admin Core)	0
	5886-003 (Admin Core)	1,750
	5887-004 (Admin Core)	1,750
	5884-005 (Admin Core)	106,695
	5885-006 (Admin Core)	1,750
	5892-007 (Admin Core)	109,649
	5893-008 (Admin Core)	163,830
	5890-009 (Admin Core)	7,099
	5891-010 (Admin Core)	187,250
	5901-001 (Core)	1,289
	5896-001 (Other)	598,862
	5897-002 (Other)	66,688
	5894-003 (Other)	43,834
	5895-004 (Other)	105,094

	5904-005 (Other)	78,360
	5905-006 (Other)	161,331
	5902-007 (Other)	2,841
	5903-008 (Other)	19,487
	5900-009 (Other)	207,434
	5898-010 (Other)	105,301
	5899-011 (Other)	115,579
	5912-012 (Other)	50,275
	5910-013 (Other)	67,279
	5911-014 (Other)	91,557
	5908-015 (Other)	98,291
	5909-016 (Other)	82,024
	5906-017 (Other)	75,331
	5907-018 (Other)	8,499
TOTALS		2,560,879
R&R Budget - Section I. Total Direct and Indirect Costs (G +H)	5888-001 (Admin Core)	6,479
	5889-002 (Admin Core)	120,446
	5886-003 (Admin Core)	6,479
	5887-004 (Admin Core)	6,479
	5884-005 (Admin Core)	395,061
	5885-006 (Admin Core)	6,479
	5892-007 (Admin Core)	405,998
	5893-008 (Admin Core)	606,614
	5890-009 (Admin Core)	26,285

	5891-010 (Admin Core)	693,332
	5901-001 (Core)	4,774
	5896-001 (Other)	2,217,408
	5897-002 (Other)	246,927
	5894-003 (Other)	162,305
	5895-004 (Other)	389,133
	5904-005 (Other)	290,145
	5905-006 (Other)	597,360
	5902-007 (Other)	10,520
	5903-008 (Other)	72,155
	5900-009 (Other)	768,066
	5898-010 (Other)	389,898
	5899-011 (Other)	427,954
	5912-012 (Other)	186,154
	5910-013 (Other)	298,709
	5911-014 (Other)	339,009
	5908-015 (Other)	363,943
	5909-016 (Other)	303,709
	5906-017 (Other)	278,929
	5907-018 (Other)	31,468
TOTALS		9,652,218

A. COMPONENT COVER PAGE

Project Title: WNPRC Director's Office

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The Director's Office of the WNPRC pursues excellence in the development and provision of scientific resources, expertise, and services for high-caliber regional and national nonhuman primate (NHP) biomedical research programs. The Director is responsible for organizing the scientific programs of the Center, and fostering new collaborations with national and international investigators engaged in NHP research. In so doing, the Director's Office strives to position the WNPRC to support research endeavors with the maximum potential for scientific breakthroughs that will be of broad impact in furthering our understanding of human and NHP biology and disease. To enhance these programs, the Director actively pursues support through the UWMadison administration, and federal, state, and private institutions for infrastructure and core service development. The Senior Management Team, consisting of the Director and three Associate Directors, also steers the WNPRC divisions and units to provide the greatest quality, efficiency, and responsiveness to the needs of our NHP researchers through our services and cores. The Senior Management Team additionally ensures rigorous adherence to federal and professional veterinary standards for the care and use of NHP in research, and safeguards the use of NHP for studies with the highest likelihood for return of knowledge that will significantly impact human and animal health. The Director's Office also oversees the WNPRC's substantial public information and outreach (PIO) activities, which inform the national public of the value of our scientific programs and promote scientific literacy and support regarding the use of NHP in research. Our overall goals are to provide resources to enhance and disseminate our basic knowledge in primatology, define the mechanisms fundamental to human health at the cellular, molecular and whole organism levels, and translate discoveries to human clinical medicine. To achieve these goals, the Director's Office - with advice and guidance from a WNPRC Executive Committee (EC) - pursues the following objectives:

Specific Aim 1: To further develop the portfolio of excellent scientific programs supported by the resources, services, and expertise of the WNPRC; to institute and facilitate the scientific interactions of our working groups, and thereby develop new internal and external collaborations and leverage new grant support.

Specific Aim 2: To oversee continual improvement and modernization of WNPRC scientific core resources, service, expertise and infrastructure; to continue to foster collaborations and sharing of knowledge and expertise with peer primate centers through consortium working groups.

Specific Aim 3: To oversee rigorous adherence to the highest standards in the care and use of NHP.

Specific Aim 4: To perform periodic external reviews of the quality and productivity of our operational, veterinary and research service units.

Specific Aim 5: To engage, inform and communicate to the public the value of NHP research, emphasizing its translational importance.

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: B.2. Accomplishments Directors_Final rec'd 02.26.2019.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?

During the next reporting period, the Director's office will continue to develop the resources, services, and scientific resources of the WNPRC, and to recruit and support investigators conducting high-impact studies in our major areas of interest. The four Working Groups will continue to engage in work-in-progress meetings, grant-planning sessions. The Director will also continue to discuss support for potential new faculty hires in Departments with overlapping interests.

Our major efforts in the coming year will be to obtain funding required to initiate two ambitious construction projects. The first of these projects consists of the construction of new holding and procedure areas for rhesus macaques utilized in HIV/SIV research projects. Construction plans entail the renovation of space within the WIMR facility, contiguous with existing WNPRC veterinary, laboratory, and husbandry areas, as well as WIMR imaging facilities, to accommodate current and future needs of our investigators. In a second project we plan to construct a new Marmoset Precision Medicine Core Facility, also adjacent to current WNPRC space in WIMR, which is designed to consolidate and expand our marmoset colonies, establish dedicated marmoset assisted reproductive technology

laboratories, and core areas for marmoset physiological and behavioral phenotyping procedures. We have already obtained commitments from the UW Vice Chancellor and the Dean of the School of Medicine and Public Health to provide a portion of the funds require, and we have submitted applications for NIH C06 construction grants to support these two vitally important projects.

DIRECTOR'S OFFICE

Accomplishments

The Director and the Senior Management Team have focused their attention to the launch of new initiatives and directions proposed within each of the component units, while continuing to oversee the recruitment and support of new projects by Core and Affiliate Principal Investigators. The Senior Management Team now has two new members who bring fresh perspectives and ideas to the management of the Center. With the retirement of Associate Director Redacted by agreement we named Redacted by agreement previously Assistant Director for Operational Services, to the Associate Director position. Redacted by agreement decided to step down as Associate Director of Research Services to focus his efforts on his expanded research portfolio; Redacted by agreement remains the head of our Genetics Services Unit and the leader of our Global Infectious Disease Working Group. Redacted by agreement a highly accomplished infectious disease and immunology researcher who moved from the New England Primate Research Center to the WNPRC in 2012, was appointed Associate Director of Research Services. Redacted by agreement joined **Director** Redacted by agreement and Associate Director for Animal Services Redacted by agreement to complete the new Senior Management Team that remains a dynamic, highly interactive group of experienced leaders that share a progressive and enterprising vision for the future of the Center. The Senior Management Team has continued to meet each Thursday morning at 11:00 AM to discuss all administrative, scientific, and veterinary matters, including ongoing issues, progress, new initiatives, and immediate, mid-term, and long-range objectives and planning. Senior Management Team meetings provide an essential vehicle for communication, debate of ideas, and decision-making that are key to achieving our basic goals – to develop, recruit, and support NHP scientific programs of the highest caliber, and to support these programs with the most advanced technologies and services achievable. The Director and the (interim)Vice Chancellor for Research and Graduate Education, Dr. Norman Drinkwater (P51 P.I.), communicate regularly on all major issues of relevance to the research, management, and strategic planning of the WNPRC. The other three members of the Senior Management Team maintain robust working relationships with the Associate Chancellor for Research Redacted by agreement the Associate Chancellor for Administration Redacted by agreement and the Assistant Chancellor for Human Resources, Redacted by agreement

The WNPRC Director expanded and intensified the duties of the **External Advisory Board (EAB)**. The EAB provides rigorous reviews of progress, priorities, and plans for each of our service and scientific components on an annual, and often semiannual basis. A 2018 EAB visit was dedicated to the assessment and strategic planning for our future infrastructure and staffing needs, with particular focus on the expansion of our Precision Medicine and marmoset monkey resources to accommodate our increasing scientific portfolio. Newest members of the EAB include Redacted by agreement D.V.M, Director of Comparative Medicine, M.D. Anderson Center, University of Texas; Redacted by agreement Ph.D., Professor, Dept. of Microbiology & Molecular Genetics, University of Pittsburgh; Redacted by agreement MD, Ph.D., Department of Pediatrics, Duke University School of Medicine; Redacted by agreement Ph.D., Emeritus Professor Yerkes NPRC, Department of Psychiatry & Behavioral Sciences. The Director has also continued to chair monthly meetings of the WNPRC **Executive Committee**, which reviews and prioritizes all proposed projects according to scientific and technical appropriateness for the WNPRC mission, capabilities, and resources. We have formalized a subset of the Executive Committee to function as a **Marmoset Working Group** to oversee the expansion, development, maintenance, and utilization of our marmoset colony in the context of increasing demand for these animals in newly funded projects.

As we entered into the second year of the P51 Grant cycle, we continued to formalize, staff, and provide new support for two newest WNPRC units. The first of these is the **Informatics and Data Services (IDS) Unit** headed by Redacted by agreement The IDS builds upon the founding and development of a LabKey Electronic Health Records (EHR) System during the previous grant cycle. In an effort spearheaded by Redacted by agreement the Senior Management Team undertook an ambitious program to completely rebuild its EHR system. The WNPRC, in close collaboration with LabKey, developed and implemented a completely web-based EHR that enables real-time data entry and retrieval by all WNPRC stakeholders (including animal care staff, veterinarians, researchers, PIs, and administrators). The new EHR is designed to accommodate new types of information as they become available, such that the entire clinical and research history of an animal can be fully captured in the system. The EHR has dramatically improved efficiency by allowing more information to be entered at point-of-care, integrating data about WNPRC animals that was previously stored in disparate

locations, and tightly linking clinical and research data. Since the entire EHR is built on a single platform, it has become relatively easy to train new users and teach existing users to access new functions. The EHR has been developed to a state at which new functionalities for research, administration, and data management and sharing will be added at an accelerated pace. The Senior Management Team thus elected to formalize a new IDS unit that will pursue these objectives separately from ITSS, with the latter returning to its traditional role of development, support, and maintenance of the WNPRC computer and networking infrastructure. Current projects in EHR services include the development of a new financial management system integrated within all aspects of Center function, new data mining capabilities, as well as other initiatives more fully described in the IDS unit report. The second new core launched in this grant cycle is the **Precision Medicine Core.** With a major goal to establish next generation animal models and innovative tools for the assessment of novel precision stem cell therapies, the WNPRC's Precision Medicine Core is developing unique resources for the WNPRC investigators and broad scientific community, including NHP models for genetic diseases such as Parkinson's disease, and preclinical models for assessing novel stem cell therapies for bone marrow suppression, genetic blood diseases and AIDS. The Precision Medicine core is now composed of two closely interconnected units: The **Embryonic Genomic Editing Subunit** headed by Redacted by agreement is focused on the development of precision disease NHP models with embryonic and in vivo somatic cell genomic editing, while the **Precision Therapies Subunit** headed **by** Redacted by agreement is focused on developing stem cell-based therapies utilizing precision disease models. New funding from NIH to support projects in both sub-units was obtained, including separate R24 grants to develop transgenic and iPSC resources for NHP models of Parkinson's disease, and to development CCR5-null macaque model to study SIV/HIV resistance. In addition, new NIH UG3 funding was obtained to develop new somatic cell genomic editing delivery vehicles – nanoparticles containing ribonucleoproteins with CRISPR/Cas9 editing capacity – for use in the deployment of gene therapy strategies in NHPs.

Other important activities overseen by the Director's Office during the current budget year include…

- Three new pilot project grant applications were selected for funding (see Pilot Project Program for full description)
- A new suite of advanced electrophysiological and behavior testing facilities is under construction
- Redacted by agreement head of our EMCD working group, has been appointed to a faculty position in the Department of Cell and Regenerative Biology
- Redacted by agreement has been appointed as a Staff Scientist and Assistant Director of S.P.I., adding Ph.D.-level expertise to enhance the qualitative and quantitative capacities of the unit.
- Plans for the expansion of our animal holding and procedure areas, and our Precision Medicine Core facility, have been completed and applications for support of these vitally important construction plans have been submitted.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5884

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Norman		Drinkwater	PhD	PD/PI	Institutional Base Salary	EFFORT			1,896.00	631.00	2,527.00
2.		Redacted by agreement			PhD	Director					94,800.00	31,568.00	126,368.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **128,895.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			50,144.00	16,698.00	66,842.00
3	Associate Director				51,669.00	17,206.00	68,875.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**135,717.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**264,612.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	7,572.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**7,572.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	2,553.00
2. Publication Costs	0.00
3. Consultant Services	13,629.00
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	**16,182.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**288,366.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	288,366.00	106,695.00
		Total Indirect Costs	**106,695.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**395,061.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Energy Metabolism and Chronic Disease Working Group

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

One component of the strategic plan of the Wisconsin National Primate Research Center (WNPRC) focuses on the development and enhancement of the WNPRC research programs. A centerpiece of this vision has been the establishment of four Working Groups that provide dynamic scientific platforms to catalyze cutting-edge collaborative nonhuman primate (NHP) research and training. The interdepartmental
groups coalesce around special research themes and include, in alphabetical order, Global Infectious Disease (GID),
Energy Metabolism and Chronic Disease (EMCD), Neuroscience, and Regenerative and Reproductive Medicine (RRM). To meet the objective of the WNPRC strategic plan, the Working Groups share the following Specific Aims:
Specific Aim 1: Capitalize on existing collaborations and interactions among WNPRC Core and Affiliate Principal Investigators and their associated programs to broaden their reach and formalize their interactions through regular work-in-progress meetings.
Specific Aim 2: Enhance the mentorship of pre- and postdoctoral trainees in the laboratories of NHP researchers by welcoming the trainees to attend and present at the regular work-in-progress meetings and by providing crucial feedback on their presentations.
Specific Aim 3: Sponsor at least two seminar speakers, annually, to present their work and consult with their University of Wisconsin-Madison colleagues.
Specific Aim 4: Host visits by potential collaborators to develop and assess the feasibility of NHP project proposals.
Specific Aim 5: Maintain an open dialogue with the WNPRC Director on emerging science to ensure the Primate Center is poised to respond to the needs of NHP researchers in an ever dynamic environment.

Aging and Nutrition:
• To continue to assess the effects of adult-onset moderate caloric restriction in rhesus macaques to determine if this paradigm is able to increase healthspan and maximum lifespan in a primate species.
• To test the ability of putative senolytic agents to remove senescent cells and improve markers of senescence in aged rhesus monkeys with the goal of informing human clinical studies.

Chronic Disease:
• To establish nutritional standards for a healthy captive common marmoset population.
• To determine the relationship between dietary fatty acid ratios, metabolic syndrome and key features of adolescent depression.
• To use an innovative “top-down” mass spectrometry-based disease proteomics platform to comprehensively examine myofilament proteins from rhesus macaque skeletal muscles in conjunction with functional studies.
• To determine the effect of estrogen on bone maintenance in common marmosets.
• To develop and evaluate cell replacement strategies in parkinsonian nonhuman primates
• To develop stem cell lines and transgenic common marmoset monkeys for modeling disease.
• To assess changes in cardiac sympathetic innervation and noncoding RNAs associated to sympathetic neurodegeneration and neuroprotection in a nonhuman primate model of Parkinson’s disease cardiac dysautonomia.
• To assess the feasibility of using oral dosing of Ivermectin to modulate the activity of a mutated chloride channel introduced by gene transfer into the subthalamic nucleus of parkinsonian rhesus monkeys.
• To engineer and optimize production of ribonucleoproteins nanoparticles of preassembled Cas9-gRNA that could cross the blood brain barrier for in vivo CRISPR/Cas9 genomic editing.
• To assess the feasibility of using a novel nanocapsule system for in vivo delivery of CRISPR/Cas9 for truncation of neuronal LRRK2 in a common marmoset model.

Hormones and Metabolism:
• To determine the role of estradiol in energy homeostasis.

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: B.2 Accomplishments_EMCD_2.25.19.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?

Over the next year of the base grant the EMCD Scientific Program will continue as a broad reaching, highly interactive and supportive working group focused around energy metabolism and chronic disease research. We will strive to recruit new members to complement our strengths, take full advantage of WNPRC resources, and expand EMCD interests. With the growing percentage of elderly and the increasing rates of obesity, MetS, and diabetes in the United States population, the impact of these studies on human health is clear.

WNPRC Working Group:	Energy Metabolism and Chronic Disease (EMCD)

2. What was accomplished under these goals?

Aging and Nutrition

EMCD investigators are continuing to assess the effects of adult-onset moderate caloric restriction (CR) in rhesus macaques to determine how effectively this paradigm is able to increase healthspan and maximum lifespan in a primate species while also working to understand the mechanisms behind the known positive effects of CR. While metabolic regulatory pathways have been implicated in the mechanisms of CR, the molecular details have not been elucidated. EMCD investigators showed that CR engages RNA processing of genes associated with a highly integrated reprogramming of hepatic metabolism. They conducted molecular profiling of liver biopsies collected from adult male rhesus monkeys at baseline and after 2 years on control or CR (30% restricted) diet. Quantitation of over 20,000 molecules from the hepatic transcriptome, proteome, and metabolome indicated that metabolism and RNA processing are major features of the response to CR. Predictive models identified lipid, branched-chain amino acid, and short-chain carbon metabolic pathways, with alternate transcript use for over half of the genes in the CR network. They conclude that RNA-based mechanisms are central to the CR response and integral in metabolic reprogramming.

Aging is the biggest risk factor for the most serious chronic diseases and disabilities. Cellular senescence, a state in which cells stop dividing but release factors that damage other cells, may contribute to both age-related and chronic diseases. EMCD affiliates have demonstrated that removal of senescent cells from aged mice delayed aging and age–related disabilities. Their goal is to develop drugs - senolytic agents - that kill senescent cells in order to ameliorate age-related diseases as a group in humans. EMCD investigators will continue to test the potential human efficacy of senolytic agents in the rhesus monkey model.

Chronic Disease

Use of the marmoset as a model in human health studies is hampered by an incomplete understanding of their nutritional requirements leading to wide variability in the type of diet provided to captive marmosets. This inconsistency results in high variation in nutrient intake both within and among marmoset colonies that may contribute unnecessary variation in experimental outcomes and may play a role in some of the most common clinical diseases seen in this species in captivity. EMCD investigators have been performing extensive studies aimed at establishing standards for a nutritionally healthy, captive common marmoset. The studies are designed to identify critical features of a standardized basic diet for captive common marmosets; determine links between diet, gut microbiome, and disease; and establish standards for healthy weights, body condition, and biomarkers of metabolic function.

We know that common marmosets vary in digestive abilities linked to intestinal inflammation which can lead to chronic diarrhea, weight loss, vitamin D deficiency, and eventually marmoset wasting syndrome and/or metabolic bone disease. EMCD investigators examined food intake and digestion in three mixed-sex groups of adult common marmosets; one at the Wisconsin National Primate Research Center (WNPRC) maintained on the WNPRC diet (n=28), and two at the Southwest National Primate Research Center (SNPRC), one maintained on the SNPRC diet (n=28) and one originally from the New England National Primate Research Center (NEPRC) and maintained on the NEPRC diet (n=25). Animals underwent two consecutive 4-day digestion trials. Feces and diet samples were assayed for Mn, fat, and gross energy. We found poor digesters on all three diets. High fecal fat in poor digesters is consistent with malabsorption syndrome which could lead to vitamin D deficiency. The SNPRC diet produced the fewest animals with high fecal fat, but also had the highest mean energy intake and the most animals above 450g, suggesting it may be obesogenic. From this study EMCD investigators learned that the concentrations of Mn in food and feces can provide an estimate of apparent digestibility of dry matter when animals are fed a restricted diet.

Worldwide prevalence of obesity has ~tripled since 1975 including a ~5-fold increase in the number of overweight and obese children aged 5-19. This has led to an increased prevalence of risk factors for cardiovascular disease, including high cholesterol, high blood pressure, and increased rates of Type 2 diabetes in this population. Like humans, captive marmosets show diet-dependent early-onset weight gain and obesity and are therefore an excellent model for examining longer term metabolic effects of early life diet. Although frequently used in captive research, little is known about the optimal energy and nutrient

WNPRC Working Group:	Energy Metabolism and Chronic Disease (EMCD)

requirements of common marmosets and obesity is rarely seen in the wild. We have been examining the metabolic effects of high fat feeding beginning in adolescence (~6 months of age) and continuing through adulthood (~24 months of age) in common marmosets. Animals are divided into 3 groups: normally fed, unhealthy fat (30% increase in saturated fats), healthy fat (30% increase in balanced fat; 1:2:1 ratio of saturated to monounsaturated to polyunsaturated fats). We have shown that 4 months of feeding a diet high in a healthy balance of fats to subadult male marmosets led to improved glucoregulatory function compared to normally fed individuals. Examination of the effects of unhealthy fat feeding are underway.

Estrogen depletion leads to bone loss in almost all mammals with frequent regular ovarian cycles. However, subordinate adult female common marmosets undergo socially induced anovulation and hypoestrogenism without clinically apparent adverse skeletal consequences. Thus, EMCD investigators speculated that this species might have evolved a mechanism to avoid estrogen-depletion bone loss. To test this possibility, they performed three experiments in which lumbar-spine (L5-L6) bone mineral content (BMC) and density (BMD) were assessed using dual-energy x-ray absorptiometry 1) cross-sectionally in 13 long-term ovariectomized animals and 12 age- and weight-matched controls undergoing ovulatory cycles, 2) longitudinally in 12 animals prior to, 3-4 and 6-7 months following ovariectomy, and 6 controls, and 3) cross-sectionally in 9 anovulatory subordinate and 9 dominant females. In Experiments 1 and 3, plasma estradiol and estrone concentrations were measured and uterine dimensions were obtained by ultrasound in a subset of animals as a marker of functional estrogen deficiency. Estrogen levels, uterine trans-fundus width, and uterine dorso-ventral diameter were lower in ovariectomized and subordinate females than in those undergoing ovulatory cycles. However, no differences were found in L5-L6 BMC or BMD. These results indicate that estrogen deficiency, whether surgically or socially induced, is not associated with lower bone mass in female common marmosets. Thus, this species may possess unique adaptations to avoid bone loss associated with estrogen deficiency.

Sarcomeric proteins, including myofilament and Z-disc proteins, play critical roles in regulating muscle contractile properties. A variety of isoforms and post-translational modifications (PTMs) of sarcomeric proteins has been shown to be associated with modulation of muscle functions and the occurrence of muscle diseases. Nonhuman primates are excellent biomedical research models due to their high genetic similarity to humans. However, the sarcomeric proteins in nonhuman primate skeletal muscle have not been well characterized. To gain a deeper understanding of sarcomeric proteins in nonhuman primate skeletal muscle, EMCD investigators employed top-down mass spectrometry (MS) to conduct a comprehensive analysis on isoforms and PTMs of sarcomeric proteins in rhesus macaque skeletal muscle. They identified 23 protein isoforms with 46 proteoforms of sarcomeric proteins, including 6 isoforms with 18 proteoforms from fast skeletal troponin T. Particularly, for the first time, a novel PDZ/LIM domain protein isoform, PDLIM7, was characterized with newly identified protein sequence. Moreover, they also identified multiple PTMs on these proteins, including deamidation, methylation, acetylation, tri-methylation, phosphorylation and S-glutathionylation. Most PTM sites were localized, including Asn13 deamidation on MLC-2S, His73 methylation on αactin, N-terminal acetylation on most identified proteins, N-terminal tri-methylation on MLC-2S and MLC-2F, Ser14 phosphorylation on MLC-2S, Ser15 and Ser16 phosphorylation on MLC-2F. In summary, a comprehensive characterization of sarcomeric proteins including multiple isoforms and PTMs in NHP skeletal muscle was achieved by analyzing intact proteins in the top-down MS approach.

Cell replacement with induced pluripotent stem cell-derived midbrain dopaminergic neuronal grafts (iPSC-mDA) is a promising therapeutic strategy for Parkinson's Disease (PD). Without the aid of immunosuppression, use of allogeneic iPSC-mDA may trigger an immune response leading to increased neuroinflammation at the site of the grafts. Compared to allogeneic iPSC-mDA, cell replacement with autologous iPSC-mDA should not trigger this response. We assessed *in vivo* using [^{18}F]FEPPA PET whether rhesus treated with autologous or allogeneic iPSC-mDA show increased microglial activation (a biomarker for neuroinflammation) at the graft sites. Our results demonstrate that [^{18}F]FEPPA PET can be used as an *in vivo* biomarker of neuroinflammation after autologous or allogeneic iPSC-mDA intracerebral grafts.

Cardiac dysautonomia is a common nonmotor symptom of Parkinson's disease associated with loss of sympathetic innervation to the heart and decreased plasma catecholamines. Disease-modifying strategies are not available, and biomarkers are lacking. EMCD investigators used systemic administration of the

WNPRC Working Group:	Energy Metabolism and Chronic Disease (EMCD)

catecholaminergic neurotoxin 6-hydroxydopmaine (6-OHDA) to recapitulate the loss of cardiac sympathetic innervation and circulating catecholamines and. They then successfully used PET imaging to visualize and quantify cardiac sympathetic neurodegeneration, increased inflammation, and oxidative stress following neurotoxin, which were attenuated in pioglitazone-treated animals compared to placebo. Post mortem characterization of heart and adrenal tissue in these animals compared to age and sex matched normal controls validated in vivo findings of 6-OHDA associated cardiac sympathetic denervation and demonstrate the ability of pioglitazone to preserve enzymes critical for catecholamine production in the adrenal medulla.

EMCD investigators have developed an efficient non-viral CRISPR/Cas9 delivery system for *in vivo* genome editing. Their strategy requires the delivery of preassembled Cas9-gRNA ribonucleoproteins (RNPs) using nanocapsules (NCs) specifically engineered for delivering an RNP payload across the blood-brain barrier (BBB). As proof-of-principle, they will target the *leucine-rich repeat kinase 2 (LRRK2)* gene in common marmoset monkeys. The *LRRK2* mutation *G2019S* (glycine to serine) is the most common mutation associated with sporadic and familial Parkinson's disease (PD). Preliminary work in common marmoset-derived neural stem cells demonstrated that CRISPR/Cas 9 can be used for editing the *LRRK2* gene in marmosets. Currently, they are working in parallel, optimizing nanoparticles for IV delivery, while performing baseline evaluations in four common marmoset monkeys.

Hormones and Metabolism

EMCD investigators proposed using a short hairpin interfering RNA-mediated mRNA knockdown approach to determine if ERα in arcuate nucleus and ventromedial nucleus neurons mediates negative feedback regulation of pulsatile GnRH release in female rhesus macaques. They found that ERα gene silencing, but not treatment with the scrambled control viral vector, produced a highly significant gain in weight and body mass index (BMI) that began at approximately 6 mo and plateaued at 12-14 mo post-surgery, rendering animals fully 25% heavier than their initial weights, and clearly obese. They have continued to more completely characterize the metabolic phenotypes of these animals, but initial indications suggest that the gradual increase in BMI following ERα gene silencing is accompanied by insulin resistance, and may be due to reduced energy expenditure rather than increased caloric intake. These metabolic findings represent the first indication in any primate, including women, that hypothalamic ERα is a critically important regulator of body weight and energy homeostasis.

They have also performed a retrospective analysis of body weight in adult female rhesus and determined that ovariectomy does not result in a significant increase in body weight up two years following surgery. At the same time, in related work in marmosets they determined that ovarian E_2 is not of major importance in the regulation of body weight and metabolism. They have inferred from these findings that a non-ovarian source of E_2, such as steroidogenic neurons in the hypothalamus, may figure more importantly in the regulation of body weight and energy homeostasis in primates versus non-primate mammals.

3. What do you plan to do during the next reporting period to accomplish the goals?

Over the next year of the base grant the EMCD Scientific Program will continue as a broad reaching, highly interactive and supportive working group focused around energy metabolism and chronic disease research. We will strive to recruit new members to complement our strengths, take full advantage of WNPRC resources, and expand EMCD interests. With the growing percentage of elderly and the increasing rates of obesity, MetS, and diabetes in the United States population, the impact of these studies on human health is clear.

WNPRC Working Group:	Energy Metabolism and Chronic Disease

4. EMCD Investigators:

Investigator	Department	Institution	Core	Affiliate
Redacted by agreement	OB/GYN	University of Wisconsin	X	
	WNPRC	University of Wisconsin	X	
	Cell and Regenerative Biology	University of Wisconsin	X	
	Medical Physics	University of Wisconsin	X	
	Pathobiological Sciences	University of Wisconsin	X	
	Cell and Regenerative Biology	University of Wisconsin	X	
	Neuroscience	University of Wisconsin	X	
Redacted by agreement	WNPRC	University of Wisconsin	X	
	Pediatrics	University of Wisconsin	X	
	WNPRC	University of Wisconsin	X	
	Medicine	University of Wisconsin		X
	Biostatistics	University of Alabama, Birmingham		X
	Population Health Sciences	Duke University		X
	Biomolecular Chemistry	University of Wisconsin		X
	Kinesiology	University of Wisconsin		X
	Psychology	Northeastern University		X
	Cell and Regenerative Biology	University of Wisconsin		X
	Neurology	University of CA, LA		X
	Nutrition	University of North Carolina		X
	Medicine	University of Wisconsin		X
	Medicine	Emory University		X
	Arlene Kogod Center on Aging	Mayo Clinic, Rochester		X
	Medicine	University of Wisconsin		X
	Stem Cell & Regenerative Med.	Harvard University		X
	Biochemistry	University of Wisconsin		X
	Biomedical Engineering	University of Wisconsin		X
	Biochemistry/Nutritional Sciences	University of Wisconsin		X
	Biochemistry	University of Wisconsin		X
	Nutrition Laboratory	Smithsonian Conservation Biology Institute		X
	Pathology	University of Washington		X
	Bacteriology	University of Wisconsin		X
	Nutrition	Univ. Federal de Pelotas		X
	Barshop Institute for Longevity and Aging Studies	University of Texas Health Sciences Center		X
	Arlene Kogod Center on Aging	Mayo Clinic, Rochester		X
	Nutritional Sciences	National Institute of Health and Nutrition		X
	Nutritional Sciences	University of Wisconsin		X

[1,2] Collaboration with Neuroscience[1], Regenerative and Reproductive Medicine[2] and Global Infectious Diseases[3] Working Groups. Such collaborative research may be described in more detail in those sections.

WNPRC Working Group:	Energy Metabolism and Chronic Disease

5. **Meeting History**:

Meeting History for 1/1/2018 – 12/31/2018 *(Insert rows as necessary)*

Date(s) of meeting	Meeting location	Guest Speaker [name, credentials, institution] *(if applicable)*	Meeting topic(s)	Notable outcomes and/or impact
1/23/18	Discovery Building	Redacted by agreement PhD, Scripps Research Institute	Expanding the Druggable Proteome	Discussion amongst participants
2/27/18	Biochemical Sciences Building	Redacted by agreement PhD, Harvard Medical School	Global Profiling of Protein Turnover	Discussion amongst participants
5/2/18	Genetics/Biotech	Redacted by agreement PhD, University of Pennsylvania	Targeting NAD Metabolism to Improve Health	Discussion amongst participants
5/2/18	WIMR	Redacted by agreement PhD, University of Southern California	Fasting Mimicking Diets, Regeneration and Rejuvenation	Discussion amongst participants, data sharing, planning for UCLA symposium
5/31/18	Nutritional Sciences	Redacted by agreement PhD, University of Utah	Lipid Metabolism in Cold Exposure	Discussion amongst participants
11/13/18	Discovery Building	Redacted by agreement PhD, University of Pennsylvania	Genetic and Environmental Influences on the Transcriptional Regulation of Metabolism	Discussion amongst participants
12/12/18	HSLC	Redacted by agreement MD, PhD, University of Sydney	Promoting Health and Longevity Through Diet: Metabolic and Molecular Effects	Discussion amongst participants, data sharing

WNPRC Working Group:	Energy Metabolism and Chronic Disease

6. List of Publications

Peer reviewed journals:

Colman RJ. Non-human primates as a model for aging. Biochim Biophys Acta Mol Basis Dis. 2018 Sep;1864(9 Pt A):2733-2741. doi: 10.1016/j.bbadis.2017.07.008. Epub 2017 Jul 17. Review. PubMed PMID: 28729086; PubMed Central PMCID: PMC5772001.

Jones CA, Duffy MK, Hoffman SA, Schultz-Darken NJ, Braun KM, Ciucci MR, Emborg ME. Vocalization development in common marmosets for neurodegenerative translational modeling. Neurol Res. 2018 Apr;40(4):303-311. doi: 10.1080/01616412.2018.1438226. Epub 2018 Feb 19. PubMed PMID: 29457539; PubMed Central PMCID: PMC6083835.

Kapoor A, Schultz-Darken N, Ziegler TE. Radiolabel validation of cortisol in the hair of rhesus monkeys. Psychoneuroendocrinology. 2018; 97:190-195.

Kraynak M, Colman RJ, Flowers MT, Abbott DH, Levine JE. Ovarian estradiol supports sexual behavior but not energy homeostasis in female marmoset monkeys. Int J Obes (Lond). 2018 Jul 18. doi: 10.1038/s41366-018-0156-4. [Epub ahead of print] PubMed PMID: 30022054.

Kraynak M, Flowers MT, Shapiro RA, Kapoor A, Levine JE, Abbott DH. Extraovarian gonadotropin negative feedback revealed by aromatase inhibition in female marmoset monkeys. Am J Physiol Endocrinol Metab. 2017; 313(5):E507-E514.

Metzger JM, Emborg ME. Autonomic dysfunction in Parkinson disease and animal models. Clin Auton Res. 2019 Jan 2. doi: 10.1007/s10286-018-00584-7. [Epub ahead of print] Review. PubMed PMID: 30604165.

Metzger JM, Moore CF, Boettcher CA, Brunner KG, Fleddermann RA, Matsoff HN, Resnikoff HA, Bondarenko V, Kamp TJ, Hacker TA, Barnhart TE, Lao PJ, Christian BT, Nickles RJ, Gallagher CL, Holden JE, Emborg ME. In vivo imaging of inflammation and oxidative stress in a nonhuman primate model of cardiac sympathetic neurodegeneration. NPJ Parkinsons Dis. 2018 Jul 13;4:22. doi: 10.1038/s41531-018-0057-1. eCollection 2018. PubMed PMID: 30038956; PubMed Central PMCID: PMC6045637. PMC5844481.

Rhoads TW, Burhans MS, Chen VB, Hutchins PD, Rush MJP, Clark JP, Stark JL, McIlwain SJ, Eghbalnia HR, Pavelec DM, Ong IM, Denu JM, Markley JL, Coon JJ, Colman RJ, Anderson RM. Caloric Restriction Engages Hepatic RNA Processing Mechanisms in Rhesus Monkeys. Cell Metab. 2018 Mar 6;27(3):677-688.e5. doi: 10.1016/j.cmet.2018.01.014. PubMed PMID: 29514073; PubMed Central PMCID:

Saltzman W, Abbott DH, Binkley N, Colman RJ. Maintenance of bone mass despite estrogen depletion in female common marmoset monkeys (Callithrix jacchus). Am JPrimatol. 2018 Aug 14:e22905. doi: 10.1002/ajp.22905. [Epub ahead of print] PubMed PMID: 30106167.

Sison SL, Vermilyea SC, Emborg ME, Ebert AD. Using Patient-Derived Induced Pluripotent Stem Cells to Identify Parkinson's Disease-Relevant Phenotypes. Curr Neurol Neurosci Rep. 2018 Oct 4;18(12):84. doi: 10.1007/s11910-018-0893-8. Review. PubMed PMID: 30284665.

Vermilyea SC, Emborg ME. In Vitro Modeling of Leucine-Rich Repeat Kinase 2 G2019S Mediated Parkinson's Disease Pathology. Stem Cells Dev. 2018 Jul 15;27(14):960-967. doi: 10.1089/scd.2017.0286. Epub 2018 Mar 29. PubMed PMID:29402177; PubMed Central PMCID: PMC6044417.

Vermilyea SC, Emborg ME. The role of nonhuman primate models in the development of cell-based therapies for Parkinson's disease. J Neural Transm (Vienna). 2018 Mar;125(3):365-384. doi:

WNPRC Working Group:	Energy Metabolism and Chronic Disease

10.1007/s00702-017-1708-9. Epub 2017 Mar 22. Review. PubMed PMID: 28326445; PubMed Central PMCID: PMC5847191.

Yamada Y, Kemnitz JW, Weindruch R, Anderson RM, Schoeller DA, Colman RJ. Caloric Restriction and Healthy Life Span: Frail Phenotype of Nonhuman Primates in the Wisconsin National Primate Research Center Caloric Restriction Study. J Gerontol A Biol Sci Med Sci. 2018 Mar 2;73(3):273-278. doi: 10.1093/gerona/glx059. PubMed PMID: 28398464; PubMed Central PMCID: PMC5861888.

Ziegler TE, Kapoor A, Binkley NC, Rice KS, Rogers J, Jolly CJ, Phillips-Conroy JE. Comparison of vitamin D metabolites in wild and captive baboons. Am J Primatol. 2018; 80(12):e22935.

Ziegler TE. Measuring peripheral oxytocin and vasopressin in nonhuman primates. Am J Primatol. 2018; e22871.

Book chapters:

Shultz J., Jones C., Emborg M.E. Parkinson's disease in humans and in non-human primate aging and neurotoxin models. (2018) In: Conn's Handbook of Models on Human Aging, 2nd edition, Elsevier/Academic Press San Diego CA. Ed. Ram J

Jones C., Shultz J., Emborg M.E. (2018) Genetic models of Parkinson's disease and their study in non-human primates. (*2018*) In: Conn's Handbook of Models on Human Aging, 2nd edition, Elsevier/Academic Press San Diego CA. Ed. Ram J

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5885

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Co-Chair	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.						Co-Chair					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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	3,783.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**3,783.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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. Speaker Meals and Incidentals	946.00
Total Other Direct Costs	**946.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**4,729.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	4,729.00	1,750.00
		Total Indirect Costs	**1,750.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**6,479.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Global and Infectious Disease Working Group

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

One component of the strategic plan of the Wisconsin National Primate Research Center (WNPRC) focuses on the development and enhancement of the WNPRC research programs. A centerpiece of this vision has been the establishment of four Working Groups that provide dynamic scientific platforms to catalyze cutting-edge collaborative nonhuman primate (NHP) research and training. The interdepartmental
groups coalesce around special research themes and include, in alphabetical order, Global Infectious Disease (GID),
Energy Metabolism and Chronic Disease (EMCD), Neuroscience, and Regenerative and Reproductive Medicine (RRM). To meet the objective of the WNPRC strategic plan, the Working Groups share the following Specific Aims:

Specific Aim 1: Capitalize on existing collaborations and interactions among WNPRC Core and Affiliate Principal Investigators and their associated programs to broaden their reach and formalize their interactions through regular work-in-progress meetings.

Specific Aim 2: Enhance the mentorship of pre- and postdoctoral trainees in the laboratories of NHP researchers by welcoming the trainees to attend and present at the regular work-in-progress meetings and by providing crucial feedback on their presentations.

Specific Aim 3: Sponsor at least two seminar speakers, annually, to present their work and consult with their University of Wisconsin-Madison colleagues.

Specific Aim 4: Host visits by potential collaborators to develop and assess the feasibility of NHP project proposals.

Specific Aim 5: Maintain an open dialogue with the WNPRC Director on emerging science to ensure the Primate Center is poised to respond to the needs of NHP researchers in an ever dynamic environment.

The WNPRC has been a leader in nonhuman primate models for HIV/AIDS for more than 20 years and currently supports a diverse research portfolio that encompasses each of the areas established as major NIH priorities in AIDS research. AIDS research remains the largest single focus area of GID core researchers and affiliates, but in recent years GID investigators have also developed an internationally recognized program in Zika virus pathogenesis.

The GID working group has the following goals:

1. Foster collaborations
2. Make investigators aware of existing resources
3. Facilitate identification of shared critical needs
4. Provide a venue for invited speakers who are leaders in their field(s) to share progress and inspire trainees

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: B.2. Accomplishments_GID_2.26.19.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?

1. Foster collaborations

Several members of the GID working group have ongoing collaborations that will continue. GID seminars have fostered both formal collaborations and informal exchanges of methods and ideas among GID core members and extramural investigators, ensuring that WNPRC remains a fertile environment in which to conduct cutting-edge infectious disease research. For example, after Redacted by Redacted visit, his laboratory assisted Redacted by group in developing new methods to improve the accuracy of deep sequencing of viral populations. Their interaction focused on influenza virus, but Redacted by group has helped others in GID apply the same approaches to sequencing Zika viruses.

2. Make investigators aware of existing resources at UW-Madison and beyond

This is an ongoing activity. We ask speakers to highlight ways in which resources (whether physical resources like facilities and equipment or virtual resources like data-analysis software) used for their studies are available to others.

3. Facilitate identification of shared critical needs

GID seminars frequently feature scientists who are making use of innovative technologies that could be useful to WNPRC investigators. Consideration of technological innovation is a criterion used to evaluate potential GID speakers. Each of this year's speakers presented technological advances as part of their presentations.

4. Provide a venue for invited speakers who are leaders in their field(s) to share progress and inspire trainees

This year's invited speakers were chosen from a list generated by GID core and affiliate investigators and included thought leaders in viral evolution and immunity to HIV/SIV, two topics that were listed as priorities for speaker recruitment in our previous RPPR.

Global Infectious Disease (GID) working group

Chair: Redacted by agreement

The WNPRC has been a leader in nonhuman primate models for HIV/AIDS for more than 20 years and currently supports a diverse research portfolio that encompasses each of the areas established as major NIH priorities in AIDS research. AIDS research remains the largest single focus area of GID core researchers and affiliates, but in recent years GID investigators have also developed an internationally recognized program in Zika virus pathogenesis.

1. Major activities and key outcomes: HIV/AIDS (according to NIH priority area)

1.1. Studies to reduce the incidence of HIV infection by developing effective vaccines. The development of a safe and effective vaccine for reducing the incidence of HIV-1 infection continues to be a major emphasis of studies at the WNPRC.

- As a novel vaccine approach, Redacted by agreement WNPRC, is exploring the potential for alloimmunization against polymorphic cellular antigens that become incorporated into virions (e.g. MHC molecules) to protect against SIV challenge in Mauritian cynomolgus macaques.
- Redacted by agreement WNPRC, recently completed studies with live-attenuated SIV in Mauritian cynomolgus macaques to test the hypothesis that focusing $CD8^+$ T cell responses on subdominant epitopes can improve T cell-mediated control of pathogenic SIV challenge (PMID:30111562).
- Redacted by agreement University of Miami, is investigating checkpoint blockade in rhesus macaques with an anti-CTLA-4 antibody as an approach for improving the efficacy T cell-based vaccines.
- Redacted by agreement University of Miami, has further investigated the efficacy of T cell-based vaccine strategies in MHC class I-defined rhesus macaques (PMID: 29875239 & PMID: 30541854).
- Following a landmark 2015 study at the WNPRC that achieved complete protection against pathogenic SHIV challenge by AAV delivery of an immunoadhesin (PMID: 25707797), Redacted by agreement Scripps-Florida, is continuing to develop AAV for "vectored immunoprophylaxis" (PMID: 30704961).
- Redacted by agreement University of Miami, will also be pursing future studies at the WNPRC following recently published work demonstrating durable vaccine protection in rhesus macaques immunized with a persistent herpesvirus vector engineered to express non-infectious SIV virus-like particles (PMID: 30642966).

1.2. Studies to find an HIV-1 cure. In line with current NIH priorities, there has been a precipitous increase in studies at the WNPRC aimed at depleting viral reservoirs in SIV/SHIV-infected macaques in an effort to find a "functional cure" for HIV-1 infection, defined as long-term, if not indefinite, containment of virus replication in the absence of antiretroviral therapy (ART).

- Redacted by agreement WNPRC, was recently awarded an R01 to determine if an IL-15 superagonist can enhance the efficacy of vaccine elicited T cells to suppress ongoing SIV replication.
- Redacted by agreement WNPRC, is currently funded to investigate antibody-dependent cellular cytotoxicity (ADCC) as an approach for containing virus replication in the absence of ART, either as a "functional cure" or as the "kill" component of a "kick and kill" strategy to eradicate virus-infected cells altogether.
- Redacted by agreement University of Miami, will test the hypothesis that treatment with the potent receptor-mimetic eCD4-Ig in combination with $CD8^+$ T cell depletion can delay virus rebound in SIV-infected macaques following withdrawal of ART. The rationale is that selective depletion of $CD8^+$ T cells will facilitate the reactivation of latently infected cells that can be eliminated by eCD4-Ig-mediated ADCC.
- Redacted by agreement University of Minnesota, recently received an R01 to test the hypothesis that targeting virus-specific T cells to B cell follicles of lymph nodes will lead to durable remission of HIV-1 replication. Virus-specific $CD8^+$ T cells do not efficiently enter $CD4^+$ T cell-rich B cell follicles, where virus replication persists in HIV-infected individuals during ART. Redacted by agreement will determine if this can be overcome using a chimeric antigen receptor (CAR) T cell approach for directing virus-specific $CD8^+$ T cells to B cell follicles in SIV-infected macaques.

- Redacted by agreement Beth Israel Deaconess Medical Center, is currently supported to evaluate several cure therapies in investigator new drug (IND)-enabling studies in SHIV-infected macaques, including IL-15 and TLR7 agonists in combination with broadly neutralizing antibodies.

1.3. Developing better treatments for HIV-associated comorbidities and co-infections. A number of studies being performed at the WNPRC, or in collaboration with WNPRC investigators, are investigating the pathogenesis of HIV-associated co-infections in nonhuman primate models.

- Redacted by agreement, WNPRC, was recently awarded a new R01 to model the impact of pre-existing HIV-1 infection on Zika virus pathogenesis in pregnant women and their developing fetuses in macaques co-infected with SIV and Zika virus. This work complements an ongoing clinical trial examining the impact of HIV-1 on Zika virus during pregnancy.
- In collaboration with Redacted by agreement at the University of Pittsburgh, Redacted by agreement WNPRC, is also modeling the pathogenesis of co-infection with HIV-1 and *Mycobacterium tuberculosis* in Mauritian cynomolgus macaques co-infected with SIV and *M. tuberculosis* (PMID: 30224552).

1.4. Reducing the severity of HIV-1 infection by developing next-generation therapies. Although most of the therapies currently under investigation at the WNPRC are aimed at achieving a cure for HIV-1 infection, a few also have the potential for reducing viral loads and disease severity.

- With the support of a TaPHIR (Targeting Persistent HIV Reservoirs) R21/R33 award Redacted by agreement WNPRC, and Redacted by agreement Scripps-Florida, are testing a Tat-inhibitor, didehydro-Cortistatin A (PMID:30723126), in SIV-infected macaques as an approach for driving HIV-1 into a deep state of transcriptional latency.
- In collaboration with Redacted by agreement Dana-Farber Cancer Institute and Redacted by agreement Université de Montréal, Redacted by is also testing a small molecule, BNM-III-170, that binds to the CD4-binding site of the HIV-1 envelope glycoprotein (Env). This compound forces Env to adopt a CD4-bound conformation that it is sensitive to antibodies that are elicited naturally during the course of HIV-1 infection (PMID: 29915222). Dose-escalation studies performed over the past year in rhesus macaques at the WNPRC have demonstrated that this compound can be administered safely by subcutaneous injection at doses sufficient to achieve effective concentrations in serum for several hours, similar to the serum half-lives of drugs currently used for antiretroviral therapy. With support provided by the Gilead Sciences HIV Cure Grants Program, we now plan to test the efficacy of this compound in SHIV-infected rhesus macaques.

1.5. Basic science research that cross-cuts multiple priorities. A number of studies at the WNPRC are contributing to our basic understanding of immunology and pathogenesis in the SIV/SHIV macaque model.

- Redacted by agreement group, WNPRC, have identified many of the first MHC class I ligands of rhesus macaque killer-cell immunoglobulin-like receptors (KIRs) (PMID:30232137) and revealed a preferential expansion of natural killer (NK) cells regulated by Bw4 ligands in gut-associated lymphoid tissues of SIV-infected rhesus macaques (PMID:30135127).
- The R01 supporting this work was renewed last fall, and will focus specific hypotheses concerning the effects of viral peptides on NK cell responses and the contribution of NK cells to the containment of immunodeficiency virus replication in tissues.
- In collaboration with Redacted by agreement, The Scripps Research Institute, La Jolla, Redacted by is also investigating Fcγ receptor-mediated antibody effector functions as mechanism of protection against immunodeficiency virus infection.

2. Major activities and key outcomes: Zika virus (ZIKV)

WNPRC investigators were among the first to develop a nonhuman primate model for ZIKV pathogenesis in pregnancy. We have continued to lead the field both scientifically and in developing best practices for using NPRC resources to respond to emerging diseases, as best evidenced by our early commitment to making all data from primate studies with ZIKV publicly available in real time to speed discovery, increase transparency, and reduce unnecessary duplication. In 2018 our Zika Experimental Science Team (ZEST) consortium was awarded a P01 grant to study ZIKV pathophysiology in pregnancy.

2.1. ZIKV research accomplishments 2018. In 2018 WNPRC investigators continued to make critical discoveries about ZIKV pathogenesis. In published studies, we:

- Led a multi-centric study combining results from multiple NPRCs to show that ZIKV infection significantly increases risk of fetal demise/pregnancy loss. This high-impact study established that miscarriage and fetal death are likely underappreciated outcomes of ZIKV infection in humans during the outbreak in the Americas. (PMID:29967348).
- Designed a ZIKV clone bearing synonymous molecular barcodes that allowed us to track within-host ZIKV evolution with unprecedented accuracy (PMID:29590202).
- Described pathologic changes in fetal eye tissue and in tissues of the maternal-fetal interface during congenital ZIKV infection in macaques (PMID:29381706).
- Used novel peptide microarray technology to describe antibody repertoires and response dynamics in ZIKV-infected pregnant and non-pregnant macaques (PMID:30481182)

2.2. New major activities in ZIKV research, 2018. In 2018, WNPRC investigators were awarded a program project (P01) grant as well as R01s to study ZIKV pathogenesis and evaluate potential interventions. Major new initiatives include:

- Collaborating with behavioral and neurocognitive researchers to conduct comprehensive neurobehavioral assessments of infant macaques born to mothers with ZIKV infection. Data from these experiments will be collected over the first year of infants' lives and could provide new insights into the potential effects of ZIKV on neurobehavioral development.
- Defining the pathways by which ZIKV crosses from mother to fetus (supported by a new R01 awarded to Redacted by
- Understanding if and how prolonged maternal viremia (which we have observed only in pregnant macaques infected with ZIKV) is associated with the outcome of ZIKV infection (P01 project 1, Redacted by agreement PI)
- Determining whether prior exposure to the antigenically related dengue virus affects risk for pathologic outcomes in congenital ZIKV infection (P01 project 2 and related R01 Redacted by agreement co-PIs)
- Determining whether post-exposure interventions can prevent or minimize fetal harm in ZIKV infection (P01 project 3, Redacted by agreement PI)

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5886

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Chair	Institutional Base	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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	3,783.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**3,783.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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. Speaker Meals and Incidentals	946.00
Total Other Direct Costs	**946.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**4,729.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	4,729.00	1,750.00
		Total Indirect Costs	**1,750.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**6,479.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Neuroscience Working Group

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

One component of the strategic plan of the Wisconsin National Primate Research Center (WNPRC) focuses on the development and enhancement of the WNPRC research programs. A centerpiece of this vision has been the establishment of four Working Groups that provide dynamic scientific platforms to catalyze cutting-edge collaborative nonhuman primate (NHP) research and training. The interdepartmental
groups coalesce around special research themes and include, in alphabetical order, Global Infectious Disease (GID),
Energy Metabolism and Chronic Disease (EMCD), Neuroscience, and Regenerative and Reproductive Medicine (RRM). To meet the objective of the WNPRC strategic plan, the Working Groups share the following Specific Aims:

Specific Aim 1: Capitalize on existing collaborations and interactions among WNPRC Core and Affiliate Principal Investigators and their associated programs to broaden their reach and formalize their interactions through regular work-in-progress meetings.

Specific Aim 2: Enhance the mentorship of pre- and postdoctoral trainees in the laboratories of NHP researchers by welcoming the trainees to attend and present at the regular work-in-progress meetings and by providing crucial feedback on their presentations.

Specific Aim 3: Sponsor at least two seminar speakers, annually, to present their work and consult with their University of Wisconsin-Madison colleagues.

Specific Aim 4: Host visits by potential collaborators to develop and assess the feasibility of NHP project proposals.

Specific Aim 5: Maintain an open dialogue with the WNPRC Director on emerging science to ensure the Primate Center is poised to respond to the needs of NHP researchers in an ever dynamic environment.

Goals:

Aim 1: Continue to perform cutting edge projects in the Neuroscience discipline.

Aim 2: Foster the excellent training of postdoctoral research fellows, graduate students, interns, and undergraduate students.

Aim 3: Establish in vivo optogenetic approach in the brain for neuroscience 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: B.2 Accomplishments_Neuroscience_2.26.19.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 perform cutting edge projects in the Neuroscience discipline.

We will continue to invite speakers for our seminar series from outside of campus.

We will continue to engaged in all mentoring activities.

Work towards establishing the new technology core unit, which includes optogenetic and nanotechnology, in the WNPRC.

NEUROSCIENCE WORKING GROUP

Working Group Co-Chairs: Redacted by agreement Ph.D.
Redacted by agreement Ph.D.

Accomplishments

Aim 1--Research Accomplishment:

- The Redacted by agreement and Redacted by agreement groups found that ERα gene silencing by infusion of shRNA for ERα into the arcuate nucleus (ARC) and ventromedial nucleus (VMN) of the hypothalamus induced a highly significant gain in weight and body mass index (BMI) that began at approximately 6 months and plateaued at 12-14 months post-surgery, rendering animals fully 25% heavier than their initial weights, and clearly obese. Preliminary observations further indicate that the gradual increase in BMI following ERα gene silencing was accompanied by insulin resistance and alternation of metabolic phenotypes in ERα knockdown animals appear to be due to reduced energy expenditure rather than increased caloric intake.
- The Redacted by agreement group found that there was a significant sex difference in the pathway involved in the control of GnRH release during sexual maturation. In prepubertal females there was little interaction between kisspeptin and neurokinin B (NKB) signaling, after puberty onset reciprocal signaling pathways (i.e., not only is NKB signaling mediated through kisspeptin neurons, but kisspeptin signaling is also medicated through NKB neurons) were established. In contrast, while the reciprocal pathways were already present in the prepubertal males, reflecting the elevated activity during the neonatal period, after puberty onset the kisspeptin signaling through NKB neurons was eliminated and NKB signaling was solely mediated through kisspeptin neurons. These results suggest that in females a more complex yet flexible regulatory mechanism of GnRH release is established at the time of puberty in preparation for cyclic ovulation and pregnancy in adulthood, whereas the regulatory mechanism of GnRH release in males is pruned to a simpler system. Preliminary data further indicate that the pubertal increase in gonadal steroids appears to greatly contribute to the establishment and modification of these pathways.
- The Redacted by agreement group is successful in establishing consistent methods for the generation of GnRH neurons from human embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC). Importantly, the group first found that treating relatively primitive neuroprogenitor cells, which contain some undifferentiated stem cells, with FGF8 was more efficient for generating GnRH neurons than treating advanced neuroprogenitor cells with FGF8. Second, the group discovered that application of kisspeptin 10 mid-way through with FGF8 treatment greatly enhanced the efficiency rate of GnRH generation.
- After the discovery of the role of neuroestradiol synthesized and released in the hypothalamus during the preovulatory surge, the Redacted by agreement group obtained new R01 support from the NICHD. In this project, her group will address the questions of whether release of neuroestradiol increases during the preovulatory GnRH surge and if so, how long after the peak elevation of estradiol it occurs. Consistent with the concept on the role of neuroestradiol in GnRH release of female rhesus monkeys, the Jon Levine and Redacted by agreement groups found that estradiol from the ovary was critical for female sex behaviors, but not metabolism regulation in marmoset females. These scientists postulate in primates, including humans, theimportance of extra-ovarian estradiol, such as neuroestradiol, in metabolic physiology.
- The Redacted by agreement group has been characterizing the interactions between the mediodorsal thalamus (MD) and prefrontal cortex (PFC) in rhesus monkeys. Using imaging obtained by diffusion MRI and linear multi-electrode arrays to simultaneously record neural activity (spikes and local field potentials, LFPs) from MD and PFC while exposing to abstract and/or concrete rules, during rule cue presentation and delay periods, it was found that the MD played an important role in processing information transmission across PFC areas according to cognitive control demands.
- The Redacted by agreement group also investigates how central thalamic deactivation influences cortico-cortical interactions in male monkeys. They recorded from interconnected sites in the central lateral thalamus (CL), frontal eye field (FEF) and lateral intraparietal area (LIP) using linear multi-electrode arrays to simultaneously record under general anesthesia (propofol or isoflurane) or during wakefulness. Results suggest that stimulation of CL at 50Hz (mimicking the spike rate of CL neurons during wakefulness) overrode effects of isoflurane and propofol anesthesia. This suggests that CL thalamic stimulation at 50Hz reconfigured cortical dynamics for arousal.

- The Redacted by agreement group investigates how neurons in the middle temporal cortex (area MT, a visual cortical area important for motion and depth processing), represent multiple visual stimuli moving in different directions and/or at different speeds. They found that neurons in area MT show a robust bias toward the near surface in response to two overlapping moving stimuli located at different depths. The group further conducted a series of computational analyses using the model, in which multiple visual stimuli by different speeds result in activity of MT by feedforward input to area MT or by local neural circuitry within MT.
- The Redacted by agreement group studies how 2D retinal images are hierarchically transformed into robust (i.e., accurate & precise) 3D percepts using rhesus monkeys. They record from multiple neurons in the primary visual cortex using multi-electrode array while monkeys responses were elicited by the visual stimuli during behavior. They propose the hypothesis that V3A is a critical juncture between 2D and 3D representations within a hierarchy of the pathway from V1 → V3A → CIP. Because the training of monkeys takes time and recording experiments are a tedious process, more data collection is necessary for the conclusion.
- Glaucoma is one of the leading causes of blindness. The primary cause of glaucoma is increased pressure of the eye chamber, which damages the optic nerve, rods and cones (photoreceptors) of the retina. The Redacted by agreement groups continue to investigate its etiology and treatment tools for glaucoma. The Redacted by agreement group has been studying two approaches. First, they are developing custom-made catheters that cannulate Schlemm's Canal (SC) in a non-human model. Second, aiming towards successful gene therapy, they are examining whether feline immunodeficiency viral vector transfection efficiency can be improved by application of the proteasome inhibitor M132, using immortalized human trabecular meshwork cells and monkey organ-cultured anterior segments. The Redacted by agreement group has been working on animal models for glaucoma with laser photocoagulation, endodiathermy/endocautery, chronic and acute elevations of intraocular pressure, and trabeculectomy. Subsequently, they examine the experimental animals ophthalmologically, testing with electroretinography and visual evoked potential, and image for visualization and documentation of posterior and anterior segments of both eyes.
- The Redacted by agreement group also investigates a pathophysiological process of presbyopia, which was due the age-related posterior restriction of the ciliary muscle. They further study how age-related presbyopia can be prevented/repaired using non-human primate models.
- The Redacted by agreement group has been studying the effects of iron deficiency on brain development. The importance of iron for brain development during the first year of life, especially for the maturation of white matter tracts in the brain, is demonstrated by cutting-edge neuroimaging methods, MRI and diffusion tensor imaging scans. Recently he discovered that more gradual repletion of iron by orally provided ferrous salts appeared to be better than the rapid increase in iron by a large bolus of iron dextran injection, as the body's regulatory control over iron absorption via the gut is significantly important and injection bypasses gut absorption.
- The Redacted by agreement group also investigates the influence of the gut-brain axis on infant behavioral and brain development using rhesus monkeys. With the materials obtained through the WNPRC Tissue Distribution program, he found that the distribution pattern of various gut microbiome relative to the digested food and feces. He also demonstrated the significant influence of maternal breast milk on the establishment of the gut bacteria in the young monkey during the first 2 months after birth. In the future he plans to culture intestinal stem cells from primates to generate enteroids to provide an *ex vivo* 3-D system for examining factors synthesized by the bacteria that are naturally present in the gut.
- Supported by the base grant Pilot study (Yr56) originally and currently by NIH R03 grant, Redacted by agreement has been investigating whether corticosterone and glucocorticoid levels measured in hair samples reflect activity of the hypothalamo-pituitary-adrenal axis. Interesting results are expected to be obtained soon.
- The Redacted by agreement group evaluated whether autologous transplantation of midbrain dopamine neurons (mDA) derived from induced pluripotent stem cells (iPSC) differs from allogenic transplantation of iPSC in MTP-induced Parkinsonian monkeys using PET scan with ^{18}F-FEPPA uptake (an inflammatory marker) and 6-^{18}F-fluorodopamine (^{18}FDA) uptake (the presence of functional dopamine neurons). The results indicate that while there was no difference with ^{18}FDA uptake, ^{18}F-FEPPA uptake in allogeneic grafts was higher than in autologous grafts, suggesting there was inflammatory reaction in allogenic transplantation, but not autologous transplantation. Preliminary data further indicate that recovery of Parkinsonian motor symptoms was better in autologous implantation than allogenic implantation.

- The *LRRK2* mutation G2019S (glycine to serine) is the most common mutation associated with sporadic and familial Parkinson's disease. Recently Redacted by agreement group was successful in producing in an *in vitro* model for Parkinson's disease from marmoset monkey ESC and iPSC using the CRISPR/Cas9 approach.
- Cardiac dysautonomia is a common nonmotor symptom of Parkinson's disease associated with loss of sympathetic innervation to the heart and decreased plasma catecholamines. After the establishment of a monkey model for cardiac dysautonomia by systemic administration of the catecholaminergic neurotoxin 6-hydroxydopmaine (6-OHDA), the Emborg group found that the PPAR-γ agonist pioglitazone protected from the neurotoxic effects of 6-OHDA.
- The Redacted by agreement group is also working on the non-viral *in vivo* gene delivery system, Cas9-gRNA ribonucleoprotein (RNP) delivery with nanocapsules (NCs) in non-human primates. Currently, they are testing modifications of the amyloid precursor protein (*APP*) gene and *LRRK2* gene, which are relevant to Alzheimer's disease and Parkinson's disease, respectively.
- Redacted by agreement groups have been investigating experience, such as social separation and high fat diet, in early life leads to adolescent depression or mood disorders such as deficits in problem solving, learning, social behavior, in marmoset monkeys. So far, they found that the marmosets at 6 months of age highly responded to the odors of their families as a social reward versus the novel family or the vehicle and that fMRI imaging studies indicated that activity of the forebrain areas including the nucleus of accumbens increased upon the exposure to the family order, not the novel order.

Aim 2--Education

- During 2018 (Yr57), three Ph.D. graduate students defended their theses. They were Redacted by agreement (Endocrinology and Reproductive Physiology Training program, Major Professor: Redacted by agreement Redacted by (Endocrinology and Reproductive Physiology Training program, Major Professor: Redacted by agreement and Redacted by agreement (Neuroscience Training program, Major Professor: Redacted by agreement Although we did not report, during 2017 (Yr56), one graduate student, Redacted by (Physiology Training program, Major Professor Redacted by agreement received Ph.D. degree.
- We provided the opportunity of a trainee poster session, in which a total of 21 posters by 23 trainees (postdoctoral research fellows, graduate students, and undergraduate students), who engage in non-human primate research, were presented. This was highly successful as seen by the enthusiasm of the trainees, the large number of attendants, and rigorous discussions.
- We also had a trainee seminar session, in which 2 graduate students gave a 30 min each. This event was very popular among trainees and attendants, as trainee's perspectives are not always the same as those of the PI (i.e., their supervisors). Furthermore, trainees had to learn how to convince an audience with different scientific disciplines, as unlike speeches or presentations given at specific meetings where they had experience before, the audience was heterogeneous.

Aim 3--Optogenetic approaches

- Optogenetic approaches are emerging powerful methods for studying neurocircuitry underlying complex brain functions. Application of this approach is particularly important in non-human primates, as obviously, we cannot use in humans. In the fall 2017, three young cognitive scientists (Redacted by Redacted by agreement) in the Neuroscience Working group were funded by the Primate Center Pilot program to obtain preliminary data for an application purchasing equipment for optogenetic approaches in the rhesus monkey brains *in vivo*. Subsequently, Redacted by obtained an approval to establish a core service unit for the optogenetic approach from the WNPRC Advisory Board. We are currently applying for additional funding to complete construction and outfitting of an optogenetic/chemogenetic/optical imaging facility.

Meeting History for 1/1/2018 – 12/31/2018

Date(s) of meeting	Meeting location	Guest Speaker [name, credentials, institution]	Meeting topic(s)/Title of talk
1/19/18	Primate Ctr.	Neuroscience Poster Session (21 posters) - Postdoc Fellows, Grad. Students and Undergrads	Neuroscience Research at the Primate Ctr.
2/16/18	Primate Ctr.	Graduate student seminars: Marissa Kraynak, Endocrinology & Reproductive Physiology Training Program, U.W.; and Jeanette Shultz, Cellular and Molecular Pathology Training Program.	"Extra-ovarian estradiol regulation via ERalpha in the hypothalamus of female sex behavior in the marmoset monkey." "Neurodegeneration & neuroproteciton in a nohuman primate model of Parkinson's disease cardiac dysautonomia."
3/2/18	Primate Ctr.	Oline K. Ronnekleiv, Ph.D., Prof., Dept. of Physiology & Pharmacology, Oregon Health & Science University, Portland, OR.	"Differential regulation by estadiol of peptide & glutamate neurotransmission by arcuate Kisspeptin neurons: Role in motivated behavior."
3/21/18	Wisconsin Institute for Discovery	Tracy L. Bale, Ph.D., Prof., Depts. of Pharmacology & Psychiatry, Director, Ctr. for Epigenetic Research in Child Health & Brain Development, Univ. of Maryland School of Medicine, Baltimore. This was a part of the Robert W.Goy Lecture Series.	"Parental stress and epigenetic programming of offspring neurodevelopment"
4/20/18	Primate Ctr.	Chris Ikonomidou, M.D., Ph.D., Prof., Child Neurology, Chief, Section of Pediatric Neurology, Vice Chair for Research, Dept. of Neurology, U.W. Madison	"Anticonvulsants, anesthetics and the pediatric brain"
9/21/18	Primate Ctr.	Victor M. Navarro, Ph.D., Assistant Prof., Harvard Program in Neuroscience, Harvard--MIT Health Sciences & Technology Faculty, Harvard Medical School & Brigham & Women's Hospital, Boston.	"New insights into the neuroendocrine control of reproductive function: Going beyond KNDy neurons."
10/19/18	Primate Ctr.	Luis C. Populin, Ph.D., Associate Prof., Dept. of Neuroscience, U.W. Madison	"Studies of CNS function and beyond in NHPs with PET/MR"
11/16/18	Primate Ctr.	Graham L. Banes, Ph.D., Clinical Assistant Prof., Dept. of Surgical Sciences, School of Veterinary Medicine, U.W. Madison	"Outbreeding depression in organgu-tans: Is it real, and does it kill?"

List of Publications

A. Peer Review Journals:

Abbott DH, Vepraskas SH, Horton TH, Terasawa E, Levine JE. Accelerated episodic luteinizing hormone release accompanies blunted progesterone regulation in PCOS-like female rhesus monkeys (macaca mulatta) exposed to testosterone during early-to-mid gestation. Neuroendocrinology. 2018;107(2):133-146.

Aktas Z, Rao H, Slauson SR, Gabelt BT, Larsen IV, Sheridan RTC, Herrnberger L, Tamm ER, Kaufman PL, Brandt CR. Proteasome inhibition increases the efficiency of lentiviral vector-mediated transduction of trabecular meshwork. Invest Ophthalmol Vis Sci. 2018; 59(1):298-310.

Emborg ME. Nonhuman primate models of neurodegenerative disorders. ILAR J. 2017; 58(2):190-201.

Fox AS, Oler JA, Birn RM, Shackman AJ, Alexander AL, Kalin NH. Functional connectivity within the primate extended amygdala is heritable and associated with early-life anxious temperament. J Neurosci. 2018; 38(35):7611-7621.

Garcia JP, Keen KL, Kenealy BP, Seminara SB, Terasawa E. Role of kisspeptin and neurokinin B signaling in male rhesus monkey puberty. Endocrinology. 2018;159(8):3048-3060.

Jones CA, Duffy MK, Hoffman SA, Schultz-Darken NJ, Braun KM, Ciucci MR, Emborg ME. Vocalization development in common marmosets for neurodegenerative translational modeling. Neurol Res. 2018; 40(4):303-311.

Kalin NH. Corticotropin-releasing hormone binding protein: Stress, psychopathology, and antidepressant treatment response. Am J Psychiatry. 2018; 175(3):204-206.

Kapoor A, Schultz-Darken N, Ziegler TE. Radiolabel validation of cortisol in the hair of rhesus monkeys. Psychoneuroendocrinology. 2018; 97:190-195.

Kaufman PL, Mohr ME, Riccomini SP, Rasmussen CA. Glaucoma drugs in the pipeline. Asia Pac J Ophthalmol (Phila). 2018; 7(5):345-351.

Kenealy BP, Keen KL, Garcia JP, Kohlenberg LK, Terasawa E. Obligatory role of hypothalamic neuroestradiol during the estrogen-induced LH surge in female ovariectomized rhesus monkeys. Proc Natl Acad Sci USA 2017; 114(52):1380413809.

Kraynak M, Colman RJ, Flowers MT, Abbott DH, Levine JE. Ovarian estradiol supports sexual behavior but not energy homeostasis in female marmoset monkeys. Int J Obes (Lond). 2018; Jul 18. doi: 10.1038/s41366-018-0156-4. [Epub ahead of print]

Kraynak M, Flowers MT, Shapiro RA, Kapoor A, Levine JE, Abbott DH. Extraovarian gonadotropin negative feedback revealed by aromatase inhibition in female marmoset monkeys. Am J Physiol Endocrinol Metab. 2017; 313(5):E507-E514.

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Martin AB, Yang X, Saalmann YB, Wang L, Shestyuk A, Lin J, Parvizi J, Knight RT, Kastner S. Temporal dynamics and response modulation across the human visual system in a spatial attention task: an ECoG study. J Neurosci. 2019; 39(2):333-352.

Metzger JM, Emborg ME. Autonomic dysfunction in Parkinson disease and animal models. Clin Auton Res. 2019 Jan 2. doi: 10.1007/s10286-018-00584-7. [Epub ahead of print]

Metzger JM, Moore CF, Boettcher CA, Brunner KG, Fleddermann RA, Matsoff HN, Resnikoff HA, Bondarenko V, Kamp TJ, Hacker TA, Barnhart TE, Lao PJ, Christian BT, Nickles RJ, Gallagher CL, Holden JE, Emborg ME. In vivo imaging of inflammation and oxidative stress in a nonhuman primate model of cardiac sympathetic neurodegeneration. NPJ Parkinsons Dis. 2018; 4:22.

Rajala AZ, Jenison RL, Populin LC. Neural correlate of auditory spatial attention allocation in the superior colliculus. J Neurophysiol. 2018; 119(4):1450-1460.

Rao R, Ennis K, Lubach GR, Lock E, Georgieff M, Coe CL. Metabolomic analysis of CSF indicates brain metabolic impairment precedes hematological indices of anemia in the iron-deficient infant monkey. Nutr Neurosci. 2018; 21(1): 40-48.

Rendina DN, Blohowiak SE, Coe CL, Kling PJ. Maternal perceived stress during pregnancy increases risk for low neonatal iron at delivery and depletion of storage iron at one year. J Pediatr. 2018; 200:166-173.

Rhoads TW, Burhans MS, Chen VB, Hutchins PD, Rush MJP, Clark JP, Stark JL, McIlwain SJ, Eghbalnia HR, Pavelec DM, Ong IM, Denu JM, Markley JL, Coon JJ, Colman RJ, Anderson RM. Caloric restriction engages hepatic RNA processing mechanisms in rhesus monkeys. Cell Metab. 2018; 27(3):677-688.

Saltzman W, Abbott DH, Binkley N, Colman RJ. Maintenance of bone mass despite estrogen depletion in female common marmoset monkeys (Callithrix jacchus). Am J Primatol. 2018; e22905.

Sison SL, Vermilyea SC, Emborg ME, Ebert AD. Using patient-derived induced pluripotent stem cells to identify parkinson's disease-relevant phenotypes. Curr Neurol Neurosci Rep. 2018; 18(12):84.

Strier KB, Ziegler TE. From the field to the lab: Muriqui endocrinology from a collaborative perspective. Am J Primatol. 2018; e22928. [Epub ahead of print]

Tan J, Fan N, Wang N, Feng B, Yang M, Liu G, Wang Y, Zhu X, Kaufman PL, Pang IH, Liu X. Effects of lentivirus-mediated C3 expression on trabecular meshwork cells and intraocular pressure. Invest Ophthalmol Vis Sci. 2018; 59(12):4937-4944.

Terasawa E, Garcia JP, Seminara SB, Keen KL. Role of kisspeptin and neurokinin B in puberty in female non-human primates. Front Endocrinol (Lausanne). 2018; 9:148.

Terasawa E. Neuroestradiol in regulation of GnRH release. Horm Behav. 2018; 104(8):138-145.

Vermilyea SC, Emborg M. In vitro modeling of leucine-rich repeat kinase 2 (LRRK2) G2019S-mediated parkinson's disease pathology. Stem Cells Dev. 2018; 27(14):960-967.

Vermilyea SC, Emborg ME. The role of nonhuman primate models in the development of cell-based therapies for Parkinson's disease. J Neural Transm (Vienna). 2018; 125(3):365-384.

Ziegler TE. Measuring peripheral oxytocin and vasopressin in nonhuman primates. Am J Primatol. 2018; e22871.

Ziegler TE, Kapoor A, Binkley NC, Rice KS, Rogers J, Jolly CJ, Phillips-Conroy JE. Comparison of vitamin D metabolites in wild and captive baboons. Am J Primatol. 2018; 80(12):e22935.

B. Book Chapters

Jones C, Shultz J, Emborg ME. (2018) Genetic models of Parkinson's disease and their study in non-human primates. In: Conn's Handbook of Models on Human Aging, 2nd edition, ed. by J. Ram, Elsevier/Academic Press, San Diego, CA. pp 641-646.

Unpublished

Shultz J, Jones C, Emborg ME. (2018) Parkinson's disease in humans and in non-human primate aging and neurotoxin models) In: Conn's Handbook of Models on Human Aging, 2nd edition, ed. by J. Ram, Elsevier/Academic Press, San Diego, CA. pp 617-638.

Terasawa, E. (2018) Postnatal development of GnRH neuronal function. In International Neuroendocrine Federation Masterclass Series: The GnRH neuron and its Control, First Edition. ed. by A.E. Herbison and T.M. Plant, John Wiley & Son, New York, NY. pp.61-91.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5887

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Co-Chair	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.					PhD	Co-Chair					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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	3,783.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**3,783.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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. Speaker Meals and Incidentals	946.00
Total Other Direct Costs	**946.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**4,729.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	4,729.00	1,750.00
		Total Indirect Costs	**1,750.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**6,479.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Regenerative and Reproductive Medicine Working Group

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

One component of the strategic plan of the Wisconsin National Primate Research Center (WNPRC) focuses on the development and enhancement of the WNPRC research programs. A centerpiece of this vision has been the establishment of four Working Groups that provide dynamic scientific platforms to catalyze cutting-edge collaborative nonhuman primate (NHP) research and training. The interdepartmental
groups coalesce around special research themes and include, in alphabetical order, Global Infectious Disease (GID),
Energy Metabolism and Chronic Disease (EMCD), Neuroscience, and Regenerative and Reproductive Medicine (RRM). To meet the objective of the WNPRC strategic plan, the Working Groups share the following Specific Aims:

Specific Aim 1: Capitalize on existing collaborations and interactions among WNPRC Core and Affiliate Principal Investigators and their associated programs to broaden their reach and formalize their interactions through regular work-in-progress meetings.

Specific Aim 2: Enhance the mentorship of pre- and postdoctoral trainees in the laboratories of NHP researchers by welcoming the trainees to attend and present at the regular work-in-progress meetings and by providing crucial feedback on their presentations.

Specific Aim 3: Sponsor at least two seminar speakers, annually, to present their work and consult with their University of Wisconsin-Madison colleagues.

Specific Aim 4: Host visits by potential collaborators to develop and assess the feasibility of NHP project proposals.

Specific Aim 5: Maintain an open dialogue with the WNPRC Director on emerging science to ensure the Primate Center is poised to respond to the needs of NHP researchers in an ever dynamic environment.

Goals:
The Regenerative and Reproductive Medicine (RRM) working group includes investigators across a variety of disciplines. In the 2016 P51 renewal application, RRM set the broad goal of establishing highly collaborative efforts with other WNPRC working groups and units. Specifically, the WNPRC proposed to:

1.Advance the use of NHP models for modeling and stem cell-based therapies for neurologic and blood diseases, diabetes and immunotherapies.

2.Derive nonhuman primate transgene-free iPSC lines form MHC homozygous donors and optimize of conditions for their maintenance.

3.Define maternal and fetal outcomes in immunological and anemic stress, intrauterine metabolic stress, and infection.

4.Refine and advance reproductive tract fertility and transgenesis opportunities.

Collectively, these efforts will expand the opportunities for translational studies in regenerative and reproductive medicine and provide exciting new breakthroughs in 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: RRM_B.2_Accomplishments_020519IS TG.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?

Redacted by agreement in collaboration with Redacted by agreement will work on establishing allogeneic TCRa/b-depleted NHP transplantation model for SHIV infection.

Redacted by agreement lab will continue collaboration with Redacted by agreement Morgridge Institute for Research) on development of iPSC-based therapies

for bone marrow failure.

Redacted by agreement will continue studies on iPSC-derived vascular transplant in NHP model.

Redacted by will initiate collaboration with Redacted by agreement (UW Departments of Medicine and Pediatrics) to explore MSCeducated macrophages for radioprotection.

Redacted by agreement lab will continue collaboration with Redacted by agreement (WNPRC) to explore iPSC-based CAR-T cell technologies for HIV therapies in NHP model.

Redacted by agreement (UW Department of Surgery) will continue collaboration with Slukvin lab to explore iPSC-derived myeloid suppressor cell in NHP model of solid organ transplantation.

The Redacted by agreement lab will work on CCR5 genomic editing in macaque embryo and generation of CCR5-mutated NHPs.

The Redacted by agreement labs will work on generation of CCR5 mutant macaque using CRISPR/Cas9 genomic editing to macaque embryos.

The Redacted by agreement labs will work to transfer CCR5 genomic editing to macaque embryos.

The Redact lab will conduct studies with Redacted by agreement to evaluate reproductive tract immune responses to Zika infection in pregnancy.

Embryonic genomic editing will be supported by the new Precision Medicine Core.

REGENERATIVE and REPRODUCTIVE MEDICINE (RRM) WORKING GROUP

Working Group Co-Chairs: Redacted by agreement Ph.D.
Redacted by agreement M.D., Ph.D.

Key Accomplishments:

1. **To advance the use of NHP models for modeling and stem cell-based therapies for neurologic, vascular and blood diseases, diabetes and immunotherapies.**

Major activities

- Continued to develop novel stem cell-based model for precision regenerative therapies. Several innovative NHP MHC-defined bone marrow transplantation models have been established i) transplantation of autologous genetically modified CD34+ cells and ii) allogeneic transplantation of TCRα/β-depleted bone marrow cells.
- Assisted UW and outside investigators in employing the BMT model, including 1) Redacted by agreement group (Department of Surgery, Division of Transplantation; UW-Madison) who, in collaboration with Redacted by agreement (Stanford University School of Medicine), explores the role of hematopoietic chimerism in establishing immune tolerance toward solid organ transplant; 2) Redacted by agreement (The Scripps Research Institute), who is developing novel approaches for highly efficient methods of genetic modification of HSCs; and 3) Redacted by agreement (Morgridge Institute for Research, Madison, WI) who is developing an NHP model for MHC homozygous iPSC banking.
- Provided a platform for executing two projects by WNPRC investigators: R24OD021322-01A1 "CCR5-mutant monkey model to facilitate the development of novel stem cell-based therapies for AIDS" Redacted by agreement PIs, Redacted by agreement Co-I), and R01 HL132891-01 entitled "Nonhuman Primate Model for Preclinical Evaluation of Haplotype-Based iPSC Banking for HLA-matched Blood Products Redacted by agreement PI and Redacted by agreement Co-I).
- New collaboration between Redacted by agreement and Redacted by agreement is initiated to study potential utility of rejuvenated through reprogramming SIV-specific TCLs for AIDS therapies.
- Assessing immune responses following arterial transplant in defined MHC-matched and mismatched settings.
- Developing methods for in vivo visualization of mechanisms of neurodegeneration in NHPs.

Significant results

- Several innovative NHP MHC-defined bone marrow transplantation models were established. These models include i) transplantation of autologous genetically modified CD34+ cells and ii) allogeneic transplantation of TCRα/β-depleted bone marrow cells. Allogeneic transplantation of TCRα/β-depleted bone marrow cells has been performed in five animals. Following optimization conditioning and post-transplant immunosuppression we were able to achieve successful HSC engraftment without a significant GVHD in MHC-matched and blood group identical Mauritian cynomolgus macaques (MCMs).
- The effect of allogeneic TCRα/β-depleted bone marrow transplantation on SHIV infected animals on retroviral therapy was evaluated in two animals. Results of these studies demonstrated that latent reservoir can persist in ART-treated macaques after profound lymphocyte depletion and allogeneic HSCT.
- The WNPRC has already performed more than 22 successful HSC transplants in rhesus and Mauritian cynomolgus macaques (MCM) in autologous and allogeneic settings.
- Transfusion of iPSC-derived blood products was performed in setting of myeloablative bone marrow transplant in MCMs.

- Novel protocol for generation of myeloid-derived suppressor cells from nonhuman primate iPSCs was established.
- New method for in vivo visualization of mechanisms of neurodegeneration in NHPs was developed.

Key outcomes

- The efficient method for MCM embryo editing using CRISPR-Cas9 technologies has been developed.
- ICTR grant "Generation myeloid-derived suppressor cells from nonhuman primate iPSCs" was awarded to support a joint project between Redacted by agreement
- Studies aimed to evaluate immune responses in setting MHC homozygous arterial transplants were completed.

2. Derive nonhuman primate transgene-free iPSC lines and optimize of conditions for their maintenance.

Significant results

- NHP iPSCs from MCMs with the most common MHC homozygous genotypes were generated.
- Protocols for reprogramming T cells into iPSCs and differentiating them back to "rejuvenated" T cells were established.
- SIV-resistant iPSC lines with homozygous CCR5 knockout were established.
- Safety of transfusion of iPSC-derived hematopoietic progenitors in NHP model was demonstrated.
- Novel method for induction blood cell production from NHP iPSCs using modified mRNA was established and published.
- Derivation of marmoset iPSC and their differentiation to neural progenitors and neurons was published.

3. Define maternal and fetal outcomes in immunological and anemic stress, intrauterine metabolic stress, and infection

Major activities

- Established transdisciplinary collaborations to develop postnatal assessment paradigms for rhesus offspring from maternal Zika infection.
- Established intrauterine inoculation with Zika virus to determine if direct fetal exposure to virus alters the trajectory of fetal injury and viral burden.
- Initiated development of high-dimensional flow cytometry with machine learning analytical paradigms to define reproductive tract responses to bacterial and viral infections.
- Determined the impact of iron oxide-containing nanoparticles used as contrast agent in MRI on fetoplacental iron content and histopathology.
- Determined the feasibility of trophoblast stem cell derivation paradigms on rhesus placental trophoblasts.
- Worked to determine the sensitivity of IVF-derived embryos to Zika virus.

Significant results

- Initial results indicate potential white matter tract alterations in rhesus infants Zika-exposed in utreo.
- Fetal brain viral RNA burden appears to be elevated with intraamniotic inoculation, possibly pointing to a platform for comparing viral genetic correlates of neuropathology and neurotropism.
- MRI with iron oxide nanoparticles does not result in fetoplacental histopathology or elevated iron burden, indicated stability as an experimental analytical paradigm.

- IVF-derived embryos are not impacted by virus in the zona-enclosed stages, however post-hatching trophoblast outgrowths demonstrate viral cytotoxicity and impact on differentiated function.

Key outcomes

- A multi-investigator P01 was awarded to further study Zika virus pathophysiology in pregnant rhesus monkeys.
- A new R01 was awarded for studying the pathways of Zika virus vertical transmission in early pregnancy.

4. Refine and advance reproductive tract fertility and transgenesis opportunities.

Major activities

- A UW2020 proposal across multiple investigators was submitted to enhance genome editing technologies with multiple species, including rhesus macaques.
- CRISPR targeting of the LRRK2 gene in marmoset pluripotent cells was moved forward to establish an in vitro model of the Parkinson's associated G2019S mutant
- Redacted by agreement was a Visiting Scientist at the WNPRC to initiate studies on nanoparticle/liposomes for delivery of therapeutic agents to the rhesus and marmoset placentas

Significant results

- Marmoset iPSC and ESC were edited to contain the G2019S LRRK2 allele that confers risk for Parkinson's disease. These cells will be the basis of further interactive studies.
- Promising results in targeted delivery of liposome cargo to the marmoset and possibly rhesus placenta in vivo were obtained.

Key outcomes

- Pending Support
- A new UW2020 proposal was awarded for extending marmoset work to rhesus embryos.

RRM CORE AND ASSOCIATE PRINICIPAL INVESTIGATORS

Investigator	Department	Institution	Core	Affiliate
Redacted by agreement	Cell and Regenerative Biology	University of Wisconsin	X	
	Pathology and Laboratory Medicine	University of Wisconsin	X	
	Comparative Biosciences, Obstetrics and Gynecology	University of Wisconsin	X	
	Medicine	University of Wisconsin	X	
	WNPRC	University of Wisconsin	X	
	Medical Physics	University of Wisconsin	X	
	Pediatrics	University of Wisconsin	X	
	Obstetrics and Gynecology	University of Wisconsin	X	
	Neuroscience	University of Wisconsin	X	
	Cell and Regenerative Biology	University of Wisconsin	X	
	Medicine	University of Wisconsin		X
	Surgery	University of Wisconsin		X
	Surgery	University of Wisconsin		X
	Surgery	University of Wisconsin		X
	Pediatrics	University of Wisconsin		X
	Surgery	University of Wisconsin		X
	Neuroscience	University of Wisconsin		X
	Surgery	University of Wisconsin		X
	Medical Physics	University of Wisconsin		X
	Psychology	University of Wisconsin		X
	Obstetrics and Gynecology	University of Wisconsin		X
	Medical Physics	University of Wisconsin		X
	Neuroscience	Northwestern University		X
	Obstetrics and Gynecology	Oxford University		X
	Pathobiological Sciences	University of Wisconsin		X
	Pathobiological Sciences	University of Wisconsin		X
	Obstetrics and Gynecology	University of Wisconsin		X
	Comparative Biosciences	University of Wisconsin		X
	Obstetrics and Gynecology	University of Wisconsin		X
	Obstetrics and Gynecology	University of Wisconsin		X
	Pediatrics	University of Wisconsin		X
	Pathobiological Sciences	University of Wisconsin		X
	Pathology and Laboratory Medicine	University of Wisconsin		X

RRM DETAILED MEETING HISTORY

Date(s) of meeting	Meeting location	Guest Speaker [name, credentials, institution] *(if applicable)*	Meeting topic(s)
3/3/16	WNPRC/HSLC UW-Madison	Anna Bakardjiev, University of California, San Francisco	Passing the TORCH: Infections at the Maternal-Fetal Interface
4/5/16	WNPRC/HSLC UW-Madison	Cynthia Dunbar, NHLBI	Investigating Pluripotent and Hematopoietic Stem Cell Biology and Therapeutic Potential in the Rhesus Macaque Model
2017-2018	WNPRC/WIMR UW-Madison	Drs. Slukvin, Kaufman, Hemati, Capitini, Reynolds, Maufort and 12 other investigators and veterinarians, UW-Madison	NHP bone marrow transplantation group holds meetings three times per year to discuss progress and develop novel strategies to advance this model.
10/28/17	WNPRC UW-Madison	Erika Sasaki, Center of Applied Developmental Biology and Central Institute for Experimental Animals, Keio University, Japan	Common marmoset transgenesis and genomic editing for human disease models
10/17/17	WNPRC/AVRL UW-Madison	Aleks Stanic-Kostic, UW-Madison	High dimensional flow cytometric and dimensionality reduction analysis at the human maternal-fetal interface
10/31/18	WNPRC UW-Madison	Erika Sasaki, Center of Applied Developmental Biology and Central Institute for Experimental Animals, Keio University, Japan	Common marmoset transgenesis and genomic editing for human disease models
12/14/18	WNPRC UW-Madison	Lynda Harris, University of Manchester	Targeted delivery of liposome nanoparticles for placental molecular therapies

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5888

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Co-Chair	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.					MD	Co-Chair					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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	3,783.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**3,783.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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. Speaker Meals and Incidentals	946.00
Total Other Direct Costs	**946.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**4,729.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	4,729.00	1,750.00
		Total Indirect Costs	**1,750.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**6,479.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Facilities and Improvement

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

To enhance the animal care and research mission of the Wisconsin National Primate Research Center (WNPRC) and support its use as a national resource, the WNPRC has a continuing need to improve and modernize its facilities and equipment, which includes the purchase of equipment to replace older items, to upgrade equipment as innovations in technologies become available, and to augment facilities and equipment in new ways as science advances. The WNPRC utilizes various funding sources, including the P51 award, to engage in improvement and modernization activities. Other sources of support include supplements from the Office of Research Infrastructure Programs (ORIP) of the Office of the Director of the National Institutes of Health (NIH), institutional support, including Facilities & Administration (F&A) cost return, and collaborative funding with other University of Wisconsin--Madison (UW--Madison) centers and departments.

Specific Aim 1: Improve and modernize facilities and equipment to meet the animal care and research mission of the WNPRC.

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: B.2. Accomplishments_Facilities.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 improve and modernize facilities and equipment to meet the animal care and research mission of the WNPRC.

FACILITIES AND IMPROVEMENT

Unit Head: Redacted by agreement Ph.D.

Accomplishments

To enhance the animal care and research mission of the Wisconsin National Primate Research Center (WNPRC) and support its use as a national resource, the WNPRC has a continuing need to improve and modernize its facilities and equipment. The WNPRC utilizes various funding sources, including the P51 award, to engage in improvement and modernization activities. Other sources of support include supplements from the Office of Research Infrastructure Programs (ORIP) of the Office of the Director of the National Institutes of Health (NIH), institutional support, including Facilities & Administration (F&A) cost return, and collaborative funding with other University of Wisconsin-Madison (UW-Madison) centers and departments. Following is a table showing the capital equipment expenditures from January 1, 2018 through December 31, 2018 for the Wisconsin National Primate Research Center (WNPRC).

2018 (01-01 to 12-31-2018)		
Description	**Cost**	**Unit/Lab**
Analysis System, Sable Systems, Serial #FX2C-1701-07	$23,279	Shared Faculty Labs
Body Composition Analyzer, Serial #E26-305-R	$81,500	Shared Faculty Labs
Micromanipulator, Hydraulic, Serial #17009	$26,500	Precision Medicine Core
Nikon TS-2R Eclipse Microscope, Serial #151017	$26,507	Precision Medicine Core
Transfection System, Neon (Invitrogen), Serial # MP924661	$ 7,173	Shared Faculty Labs
Cryostat, Serial #7065	$ 46,592	Shared Faculty Labs
Nikon Microscope, Eclipse Ti2-E, Serial #548680	$145,760	Shared Faculty Labs
Motorized Tug, Serial #WI-1087	$7,588	Colony Management
Film Processor, Serial #5382	$ 5,100	Shared Faculty Labs
Centrifuge, Sorvall Legend	$6,998	Shared Faculty Labs
Nucleic Acid Purification System, Serial #20000064	$122,620	Shared Faculty Labs
Gait Anaylsis System, Catwalk, Serial #170356.002	$49,996	Shared Faculty Labs
Portable Ultrasound, Serial #637571WX0	$37,187	Veterinary Services Unit
Particle Tracking Analyzer	$40,951	Shared Faculty Labs
Anesthesia Workstation	$5,984	Veterinary Services Unit
CO2 Incubator	$5,909	Precision Medicine Core
Centrifuge, Serial #5811GI181154	$9,949	Levine Laboratory
Freezer, TSX Series Ultra-Low, Serial #175AT0501A	$15,986	Assay Services
ABR System, Serial #NV2009-1A	$29,866	Veterinary Services Unit
ABAXIS, Handheld Analyzer, i-STAT 1 Serial#707855	$6,108	Veterinary Services Unit
ABAXIS, Handheld Analyzer, i-STAT 1 Serial#708059	$6,108	Veterinary Services Unit
Freezer, TSX Series Ultra-Low, Serial #TLE60086A	$11,692	Pathology Service Unit
Digital Camera, ORCA-FLASH 4.0	$26,271	Shared Faculty Labs
Total Expenditures for 2018	**$745,623**	

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5889

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Project Lead	Institutional Base	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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

C. Equipment Description

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

Equipment Item	Funds Requested ($)*
1. Flow Cytometer - Immunology Services Unit	120,446.00
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**120,446.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**120,446.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	0.00	0.00
		Total Indirect Costs	**0.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**120,446.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Operational Services Division

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The Operational Services Division of the Wisconsin National Primate Research Center (WNPRC) consists of the following three units:
• Administrative Services Unit
• Facilities and Shop Services Unit
• Information Technology & Systems Services (ITSS) Unit

To support the research and animal care mission of the WNPRC, the Division is tasked with providing all necessary administrative and operational services and support required for the WNPRC's
infrastructure and for the successful conduct of the independently funded research projects of WNPRC principal investigators and collaborators. While each of the units has its own individual Specific Aims,
they collaborate with each other and communicate on a daily basis to deliver proactive leadership and outstanding service to fulfill the over--arching Specific Aims of the Operational Services Division and to
ensure WNPRC's mission attainment:

Specific Aim 1: Assist WNPRC investigators and staff to ensure compliance with applicable Federal, State, and University policies and procedures with respect to the Center's operations, including facilities, finance, grants, human resources, information technology, network systems, and procurement.

Specific Aim 2: Provide a compliant, secure, and safe environment for all human and nonhuman occupants of WNPRC facilities.

Specific Aim 3: Develop strategies and implement process across Center operations to increase operational efficiencies and reduce costs whenever and wherever possible.

Specific Aim 4: Collaborate with WNPRC investigators and staff to devise strategies for increasing funding and revenue for Center programs.

Specific Aim 5: Leverage University of Wisconsin--Madison resources to improve WNPRC operations whenever and wherever possible.

Specific Aim 6: Collaborate with WNPRC investigators and staff to develop new approaches, ideas, or methods with respect to operational support in order to further the research and animal care mission.

Specific Aim 7: Fulfill the Specific Aims of each unit within the Operational Services Division.

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: B.2. Accomplishments Operational Srvcs.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: Assist WNPRC investigators and staff to ensure compliance with applicable Federal, State, and University policies and procedures with respect to the Center's operations, including facilities, finance, grants, human resources, information technology, network systems, and procurement.

A few key plans include the HR Team working with managers to ensure all position descriptions are updated according to the new campus guidelines as part of the Title and Total Compensation Study for UW-Madison; the Shop Unit working with UW-Madison Facilities to replace a rusted ceiling grid in one of the facilities in the least invasive manner to the researchers and animal care staff; and the ITSS Unit working with the UW-Madison Cybersecurity Office and DoIT to migrate to the next generation firewall service.

Specific Aim 2: Provide a compliant, secure, and safe environment for all human and nonhuman occupants of WNPRC facilities. The HR team will continue to collaborate with the Compliance Unit, specifically the Occupational Health and Safety Coordinator, on ways to

increase safety throughout the Center, including the annual review of Worker's Compensation claims to determine if there are patterns and to address any areas of concern. The Shop Unit will initiate work with UW-Madison Facilities to relocate the Fire Alarm Annunciator Panel from behind the animal barrier to the main lobby to facilitate easier access for emergency personnel.

Specific Aim 3: Develop strategies and implement process across Center operations to increase operational efficiencies and reduce costs whenever and wherever possible. All Units continue to work on this aim; some specific examples include: The Admin and ITSS teams will collaborate with the ES Unit on the development of an online procurement module within the LabKey system, and the Shop will coordinate with UW-Madison Facilities to install a new auxiliary heat exchanger for the cage washer at the 1220 Capitol Court location.

Specific Aim 4: Collaborate with WNPRC investigators and staff to devise strategies for increasing funding and revenue for Center programs. The Admin and ITSS teams will work with the ES Unit to rollout the financial module in LabKey, and the Admin team will continue to work with faculty and units heads to reduce procurement costs wherever possible and increase customer base wherever possible.

Specific Aim 5: Leverage University of Wisconsin-Madison resources to improve WNPRC operations whenever and wherever possible. The Admin and ITSS Units will participate in the UW Mobile Device Management (MDM) pilot program to manage the Center's tablets and smartphones. If pilot is successful, adopt MDM for all devices to include desktop computers and laptops. The Shop Unit will continue to assist with the planning and coordination of the Facilities project to provide a new back-up generator to the 1223 Capitol Court location.

Specific Aim 6: Collaborate with WNPRC investigators and staff to develop new approaches, ideas, or methods with respect to operational support in order to further the research and animal care mission. The Shop Unit will begin fabricating eight enrichment devise basket racks after completion of 10 new Marmoset husbandry units. The Admin team intends to develop a Quality Improvement Plan to research ways to enhance operational support across all areas.

Specific Aim 7: Fulfill the Specific Aims of each unit within the Operational Services Division.

Please see attached progress reports from each unit which includes detailed future plans.

OPERATIONAL SERVICES DIVISION

Division Head: Redacted by agreement

Accomplishments

Specific Aim 1: Assist WNPRC investigators and staff to ensure compliance with applicable Federal, State, and University policies and procedures with respect to the Center's operations, including facilities, finance, grants, human resources, information technology, network systems, and procurement.

All three units within the Division of Operational Services – Administrative Services (Admin) Unit, Facilities and Shop Services (Shop) Unit, and the Information Technology & Systems Services (ITSS) Unit – are charged with ensuring compliance in their areas of expertise and assisting the other Divisions with other compliance matters. A few notable accomplishments include successful completion of UW-System and the State of Wisconsin Legislative Audit Bureau (LAB) audits of awards, equipment, and human resources without any findings; successful completion of regular Institutional Animal Care and Use Committee (IACUC) inspections without major deficiencies; and continued administration of the Center's IT systems and servers to ensure a high level of security.

Specific Aim 2: Provide a compliant, secure, and safe environment for all human and nonhuman occupants of WNPRC facilities.

The Shop Unit provides a compliant, secure and safe environment for all human and non-human occupants. Acting as lead liaison between the WNPRC and the University of Wisconsin-Madison Physical Plant, Redacted by agreement Redacted Shop Unit Head, coordinates and implements all repairs, system upgrades, and remodeling projects. The Unit continues to provide 24/7 monitoring of the major operational systems including heating, ventilation and cooling (HVAC), electrical, plumbing, and freezer controls. In response to the last AAALAC inspection, Redacted spearheaded the effort to provide controlled cooling for the animal chow storage room in one of the Center's facilities, and this project was completed in October 2018. In addition Redacted has coordinated with UW-Madison Physical Plant on the effort to provide standby, back-up power by installing a 350kW generator for the WNPRC Building 1. Additionally, the ITSS Unit collaborates with the UW-Madison's Cyber Security team to protect the Center's network though use of a new web-based firewall service. Implemented in May 2018, this new service enables the design of security policies based on analysis of all traffic, including applications and content. See the Unit progress report for specific details.

Specific Aim 3: Develop strategies and implement processes across Center operations to increase operational efficiencies and reduce costs whenever and wherever possible.

All three units within the Division are tasked with this aim and often collaborate on efforts. The Admin team continues to collaborate with the Information and Data Services (IDS) Unit (formerly the Electronic Health Records Unit) to further develop and implement the financial module within the LabKey server. The Shop and Admin team worked with the Colony Management supervisor at the Blue Mounds Quarantine facility to develop a more efficient and effective office furniture layout, and new furniture was procured and installed in late 2017. In 2018 the WNPRC upgraded the technology in our main conference room. The ITSS team spearheaded this project to bring state-of-the-art video and web conferencing to the Center, thereby increasing the efficiency of meetings between units not physically located together. See all of the units' progress reports for further details.

Specific Aim 4: Collaborate with WNPRC investigators and staff to devise strategies for increasing funding and revenue for Center programs.

The Grants and Finance Team continue to meet with WNPRC investigators regularly to discuss their funding portfolios and potential grant opportunities. Over the course of 2018, the team assisted the faculty and scientists with 37 new grant applications, 4 competing renewals, and 13 renewal progress reports. Additionally, the team meets with service unit leadership to review revenue generation and discuss avenues for attracting new customers, as needed.

Specific Aim 5: Leverage University of Wisconsin-Madison resources to improve WNPRC operations whenever and wherever possible.

The ITSS Unit works with UW-Madison Division of Information Technology (DoIT) to leverage campus centralized services. In 2018 the ITSS Unit began using the University's centralized Domain Name Service (DNS) and Dynamic Host Configuration Protocol (DHCP) service, and two members of the team were trained in the use of the web-based administration platform. See the ITSS Unit's progress report for specific details.

Specific Aim 6: Collaborate with WNPRC investigators and staff to develop new approaches, ideas, or methods with respect to operational support in order to further the research and animal care mission.

The Shop Unit supports research and the Colony Management Unit with the design and fabrication of specialized equipment. Some notable accomplishments from the past year include novel modifications to a CatWalk XT gait analysis system, providing marmoset nesting box interface; design and fabrication of several pieces of specialized research equipment, including a marmoset metabolism 4-unit rolling rack, a rhesus macaque metabolic metabolism chamber, and a marmoset indirect calorimetry chamber; and development of a prototype transfer box equipped with a multi-position hook to allow staff to hook the transfer box to multiple different cages front, which helps secure the transfer box in position. Throughout 2018, the WNPRC HR team worked with 17 different faculty and staff to secure the donation of 952.5 hours of personal leave for WNPRC employees in need of catastrophic leave due to serious medical conditions (either for personal or family needs).

Specific Aim 7: Fulfill the Specific Aims of each unit within the Operational Services Division.

Please see attached progress reports from each unit which includes specific aims, accomplishments, goals and future plans.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5890

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Associate Director	Institutional Base Salary	EFFORT			14,393.00	4,793.00	19,186.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **19,186.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	**0.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**19,186.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**19,186.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	19,186.00	7,099.00
		Total Indirect Costs	**7,099.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**26,285.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Administrative Services Unit

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1: Collaborate with the Electronic Health Record Services (ES) Unit to further develop and implement the financial module within the LabKey server. The implementation of this financial module, which is in use currently at the Oregon National Primate Research Center (ONPRC), will help streamline the chargeback and billing process for all WNPRC service units, expand reporting features, and provide a more robust audit trail of financial and grant activity.

Specific Aim 2: Collaborate with the Compliance and Training Unit and the ES Unit to develop and implement a user-friendly system within the LabKey server for enhanced tracking of facility access requests and the corresponding compliance requirements. The development and implementation of a centralized tracking system will increase efficiency and efficacy of communication across and between WNPRC units, as well as with the investigators and research staff.

Specific Aim 3: Implement and ensure compliance with new policies and procedures initiated by the UW-Madison Office of Human Resources (OHR) as part of Human Resources (HR) Design, including but not limited to Recruitment, Selection, and Assessment of Academic, Faculty, Limited, and University Staff Employees (OHR Policy 3.01); New Employee Onboarding (OHR Policy 6.01); and Performance Management for Managers and Supervisors (OHR Policy 8.01).

Specific Aim 4: Collaborate with the IDS Unit to develop and implement a new, user-friendly procurement request module within the LabKey server to help streamline the process for staff to submit requests for supplies, equipment (minor and capital), and non-UW services needed for the operational and research needs of the Center. The development and implementation of such a system will expand reporting features and provide a more robust audit trail of financial and grant activity.

Specific Aim 5: In collaboration with the Colony Management team, the Compliance and Training Unit, and key UW-Madison departments, such as Environmental Health & Safety (EHS) and University Health Services (UHS), expand the implementation of ergonomic practices and principles wherever and whenever possible to mitigate occupational safety risks to employees.

Specific Aim 6: In consultation with staff within the Office of Industrial Partnerships (OIP), tighten the Terms and Conditions of Fee-for-Service Agreements to include language aimed at ensuring recipient organizations understand their responsibilities should the recipient share nonhuman primate biological materials with other researchers.

Specific Aim 7: Develop and implement a Quality Improvement Process (QIP) Plan to review operational services across the Center and to identity areas for increasing efficiency and effectiveness.

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: B2_Accomplishments_Administrative Srvcs.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: Collaborate with the Information and Data Services (IDS) Unit (formerly the Electronic Health Record Services Unit) to further develop and implement the financial module within the LabKey server. The implementation of this financial module, which is in use currently at the Oregon National Primate Research Center (ONPRC), will help streamline the chargeback and billing process for all WNPRC service units, expand reporting features, and provide a more robust audit trail of financial and grant activity.

- Given the delays due to procurement policies, implementation has been moved from July 1, 2018 to July 1, 2019.

Specific Aim 2: This Specific Aim was transitioned to the Compliance and Training Unit in April 2017, as responsibility for facility access was moved from the Human Resources team to the Compliance team

Specific Aim 3: Implement and ensure compliance with new policies and procedures initiated by the UW-Madison Office of Human Resources (OHR) as part of Human Resources (HR) Design, including but not limited to Recruitment, Selection, and Assessment of

Academic, Faculty, Limited, and University Staff Employees (OHR Policy 3.01); New Employee Onboarding (OHR Policy 6.01); and Performance Management for Managers and Supervisors (OHR Policy 8.01).

• The HR team will continue to utilize the online Talent Recruitment and Engagement Management System (TREMS) to streamline communication with applicants and hiring managers at all stages of the recruitment process.
• The WNPRC HR team will continue to utilize the Employee Management System (EMS) developed by the Office of the Vice Chancellor for Research and Graduate Education (OVCRGE) HR office, and to train managers/supervisors on its use.
• The WNPRC HR team will continue to work with all managers/supervisors to ensure that all employees are being reviewed at least twice per year in accordance with UW-Madison policy.
• UW-Madison Office of Human Resources will continue to work on a Title and Total Compensation (TTC) Study. The HR team will continue to work closely with Jurmu to reassess equity across job categories until the TTC is fully implemented, a target for which has not been released. One critical step in this process is for the revision of all employees' position descriptions, and the updated target date for this is the summer of 2019 (original target was early in 2018).
• Recently, the WNPRC HR team began work on transitioning to the online Employee Self-Service (ESS) module for time and absence tracking. The HR team is researching options for a web-based "time clock" to assist hourly paid staff in the accurate and timely data entry of their hours. The transition to ESS is being phased and the HR team has established a goal of July 1, 2019 to have it implemented for all Center employees.

Specific Aim 4: Collaborate with the IDS Unit to develop and implement a new, user-friendly procurement request module within the LabKey server to help streamline the process for staff to submit requests for supplies, equipment (minor and capital), and non-UW services needed for the operational and research needs of the Center. The development and implementation of such a system will expand reporting features and provide a more robust audit trail of financial and grant activity.

• The development of a procurement request module will start after the successful rollout of the financial module. Due to the delay with the financial module, the projected timeline is to launch the procurement module project in late fall 2019 with LabKey.

Specific Aim 5: In collaboration with the Colony Management team, the Compliance and Training Unit, and key UW-Madison departments, such as Environmental Health & Safety (EHS) and University Health Services (UHS), expand the implementation of ergonomic practices and principles wherever and whenever possible to mitigate occupational safety risks to employees.

• Another initiative that has been launched is a WNPRC "U-Well" Committee as part of an overall UW-Madison "campus-wide effort committed to benefitting and promoting wellness on campus." A joint effort between the WNPRC HR team and the Compliance/Training Unit will be launched in the spring of 2019, including a survey of all employees to assess what activities are of most interest.

Specific Aim 6: In consultation with staff within the Office of Industrial Partnerships (OIP), tighten the Terms and Conditions of Fee-for-Service Agreements to include language aimed at ensuring recipient organizations understand their responsibilities should the recipient share nonhuman primate biological materials with other researchers.

• The Office of Industrial Partnerships was dissolved by the UW-Madison Research and Sponsored Programs (RSP) office in the summer of 2018, and the work of OIP was transitioned to pre-award staff in RSP. In September 2018, Jurmu and her staff worked with an RSP team member to add clauses on "Export Control" and on "Compliance with Laws" to the WNPRC standard Terms and Conditions. The "Compliance with Laws" clause includes language on the "Convention on International Trade in Endangered Species (CITES) of Wild Fauna and Flora." Therefore, this SA is completed.

Specific Aim 7: Develop and implement a Quality Improvement Process (QIP) Plan to review operational services across the Center and to identity areas for increasing efficiency and effectiveness.

• Phase 2 for the Animal Services Division will be completed in early March 2019. The exact configuration for Phase 3 is being finalized with an expected completion in summer 2019. Once the reconfiguration of Room 210 has been completed, a review of other areas will be conducted to try to maximize the utilization of the Center's space.

ADMINISTRATIVE SERVICES UNIT

Unit Head: Redacted by agreement

Accomplishments

Specific Aim 1: Collaborate with the Information and Data Services (IDS) Unit (formerly the Electronic Health Record Services Unit) to further develop and implement the financial module within the LabKey server. The implementation of this financial module, which is in use currently at the Oregon National Primate Research Center (ONPRC), will help streamline the chargeback and billing process for all WNPRC service units, expand reporting features, and provide a more robust audit trail of financial and grant activity.

As noted in the Yr 56 RPPR, a contract was executed with LabKey in August 2017 to develop the financial module, and the project kicked off in September 2017. Unfortunately, the project had to be halted in February 2018 when a reassessment of the budget became necessary and, due to State of Wisconsin procurement policies, UW-Madison Business Services determined that a formal Request for Bid (RFB) was required before further development work could be undertaken. UW-Madison Purchasing Services released the RFB on June 27, 2018. LabKey was the only bidder and was awarded the contract on July 18, 2018. The project was recommenced in August 2018. Given the delays due to procurement policies, implementation has been moved from July 1, 2018 to July 1, 2019.

While the project is adapting the financial module developed at the ONPRC, there is one significant difference in billing practices that has resulted in further refinement for the WNPRC. At the ONPRC, their host institution handles external billing for the Primate Center, including accounts receivable activity. At the WNPRC, all billing, including external clients, is handled by Primate Center staff, including accounts receivable monitoring and follow-up on delinquent payments. This has necessitated additional programming for the WNPRC's version of the financial module.

Specific Aim 2: Collaborate with the Compliance and Training Unit and the IDS Unit to develop and implement a user-friendly system within the LabKey server for enhanced tracking of facility access requests and the corresponding compliance requirements. The development and implementation of a centralized tracking system will increase efficiency and efficacy of communication across and between WNPRC units, as well as with the investigators and research staff.

As reported in the Yr 56 RPPR, this Specific Aim was transitioned to the Compliance and Training Unit in April 2017, as responsibility for facility access was moved from the Human Resources team to the Compliance team

Specific Aim 3: Implement and ensure compliance with new policies and procedures initiated by the UW-Madison Office of Human Resources (OHR) as part of Human Resources (HR) Design, including but not limited to Recruitment, Selection, and Assessment of Academic, Faculty, Limited, and University Staff Employees (OHR Policy 3.01); New Employee Onboarding (OHR Policy 6.01); and Performance Management for Managers and Supervisors (OHR Policy 8.01).

This is a dynamic aim for the HR team, as UW-Madison continues to develop and refine policies and procedures as part of HR Design, which was effective July 1, 2015 and defined as "a campus-wide effort to build a more efficient and effective UW-Madison human resource system that best serves the needs of a public university in the 21st century." A few key accomplishments include:

- The HR team continues to utilize the online Talent Recruitment and Engagement Management System (TREMS) to streamline communication with applicants and hiring managers at all stages of the recruitment process. Additionally, UW-Madison upgraded the system to allow it to be used for advertising and recruiting for student hourly workers, allowing for better integration of recruitment processes across all job types.
- The WNPRC HR team continues to utilize the Employee Management System (EMS) developed by the Office of the Vice Chancellor for Research and Graduate Education (OVCRGE) HR office, and to train managers/supervisors on its use. This system is designed to help manage the integration of new

employees into departments/centers and allows for tracking of critical onboarding tasks, such as dissemination of key policies to new employees.

- In fall 2017, UW-Madison rolled out a new online system, Performance Management and Development Program (PMDP), for completing performance management of all employees. The WNPRC, along with the other research centers on campus, were among the first adopters of the new system. The HR team continues to work with all managers/supervisors to ensure that all employees are being reviewed at least twice per year in accordance with UW-Madison policy. Unfortunately, the system does not have robust tracking tools as of yet; therefore, the HR team works with managers/supervisors to manually track deadlines to ensure compliance with the policy.
- UW-Madison Office of Human Resources continues to work on a Title and Total Compensation (TTC) Study. Since this study has been in development for some time, the WNPRC HR team completed several equity reviews, including for Animal Research Technicians (ARTs), Laboratory Technical Support Supervisors (Colony Management Supervisors), and Research Specialists. The HR team will continue to work closely with Redacted to reassess equity across job categories until the TTC is fully implemented, a target for which has not been released. One critical step in this process is for the revision of all employees' position descriptions, and the updated target date for this is the summer of 2019 (original target was early in 2018). The WNPRC HR team will continue to flex to meet the Center's goals, as well as the University's.
- Recently, the WNPRC HR team began work on transitioning to the online Employee Self-Service (ESS) module for time and absence tracking. ESS allows hourly-paid staff to directly enter their "punch in/punch out" times instead of completing paper timesheets that must be manually entered by HR staff. In addition, all employees will enter their absences directly, eliminating the need for paper leave reports for monthly paid employees. The HR team is researching options for a web-based "time clock" to assist hourly paid staff in the accurate and timely data entry of their hours. The transition to ESS is being phased and the HR team has established a goal of July 1, 2019 to have it implemented for all Center employees.

Specific Aim 4: Collaborate with the IDS Unit to develop and implement a new, user-friendly procurement request module within the LabKey server to help streamline the process for staff to submit requests for supplies, equipment (minor and capital), and non-UW services needed for the operational and research needs of the Center. The development and implementation of such a system will expand reporting features and provide a more robust audit trail of financial and grant activity.

The development of a procurement request module will start after the successful rollout of the financial module. Due to the delay with the financial module, the projected timeline is to launch the procurement module project in late fall 2019 with LabKey.

Specific Aim 5: In collaboration with the Colony Management team, the Compliance and Training Unit, and key UW-Madison departments, such as Environmental Health & Safety (EHS) and University Health Services (UHS), expand the implementation of ergonomic practices and principles wherever and whenever possible to mitigate occupational safety risks to employees.

A member of the HR team continues to participate in the WNPRC Safety Committee to assist in implementing new or modified practices to minimize occupational safety risks to employees. Additionally, Administrative Services Unit staff continue to purchase ergonomic mice, mouse pads, and wrist rests, standing desks, and anti-fatigue mats for staff who wish to use them to improve their wellness at work.

Another initiative that has been launched is a WNPRC "U-Well" Committee as part of an overall UW-Madison "campus-wide effort committed to benefitting and promoting wellness on campus." The UWell program defines "wellness in its seven dimensions: physical, spiritual, career/academic, emotional, social/cultural, financial, and environmental." Efforts by a formal committee have been delayed due to staff medical leaves. A joint effort between the WNPRC HR team and the Compliance/Training Unit will be launched in the spring of 2019, including a survey of all employees to assess what activities are of most interest. While the WNPRC UWell Committee has not been as active as intended, WNPRC Administrative Services staff organized a step challenge to help Center employees participating in the State of Wisconsin's StayWell program, which provides

a monetary incentive to State employees who meet required physical activity milestones, such as logging 1 million steps in the calendar year or completing a 21-day online meditation module.

Specific Aim 6: In consultation with staff within the Office of Industrial Partnerships (OIP), tighten the Terms and Conditions of Fee-for-Service Agreements to include language aimed at ensuring recipient organizations understand their responsibilities should the recipient share nonhuman primate biological materials with other researchers.

The Office of Industrial Partnerships was dissolved by the UW-Madison Research and Sponsored Programs (RSP) office in the summer of 2018, and the work of OIP was transitioned to pre-award staff in RSP. In September 2018, Redacted by and her staff worked with an RSP team member to add clauses on "Export Control" and on "Compliance with Laws" to the WNPRC standard Terms and Conditions. The "Compliance with Laws" clause includes language on the "Convention on International Trade in Endangered Species (CITES) of Wild Fauna and Flora." Therefore, this SA is completed.

Specific Aim 7: Develop and implement a Quality Improvement Process (QIP) Plan to review operational services across the Center and to identity areas for increasing efficiency and effectiveness.

The number of active research projects being supported by the WNPRC has grown tremendously and, with this, the number of staff needed to accomplish the Center's aims across all Divisions is increasing, as well. At this time, the Center needs additional space, not only for nonhuman primates, but also for employees and for storage. Since early 2018, Redacted by agreement have been working with one of the UW-Madison approved vendors to reconfigure space in Room 210 of Building 2 that has been underutilized. Phase 1 for the Administrative Services Unit has been completed, and Phase 2 for the Animal Services Division will be completed in early March 2019. The exact configuration for Phase 3 is being finalized with an expected completion in summer 2019. Once the reconfiguration of Room 210 has been completed, a review of other areas will be conducted to try to maximize the utilization of the Center's space.

Other key accomplishments for the Administrative Services Unit:

- WNPRC HR team members, Redacted by agreement, passed their Society for Human Resource Management (SHRM) certification exams in February 2018;
- Redacted by agreement Grants Manager, completed the "Principles of Supervision and Management (PSM)" course offered through the UW-Madison OHR in March 2018;
- Redacted by agreement joined the team on April 30, 2018 as an HR Assistant, transferring from the School of Medicine and Public Health, Department of Cardiovascular Medicine where she was a Medical Program Assistant-Senior;
- Redacted by agreement were promoted from HR Assistant Advanced positions to HR Manager positions in June 2018;
- Redacted by agreement joined the team on June 11, 2018 as a University Services Program Associate (USPA) to assist with grants and purchasing activity, transferring from a limited term position as a University Services Associate 1 at the UW-Madison Memorial Union;
- Redacted by agreement Senior Grants Manager, completed the "Principles of Supervision and Management (PSM)" course offered through the UW-Madison OHR in October 2018;
- In December 2018, Redacted by agreement was nominated by several Primate Center faculty and staff for the 2018 HR@UW Business Partnership Award, which is meant to recognize and celebrate the dedicated, but often unnoticed, work of those who model the spirit of partnership while fostering HR service delivery on campus; and
- Throughout 2018, the WNPRC HR team worked with 17 different faculty and staff to secure the donation of 952.5 hours of personal leave for WNPRC employees in need of catastrophic leave due to serious medical conditions (either for personal or family 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

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5891

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Unit Head	Institutional Base	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						
2	Undergraduate Students	EFFORT			10,100.00	314.00	10,414.00
9	Secretarial/Clerical				279,857.00	110,648.00	390,505.00
11	**Total Number Other Personnel**					**Total Other Personnel**	**400,919.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**400,919.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	11,351.00
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	93,812.00
Total Other Direct Costs	**105,163.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**506,082.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	506,082.00	187,250.00
		Total Indirect Costs	**187,250.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**693,332.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Information Technology and Systems Services

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The objectives of the Information Technology and Systems Services (ITSS) Unit are to provide data management, computer services, and networking services to support research, service units, and daily operations of the Wisconsin National Primate Research Center (WNPRC). The ITSS Unit is led by Redacted by agreement who oversees the provision of these services for the core activities within the Director's Office, and the Divisions of Animal Services, Operational Services, and Research Services. ITSS Unit will also continue striving to optimize the Center's information technology infrastructure, as it administers desktop computers, provides network and cyber security services, provides general-purpose timesharing service and file access on UNIX hosts, and provides graphics and digital image processing to investigators, staff, and affiliates.

To enhance the ITSS Unit's ability to meet these objectives the next grant period, the following Specific Aims are proposed:

Specific Aim 1: Administration - To leverage University of Wisconsin-Madison (UW-Madison) services to improve the cyber infrastructure of the WNPRC. By taking advantage of UW-Madison campus machine virtualization, tiered storage, collaboration (email and calendaring), network, and security services, the ITSS Unit will continue to save costs in both time and money allowing the Unit to quickly react to the changing needs of the researchers, administrators, and service units of the WNPRC.

Specific Aim 2: Support - To continue to support the Electronic Health Record Services (ES) Unit by administering the LabKey production, test, and staging systems environment; provide comprehensive end-user support including troubleshooting hardware, software, and networking issues; managing device upgrades; and provide centralized backups of computers and servers along with providing solutions to enhance the integration between local services, such as the Electronic Health Records (EHR) systems, the LabKey platform, and UW-Madison centralized services, including programming custom software and scripts as needed.

Specific Aim 3: Security - To emphasize secure access to data and intellectual property using robust operating systems, networking hardware, and software.

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: B.2. Accomplishments_ITSS_1.16.19 rev1.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:
Migrate local Domain Name Services to the UW shared DNS system.
Participate in the UW Mobile Device Management pilot program to manage our tablets and smartphones. Adopt MDM if pilot is successful for all devices including desktop computers and laptops.
Plan migration of local directory system LDAP to UW Active Directory system.

Specific Aim 2
Assist ES Unit in use of "Docker" containers to streamline the process of upgrading the EHR / LabKey software system.
Assist ES Unit in implementation of the new LabKey Financials module.
Work with ES Unit and LabKey to plan for use of UW Active Directory system.

Specific Aim 3
Work with UW Cybersecurity Office and DoIT to migrate to the next generation firewall service.
Work with UW Cybersecurity Office on new security gap analysis.

INFORMATION TECHNOLOGY & SYSTEM SERVICES UNIT (ITSS)

Unit Head Redacted by agreement

Accomplishments

ITSS continues to administer the computer systems and servers used by the EHR production and development platforms. All EHR servers are deployed on the UW Campus Computing Infrastructure (CCI) as virtual machines (VM). The Dell PowerEdge Enterprise Server was retired in 2018 and replace by a VM.

ITSS continues to administer the two WordPress virtual machines one machine for development and the other machine is the main WNPRC production website. The ITSS web administrator provides support and training to the WNPRC Outreach specialist and to the Research Services Division.

ITSS continued to support the Center's web-based business systems for charge entry, invoicing, reporting, and purchase order requests. In 2017 a project to migrate the systems to the EHR Labkey platform was initiated led by the Administrative Services Unit and supported by ITSS. LabKey corporation is providing the development support which is based on modules initially developed by Oregon National Primate Research Center. Development continued throughout 2018 on the Financials module.

ITSS continues to work with UW Madison Division of Information Technology (DoIT) to leverage campus centralized services. In 2018 we started using the UW's centralized Domain Name Service (DNS) and Dynamic Host Configuration Protocol (DHCP) service. Two members of the ITSS Unit were trained in the use of the web-based administration platform. This service enabled us to retire two servers that provided Domain Name Service (DNS) to the WNPRC network and to turn off the DHCP service on another server.

ITSS continues to follow the replacement cycle for servers and desktop systems. Servers have a lifetime of 4-6 years on average. Most physical servers are being replaced by CCI virtualized servers as they age out. Desktop systems are replaced by cascading three- to four-year-old systems to less critical locations before they are obsolete. Between January 1 and December 31, 2018, ITSS cycled 27 new desktop computers and 15 new laptop computers into operation.

In 2018 the WNPRC upgraded the technology in our main conference room. The project brings state of the art video and web conferencing to the Center. The room can be divided into two separate rooms each providing audio and video services. Table top microphones allow everyone in the room to be heard locally by providing audio uplift to the rooms speaker system and remotely over the network. The system is controlled by a wall mounted tablet computer.

ITSS collaborates with the UW's Cyber Security team to protect the Center's network though use of a new web-based firewall service. This new service enables us to design security policies based on analysis of all traffic including applications and content. The new system was implemented in May of 2018. We rolled out the system to each of our virtual local area networks (VLAN) at our 4 physical locations and to our virtual network on the UW CCI starting and May, 2018 and completed the roll-out in October, 2018. Two ITSS Unit members were trained to manage the firewall system.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5892

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Unit Head	Institutional Base	EFFORT			89,252.00	29,721.00	118,973.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **118,973.00**

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						
1	Undergraduate Students	EFFORT			5,050.00	157.00	5,207.00
	Secretarial/Clerical						
3	IT Specialist				109,818.00	38,837.00	148,655.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**153,862.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**272,835.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	15,814.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. iPads for Veterinary Services Division	7,700.00
Total Other Direct Costs	**23,514.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**296,349.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	296,349.00	109,649.00
		Total Indirect Costs	**109,649.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**405,998.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Facilities Management and Instrument Maker Shop Services

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

1. To monitor and maintain all aspects of WNPRC facility operations and coordinate systems upgrades.
2. Participate in the planning and execution of all facility renovation and construction initiatives at the WNPRC.
3. To support research and colony management staff with the design and fabrication of specialized equipment.
4. To prioritize and coordinate repairs of equipment, minimizing the interruption of science.
5. To continue on extensive animal holding room refurbishing projects.
6. To focus on staying compliant and surpassing all regulatory guidelines along with improving husbandry and housing operations.
7. To provide support and service in the design and construction of new quarantine facility.

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: B.2. Accomplishments_Facilities and Shop.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?

1. To monitor and maintain all aspects of WNPRC facility operations and coordinate systems upgrades.
Annex building 0782 is slated for an upgraded fire alarm system in 2019. We were told last year that we should be next on the list for this campus-wide initiative. Campus will be funding this project. The upgraded system would include the re-location of the annunciator panel which is currently located Specific Animal Location

Annex B181: Building main backflow prevention devises need to be reconfigured and replaced.

2. Participate in the planning and execution of all facility renovation and construction initiatives at the WNPRC.
Future plans include completing both Center projects currently under construction. This includes Specific and Specific Animal Location

Generator projects for both the Annex and Center: Plans include approving final design and budget for the Annex generator with hopes of a late 2019 start date. Center Building goals include staging or combining the chilled water extension and standby generator project together in the most logical manner.

3. To support research and colony management staff with the design and fabrication of specialized equipment.
Develop a new sliding door panel for our BRITZ Flexagon holding pens. Existing panels are difficult to operate and breaking. The new panel will assist in separating and transferring animals more efficiently.

4. To prioritize and coordinate repairs of equipment, minimizing the interruption of science.
New pultruded fiberglass grating was researched, specified and ordered for our rack washer exit area. Upon delivery the new grating will be installed.

5. To continue on extensive animal holding room refurbishing projects.
As opportunities arise, holding rooms will be emptied and cleaned for assessment and scheduling of required repairs and renovations.

6. To focus on staying compliant and surpassing all regulatory guidelines along with improving husbandry and housing operations.
Specific Animal Location It was recommended at our last safety inspection that we add two flammable cabinets. We plan to reduce our inventory of flammables, tabulate a working list and update our MSDS binder. Cabinet sizes will be determined and purchased.

7. To provide support and service in the design and construction of new quarantine facility.
We have requested the landlord to provide a roof extension to the front of the building to block snow and ice build-up, planning on this being completed in 2019.

FACILITIES & SHOP SERVICES (SHOP)

Unit Head: Redacted by agreement

Accomplishments

1. To monitor and maintain all aspects of WNPRC facility operations and coordinate systems upgrades.

Annex B181 mechanical room: 3 high efficiency water softeners were installed replacing the original 2. This will reduce salt usage and better serve the high-water demand introduced by the cage washer and holding room washdowns.

WNPRC Shop room 303: New frequency drive 20” drill press, Passivation style weld cleaning system and additional TIG welder were all purchased and put into use in 2018.

Center loading dock 6: New Ice flaking machine was researched, purchased and installed.

2. Participate in the planning and execution of all facility renovation and construction initiatives at the WNPRC.

Listed below are several projects in different phases within our facilities. Given the nature of our work, close attention is paid to scheduling work, obtaining access and meeting regulatory requirements. The Facilities and Shop unit is very knowledgeable in the operations and common goals here at the Center. The unit is very involved in the planning and execution of all such projects.

Specific Animal Location renovation project 0526-1602: Existing lab will be renovated to include 3 new RF (radio frequency) shielded research chambers. Under close direction from the unit, UW Physical Plant CRS (campus renovation services) will conduct the work. This project is under construction and scheduled for completion in April 2019.

Specific Animal Location renovation project 0526-1701: Renovate lab space to accommodate new autoclave. This project is under construction and scheduled for completion in March 2019.

Center Project 0526-1601: Provide standby, back-up power by installing a 350kW generator. A&E firm Mead Hunt was awarded the contract. Budget and design are approved with a tentative construction start date of April 2019. Current start date is heavily impacted by project 18A1Z: Primate Center Chilled Water Extension. University FP&M, WNPRC and The Department of Administration staff are working on a comprehensive plan to coordinate both projects.

Annex DFD (division of facilities development) project 18L2G: Provide standby, back-up power by installing 200kW generator. This project has an accepted budget of 234K and is in the design phase.

Annex Project 0782-1701: Provide controlled cooling to animal chow storage room. This project was completed October 2018.

3. To support research and colony management staff with the design and fabrication of specialized equipment.

The Shop recently fabricated the following pieces of equipment to match existing. The original designs were developed by the WNPRC Shop. The equipment was requested by Colony Management.

: 3 scale carts.
: 10 single marmoset cages.
: 8 enrichment devise storage / wash racks.

The Shop designed and built the following pieces of specialized research equipment based on specific PI and vendor requirements. The Shop provided a design and estimate prior to fabrication.

: Marmoset metabolism 4 unit rolling rack.
: Rhesus metabolic metabolism chamber.
: Marmoset indirect calorimetry chamber.

In a continuing effort to reduce primate escapes the shop developed a prototype transfer box equipped with a multi-position hook. Staff are able to hook the transfer box to multiple different cages fronts aiding in holding the transfer box in position.

Recently made novel modifications to a CatWalk XT gait analysis system providing Marmoset nesting box interface.

4. To prioritize and coordinate repairs of equipment, minimizing the interruption of science.

Center walk–in -20 freezer was upgraded with a new compressor and control lines.

Annex rack washer B171A: Hot water heater tube and shell bundle was removed and de-limed. New auxiliary heat exchanger was researched, specified and purchased. Installation should be completed next month.

5. To continue on extensive animal holding room refurbishing projects.

Specific Animal Location animal holding hallways: Approximately sq. ft. of dropped ceiling grid and tile were replaced. Some of the existing grid was starting to rust. New all-aluminum 24” x 24” grid was installed along new 5/16” PVC ceiling tile. Tradespeople include carpenter, electric, sheet metal and paint.

Center holding pens Specific Animal Location received all new stainless-steel drinking lines. The existing PVC lines had signs of slow leaks and calcification. New weighted drain covers were also designed and built for the pens in preparation for a new study introducing bedding to the pen floors. Additional pass thru doors were fabricated and installed between pens Specific Animal This was in preparation for a large incoming family of Cynos. The pass thru doors are operated outside of the pen allowing staff to separate animals.

6. To focus on staying compliant and surpassing all regulatory guidelines along with improving husbandry and housing operations.

Specific Animal Location were upgraded with the addition of electronic differential pressure transducers. This will allow room pressures to be monitored and alarmed in addition to the existing visual magnehelic gauge.

7. To provide support and service in the design and construction of new quarantine facility.

BMQ Quarantine: Several housing pens and cages were disassembled and moved into a quarantine room to accommodate a large primate shipment. After the required quarantine the caging was moved back to its original location.

BMQ Quarantine: New office furniture was purchased and installed creating individual and group work stations.

SPECIAL PROGRESS:

WNPRC sent volunteers to Punta Santiago, Humacao, Puerto Rico to help with rebuilding efforts on Cayo Santiago after Hurricane Maria hit in September 2017. A team deployed in August 2018 included two members from the WNPRC Facilities and Shop Services Unit, Redacted by agreement They and colleagues from the other NPRCs rebuilt the island’s rain collection roof and monkey health-check corral. Research station staff had been transporting all of the monkeys’ fresh water by boat. They were transporting food, as well, because

the station's infrastructure was devastated and the hurricane had stripped the island of its vegetation. The rebuilding effort, called Project Monkey Island, is all about helping the people in the Punta Santiago community rebuild their lives, as well as helping the monkeys on Cayo Santiago.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Admin Core-5893

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Unit Head	Institutional Base Salary	EFFORT			67,542.00	28,705.00	96,247.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **96,247.00**

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	Instrument Maker / Mechanician	EFFORT			72,159.00	30,668.00	102,827.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**102,827.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**199,074.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	166,710.00
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	77,000.00
Total Other Direct Costs	**243,710.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**442,784.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	442,784.00	163,830.00
		Total Indirect Costs	**163,830.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**606,614.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Animal Services Division (Animal-Resources-001)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The Animal Services Division (ASD) of the WNPRC consists of the following six units and one core:

Colony Management Unit
Scientific Protocol Implementation Unit
Veterinary Services Unit
Behavioral Services Unit
Pathology Services Unit
Compliance and Training Unit
Nonhuman Primate Biological Materials Distribution Core

While each of the Units has its own individual Specific Aims, they work in unison and communicate on a daily basis as a centralized full service entity to fulfill the following over-arching Specific Aims of the Division:

Specific Aim 1: To provide for the daily medical, psychological, and husbandry needs of each nonhuman primate (NHP) living at the WNPRC from the moment of their conception or acquisition to the endpoint of their study or lifetime at the Center.

Specific Aim 2: To provide research support from the inception of a study (grant/IACUC protocol preparation) through experimental execution, data collection and analysis, and manuscript preparation/publication.

Specific Aim 3: To ensure the safety of all personnel working at the WNPRC with NHP or their tissues through the implementation of a rigorous and detailed training, re-training, and continuing education program.

Specific Aim 4: To ensure that all university, state, and federal laws, regulations, and guidelines governing the utilization of NHP in laboratory animal research are adhered to by all WNPRC personnel, investigators, and 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: Animal Services Division Report_02222019.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?

Please see related Unit Reports, which includes future goals for the next reporting period.

ANIMAL SERVICES DIVISION

UNIT REPORTS

DIVISION OVERVIEW AND SUMMARY OF ACTIVITIES

Division Head: Redacted by agreement **D.V.M., D.A.C.L.A.M.**

The **Animal Services Division** (ASD) consists of 6 units (Veterinary Services, Colony Management, Scientific Protocol Implementation, Pathology Services, Compliance and Training, and Behavioral Management) and one core (Nonhuman Primate Biological Materials Distribution). While each of the units has their own individual specific aims, they work in unison and communicate on a daily basis as a centralized full-service entity to fulfill the following over-arching goals of the Division:

1. To provide for the daily medical, psychological, and husbandry needs of each nonhuman primate (NHP) housed at the WNPRC from the moment of their conception or acquisition to the endpoint of their study or lifetime at the Center
2. To support the scientific needs of all investigators performing research at the WNPRC
3. To ensure the safety of all personnel working with NHP or their tissues at the WNPRC through the implementation of a rigorous and detailed training and re-training program
4. To ensure that all university, state, and federal laws, regulations, and guidelines governing the utilization of NHP in laboratory animal research are adhered to by all WNPRC personnel, investigators, and staff

The ASD also employs one divisional program assistant who executes a variety of administrative tasks (e.g., ordering and purchasing office supplies, making travel arrangements, taking meeting notes, submitting ASD charges to Operational Services, processing USDA transport documents, etc.) and three assistants to provide administrative support for NHP colony records and the WNPRC Electronic Health Records System (EHR).

The **Veterinary Services Unit** maintains four clear-cut specific aims in coordination with the overall aims of the ASD:

1. To provide consistent and exemplary clinical care to the nonhuman primate (NHP) colonies housed at the WNPRC
2. To provide excellent technical support for the investigators performing research at the WNPRC
3. To provide training for personnel working with NHPs at the WNPRC and at other institutions
4. To maintain continuous academic output

In pursuit of these aims over the current reporting period, the Veterinary Services Unit has performed the following tasks:

- Acquired and quarantined rhesus and cynomolgus macaques from outside sources
- Performed or provided support for clinical and research oriented imaging and surgical procedures
- Performed diagnostic procedures in the support of clinical health and research protocols
- Trained numerous undergraduates, veterinary technician students, veterinary students, and veterinarians
- Presented at professional meetings and co-authored manuscripts which were published in peer-reviewed journals

The **Colony Management Unit** maintains five specific aims in coordination with the overall aims of the ASD:

1. To provide a consistent and excellent husbandry program compliant with all laws, regulations, and guidelines governing the care of captive NHP utilized in research
2. To perform, document, and communicate daily health observations for the NHP colonies

3. To execute the delivery of environmental enrichment (food treats and manipulanda) to the NHP colonies
4. To support the clinical, behavioral, and research initiatives of the WNPRC by providing personnel to administer medical and experimental treatments, collect biological samples, transport animals and biological samples, and collect behavioral and scientific data in collaboration with the WNPRC SPI unit
5. To meet the animal subject requirements of investigators by managing the NHP breeding and stock colonies of the WNPRC

In pursuit of these aims over the current reporting period, the Colony Management Unit has performed the following tasks:

- Increased and enhanced the housing opportunities for the WNPRC's NHP colonies
- Contributed to AAALAC reaccreditation process for the UW-Madison
- Performed almost 500,000 daily health observations and greater than 6,000 reproductive cycle checks on WNPRC NHP
- Ensured that the food component of the WNPRC Environmental Enhancement Program was executed
- Assisted with the clinical and research initiatives of the WNPRC by collecting diagnostic samples and administering clinical and research treatments
- Provided the required number of animals to WNPRC PIs by maintaining the SPF rhesus breeding colony and acquiring needed animals from outside sources

The **Pathology Services Unit** maintains three specific aims in coordination with the overall aims of the ASD:

1. To continue to support NHP colony health and experimental investigations by providing rapid diagnosis of disease, characterization of current and developing NHP models, and collaborative development of experimental paradigms
2. To continue to curate and expand the NIA Tissue bank and manage the NHP Biological Materials Distribution (NHPBMD) Core in cooperation with SPI.
3. To serve as a resource for primate research, education, and conservation through participation in pathology consortium activities, scientific meetings, serving as advisors/consultants and training of students at the WNPRC

In pursuit of these aims over the current reporting period, the Pathology Services Unit has performed the following tasks:

- Performed a record number of routine diagnostic and screening procedures and developed innovative diagnostic methods and experimental techniques
- Processed nine donations to the NIA Tissue Bank and distributed 124samples to bank users
- Trained numerous veterinary students, veterinary residents, and veterinarians
- Presented at professional meetings and co-authored manuscripts which were published in peer-reviewed journals

The **Behavioral Services Unit** maintains four aims in coordination with the overall aims of the ASD:

1. To ensure the psychological well-being of the WNPRC NHP colonies
2. To provide research support to investigators
3. To provide NHP behavior training for personnel and NHP
4. To disseminate BSU research results through interaction with colleagues, scientific presentations and peer-reviewed publications

In pursuit of these aims over the current reporting period, the Behavioral Services Unit has performed the following tasks:

- Worked diligently to ensure that macaques held by the WNPRC were housed in social situations when possible
- Coordinated, enhanced, and expanded the WNPRC Environmental Enhancement Program

- Assisted WNPRC investigators with animal transfer training, shaping techniques, and positive reinforcement training to ensure the fulfillment of research objectives
- Provided prerequisite training in NHP behavior to all University staff that encounter NHP as a work requirement
- Presented at professional meetings and co-authored manuscripts which were published in peer-reviewed journals

The **Scientific Protocol Implementation Unit** maintains three aims in coordination with the overall aims of the ASD:

1. Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators
2. Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities
3. Contribute to NHP knowledge and translational models through academic output

In pursuit of these aims over the current reporting period, the Scientific Protocol Implementation Unit has performed the following tasks:

- Provided research support for numerous new experimental projects and presented multiple new potential projects to the WNPRC Executive Committee
- Added new research specialists to the unit and ensured that all new personnel were appropriately trained and senior specialists received appropriate continuing education opportunities
- Presented at professional meetings and co-authored manuscripts which were published in peer-reviewed journals

The **Compliance and Training Unit** maintains three aims in coordination with the overall aims of the ASD:

1. Educate, train, re-train and update training records for all WNPRC staff, support personnel, and visitors who may come into contact with NHP or their tissue to ensure that they understand and follow WNPRC standard operating procedures
2. Ensure a safe working environment for all WNPRC staff and students and to further develop the WNPRC Occupational Health and Safety Program (OHP) to maintain compliance with new and existing standards
3. Ensure that WNPRC personnel and facilities remain compliant with all institutional, state, and federal regulations governing the use of NHP in laboratory animal research

In pursuit of these aims over the current reporting period, the Compliance and Training Unit has performed the following tasks:

- Provided training and retraining to personnel including animal research technicians, research staff, personnel using primate tissues, visitors, vendors, and maintenance staff
- Ensured SOPs were routinely reviewed and updated
- Developed and enhanced the WNPRC Occupational Health and Safety Program with the assistance of the staff of the UW-Madison's Department of Environment, Health and Safety (UW Safety) and the University Health Services Occupational Medicine Department (UHS).
- Provided animal care and use protocol development and review services for all investigators utilizing NHP at the WNPRC

The **Nonhuman Primate Biological Materials Distribution (NHPBMD) Core** maintains four aims in coordination with the overall aims of the ASD:

1. To continue to maximize the investigative use of each animal scheduled for post-mortem examination
2. To increase the investigative usage of colony animals through minimally invasive manipulations
3. To coordinate complex collection needs through ante-mortem manipulations prior to sample collections for both *in vivo* and post-mortem sampling

4. To leverage and develop collaborative relationships with investigators, who may originally make simple research requests for pilot data, into projects utilizing full WNPRC research support in NHP models

In pursuit of these aims over the current reporting period, the **Nonhuman Primate Biological Materials Distribution Core** has performed the following tasks:

- Assigned NHP for the minimally invasive collection of biological samples, short-term experimental manipulations followed by specific post-mortem collection of tissues, traditional post-mortem sample collection, as well as access to numerous banked samples. This has resulted in significant peer reviewed publications and increased recognition of NHPBMD Core as a national resource

During the current reporting period, the divisional program assistant processed 8 CITES permits, 7 US Fish and Wildlife Service declarations, and 12 NHP Letters of Origin.

VETERINARY SERVICES UNIT

Unit Head: Redacted by agreement D.V.M., D.A.C.L.A.M.

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1- To provide consistent and exemplary clinical care to the nonhuman primate (NHP) colonies housed at the WNPRC

To achieve this aim, the well-trained and experienced veterinarians and veterinary technicians of the Veterinary Services unit utilize a rigorous preventative medicine program, an intensive daily health evaluation system, aggressive clinical and surgical practices, modern equipment, and a state-of-the-art electronic health records system to ensure that each NHP housed at the WNPRC receives excellent clinical care. The multifaceted health care program implemented by the unit ensures WNPRC investigators have access to healthy animals for their projects and that these animals' health is maintained once they are enrolled in experimental studies.

Specific Aim 2 – To provide excellent technical support for the investigators performing research at the WNPRC

The veterinarians and veterinary technicians of the Veterinary Services Unit provide intellectual and experienced-based pre-project input and technical project support to WNPRC investigators to achieve this aim. Prior to the initiation of a project (and often prior to the submission of a grant proposal), personnel from each unit of the Animal Services Division (including the Veterinary Services unit) meet with an investigator to discuss important aspects of experimental design such as species choice, equipment needs, specialized procedure requests, and experimental timelines to ensure that all aspects of the proposed study are feasible and will be executed properly. Once a project has been initiated, Veterinary Services unit personnel provide all the clinical care required for experimental animals (as outlined in Specific Aim 1), technical support for research procedures, and virtually all anesthesia support for experimental procedures (e.g., imaging, surgical procedures).

Specific Aim 3 - To provide training for personnel working with NHPs at the WNPRC and at other institutions

Through didactic and applied instruction, the unit provides training to residents, veterinary students and veterinary technical students, visiting veterinarians and veterinary technicians, WNPRC and visiting investigators, and scientific support staff to achieve this aim. Training ranges from a two- to three-year laboratory animal medicine residency program that prepares residents to sit for ACLAM boards to short externships that teach basic NHP medical techniques and research procedures to students and WNPRC research staff. Veterinary Services personnel also participate in various training teleconferences established by the National Primate Research Center consortia (i.e., NPRC Training Consortium Virtual Grand Rounds, Clinical and Surgical Techniques Working Group)

Specific Aim 4 - To maintain continuous academic output

To maintain the academic production of the unit, veterinary personnel strive to:

- Utilize clinical and research data collected at the WNPRC to disseminate information to their veterinary colleagues pertaining to novel techniques and treatments through the presentation of clinical case reports at national meetings and NPRC consortium teleconferences.
- Utilize clinical and research data collected at the WNPRC to publish case reports, retrospective studies, and hypothesis-based clinical research in peer-reviewed veterinary journals or collaborate with WNPRC investigators and contribute as co-authors on hypothesis-based studies published in peer-reviewed, high-impact journals.
- Determine the feasibility and their desire to gain accreditation in a veterinary specialty of his/her choosing.

Accomplishments

To fulfill the primary aim of the unit, (i.e., **providing consistent and exemplary clinical care to the WNPRC's NHP colonies**), the Veterinary Services unit employs a group of well-trained and experienced veterinarians and veterinary technicians to implement a multifaceted animal health program consisting of a rigorous preventative medicine program, an intensive daily health evaluation system, aggressive clinical and surgical practices, modern equipment, and a state-of-the-art electronic health records system. The animal health care program implemented by the unit also ensures WNPRC investigators have access to healthy animals for their projects and that these animals' health is maintained once they are enrolled in experimental studies.

The WNPRC maintains a veterinary staff consisting of 6 full-time veterinarians, 1 part-time veterinarian 10 full-time veterinary technicians, 2 part-time veterinary technicians, and 6 veterinary student assistants. Two full-time veterinary technicians were added to the unit and 1 full-time veterinarian left the unit during the current reporting period.

As part of the WNPRC's preventative medicine program, NHP obtained from domestic sources are held in quarantine for a minimum period of 30 days and newly imported foreign source animals or foreign source animals housed in the U.S. for less than one year are held for at least 90 days as outlined in WNPRC SOP 3.06 (Quarantine of Newly Arrived Nonhuman Primates). During the current reporting period, **210** newly acquired nonhuman primates underwent quarantine at the WNPRC's Blue Mounds Quarantine facility including **85** cynomolgus macaques and **125** rhesus macaques.

The Veterinary Services Unit currently maintains five functional operating rooms (one in WNPRC Building 1, two in Building 2, and two in the WIMR NHP vivarium) to support clinical and research procedures performed at the WNPRC. Maintaining surgical suites in three separate buildings virtually eliminates the need to transport an animal out of the building it is housed in to perform a major clinical or research surgical procedure, thus reducing the level of distress an animal may experience associated with the procedure. During the current reporting period, Veterinary Services personnel performed or provided support for **21** clinical surgeries (20 macaque, 1 marmoset) and **222** research surgical procedures (197 macaque, 25 marmoset). Veterinary personnel also provide support for a variety of research imaging procedures (e.g., MRI, CT, PET scans During the current reporting period, the unit provided anesthetic support for **227** research imaging procedures (CT- 11, PET – 38, MRI – 178).

The Veterinary Services Unit uses contemporary diagnostic modalities (e.g. ultrasonography and digital radiology) to perform clinical and experimental evaluations of NHP housed at the WNPRC. During the current reporting period, Animal Services personnel performed radiographic procedures on 248 animals and **4,143** ultrasound procedures (2,455 macaque, 1,688 marmoset).

The Veterinary Services Unit continues to maintain a multi-faceted training program for undergraduates, veterinary technician students, veterinary students, and veterinarians. The program, which consists of externships, paid student positions, and an ACLAM accredited Laboratory Animal Medicine Residency Training Program, provides training opportunities for individuals interested in an introduction to, or extensive experience with NHP medicine and husbandry. During the current reporting period, the WNPRC veterinary staff hosted two veterinary students through the externship program.

During the current reporting period, Veterinary Services personnel presented **11** presentations at national/international meetings in 2017, presented on **2** national teleconferences, and co-authored **7** manuscripts in peer-reviewed journals.

FUTURE GOALS

WNPRC Animal Health Program (Specific Aim 1)

The Veterinary Services Unit will continue to implement and hone each component of the PMP to ensure the ongoing health of all breeding colony, stock colony, and research assigned animals at the WNPRC. In collaboration with the EHR Services Unit, Veterinary Services personnel will continue to improve the capabilities of the EHR system to further reduce the need for paper records and to improve the ease and quickness of tracking clinical data.

Research Support (Specific Aim 2)

Over the next funding period, the Veterinary Services Unit will continue to work closely with the other units of the Animal Services Division and all other WNPRC Divisions to provide the Center's PIs with excellent research support to ensure the health of all experimental animals and the success of all experimental protocols.

Training (Specific Aim 3)

The Veterinary Services Unit will continue to advertise the externship-training program with the AVMA and AALAS to continue to recruit students interested in obtaining NHP experience. The unit will also continue to offer paid veterinary student assistant positions to UW veterinary students who can make a multi-year commitment.

Academic Output (Specific Aim 4)

Redacted by agreement will continue to expect each veterinarian employed by the unit to present at one national conference per year. In addition, Redacted by agreement will also expect and encourage the veterinary technicians employed by the unit to attend and present at appropriate meetings. With the assistance of Redacted by agreement and in collaboration with Redacted by agreement of the SPI unit and the core and affiliate PIs of the Center, Dr. Capuano will ensure that WNPRC veterinary personnel have continuing opportunities to hone their skills as pivotal research collaborators which should increase their opportunities to be first author or co-authors on peer-reviewed manuscripts over the next grant cycle. Redacted by agreement will provide ample opportunity for Redacted to complete his research project and will allow Redacted by agreement to study for the ACLAM Boards over the next funding period to ensure they becomes board certified.

COLONY MANAGEMENT UNIT

Unit Head: Redacted by agreement

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1 - To provide a consistent and excellent husbandry program compliant with all laws, regulations, and guidelines governing the care of captive NHP utilized in research

The primary goal of the Colony Management Unit (CM) of the WNPRC is to provide the highest quality animal husbandry program for the NHP colonies of the Center. The main components of the husbandry program include the provision of food and water, consistent and thorough sanitation of the NHP enclosures and support areas, and the implementation of a rigorous pest management program in collaboration with a commercial vendor. The husbandry program is supervised by a colony manager and five animal care supervisors with extensive NHP husbandry experience.

Specific Aim 2 - To perform, document, and communicate daily health observations for the NHP colonies

An Animal Research Technician (ART) of the CM evaluates each animal in the WNPRC's NHP colony a minimum of two times per day for evidence of disease or injury. This information is crucial to the well-being of the colony as it is used by the WNPRC Veterinary Staff to triage animals that may require clinical treatment. Each ART undergoes intensive instruction from WNPRC supervisors, Compliance and Training, and Behavioral Services Unit (BSU) personnel to ensure that they are able to identify common and abnormal behaviors exhibited by captive NHP.

Specific Aim 3 - To execute the delivery of environmental enrichment (food treats and manipulanda) to the NHP colonies

The staff of CM play a pivotal role in assisting the BSU with implementing the WNPRC Environmental Enhancement Plan (EEP) by delivering a majority of the edible and inanimate enrichment objects to the NHP colonies of the center. The ARTs also execute the remainder of the food-based portion of the EEP by offering fruit or vegetable pieces to the NHPs each day and by preparing and delivering a majority of the foraging opportunities offered to the colonies each week.

Specific Aim 4 - To support the clinical, behavioral, and research initiatives of the WNPRC by providing personnel to administer medical and experimental treatments, collect biological samples, transport animals and biological samples, and collect behavioral and scientific data in collaboration with the WNPRC SPI unit

Colony Management personnel play a critical support role for the clinical, behavioral, and research units of the WNPRC. The ARTs administer a majority of the clinical treatments prescribed by veterinary staff and, in collaboration with the Scientific Protocol Implementation (SPI) and Veterinary Services Units (VS), ARTs are also responsible for weighing animals, administering experimental agents, collecting tissue samples, and collecting data for various experimental protocols and clinical evaluation.

Specific Aim 5 - To meet the animal subject requirements of investigators by managing the NHP breeding and stock colonies of the WNPRC

In collaboration with the other units of the Animal Services Division, CM personnel are responsible for maintaining the NHP colonies of the Center by utilizing contemporary methods to track and maintain the genetic integrity of breeding populations and by breeding or purchasing animals to fulfill the needs of investigators.
of investigators.

Accomplishments

<u>Specific Aim 1</u> - To provide a consistent and excellent husbandry program compliant with all laws, regulations, and guidelines governing the care of captive NHP utilized in research

- CM personnel performed daily cleaning, feeding, and bi-weekly cage sanitation for the entire WNPRC population of nonhuman primates, which consists of, on average, 1120 rhesus macaques, 188 cynomolgus macaques, and 258 marmosets during the reporting period.
- In collaboration with the Behavioral Services Unit (BSU), CM has helped introduce 122 animals into social breeding groups during the reporting period.
- To help support the Environmental Enhancement Plan (EEP), CM has placed 131 c-tunnels and 298 cage extensions to enhance the housing environment for the macaque colonies in Building 2 and BMQ during the reporting period.

<u>Specific Aim 2</u> - To perform, document, and communicate daily health observations for the NHP colonies

- CM submitted 755,164 daily observation reports on individual animals that needed to be addressed by the WNPRC veterinary and/or Behavioral Management staff. These morning and afternoon health observations are pivotal to ensuring that clinically compromised animals receive rapid and appropriate care during this reporting period.
- During this same time period, CM personnel performed 121,629 menses checks on female macaques. Data from these menstrual checks is used to populate monthly menstruation tables for each female animal in the macaque colony. This information is extensively used by the rhesus breeding coordinator to determine the most appropriate time to breed an animal and to increase the possibility of conception. In addition, the data on stock animals is used by investigative groups for reproductive, neurological, and infectious disease research.

<u>Specific Aim 3</u> - To execute the delivery of environmental enrichment (food treats and manipulanda) to the NHP colonies

- CM personnel continue to support, up to six days per week whenever possible, foraging opportunities for the entire colony at the WNPRC.
- In addition to the foraging opportunities listed above, CM personnel delivered 958 additional foraging opportunities to animals exhibiting self-injurious behavior or recovering from surgery/injuries to assist in the improvement of their psychological wellbeing and physical recovery.

<u>Specific Aim 4</u> - To support the clinical, behavioral, and research initiatives of the WNPRC by providing personnel to administer medical and experimental treatments, collect biological samples, transport animals and biological samples, and collect behavioral and scientific data in collaboration with the WNPRC SPI unit

- CM personnel performed 9056 blood collections for experimental and clinical purposes during this reporting period.
- CM personnel performed 2614 ART therapy applications for experimental support during this reporting period.
- CM personnel performed 331,273 clinical and experimental treatments that were prescribed during this reporting period.

- CM personnel performed daily observations on newly formed social groups and reported any evidence of incompatibility to BSU.
- Starting August 2018, CM personnel has performed 5677 vaginal swabs for various research projects.
- CM personnel collected 293 urine and 50 fecal samples to support the Zika and Listeria research projects during this reporting period.

Specific Aim 5 - To meet the animal subject requirements of investigators by managing the NHP breeding and stock colonies of the WNPRC

- The SPF macaque-breeding colony produced 106 offspring and the marmoset-breeding colony produced 52 offspring.
- CM personnel assisted in acquiring 235 macaques (150 rhesus, 85 cynomolgus) to fulfill PI needs that could not be fulfilled by animals from the existing WNPRC colonies.
- The WNPRC acquired two established Mauritius cynomolgus breeding colonies (n=34, n=16) to support infectious disease research.
- In collaboration with the WNPRC Genetic Services Unit and the NPRC Genetics Consortium, the CM unit continues to obtain samples that have been utilized to identify the MHC type of each new offspring of the macaque-breeding colonies.
- In collaboration with the VS and in response to the needs of multiple investigators, the CM continues to collect samples that are used to identify SPF macaques that are also negative for Adeno-Associated virus (AAV) and/or Rhesus Rhadinovirus (RRV).

FUTURE GOALS

During the next funding period, the personnel of the Colony Management Unit will continue to provide an excellent and compliant standard of NHP husbandry, assist the other units within the Animal Services Division, and support the ongoing and new projects of the Center's core and affiliate PIs.

Specific Aim 1 – **To provide an excellent and compliant standard of animal husbandry**, the Colony Manager and the animal care supervisors will continue to nurture and motivate the existing animal care staff through close evaluation of their daily performance, positive feedback, and advice on how to improve their skill sets and efficiency. With the assistance of the WNPRC Human Relations Unit, the Colony Manager and supervisors will ensure that deserving Animal Research Technicians (ART) receive merit raises and promotions. Similarly, ARTs who are underperforming will receive retraining from the supervisors and personnel of the Compliance and Training Unit to ensure that their performance improves. The WNPRC continually supports the career development of our ARTs by providing continuing education opportunities to attend leadership lecture series offered by the UW, becoming certified through the American Association of Laboratory Animal Research, and successfully obtaining positions as colony management supervisors, research associate positions, veterinary technician positions, and attending veterinary and post-graduate school.

In collaboration with the Attending Veterinarian and BSU personnel, CM personnel will continue to play a crucial role in the WNPRC's commitment to socializing NHPs. ARTs immediately report any evidence of aggression or wounding between pairs and groups of animals to Behavioral and Veterinary Services personnel to ensure timely intervention. CM personnel will work in unison with BSU and the WNPRC shop personnel to identifying any structural modifications that are required in animal housing to promote wellbeing and investigate innovative social enclosures to help enhance animal housing.

Specific Aim 2 – CM personnel will continue to **perform daily health observations** that are crucial to ensuring that animal needs are addressed in a timely fashion by both VS and BSU. CM personnel will work

closely with Informatics and Data Services (IDS) personnel to continue to hone the electronic health record (EHR) system to improve data entry and to further reduce the need of hardcopy forms.

In addition, CM will continue working with IDS to streamline the newly added pregnancy and breeding module in EHR.

Specific Aim 3 – CM personnel will continue to support the **EEP** by providing edible and destructible enrichment, foraging opportunities, and audio and visual stimulation. ARTs will assist Behavioral Services in improving the plan by reporting on which components of the EEP are most well used by the animals and which components need to be altered or eliminated from the plan. The positive psychological bond build between the ARTs and the animals will continue to be emphasized as an important part of the EEP.

Specific Aim 4 – CM personnel will **provide support to the clinical, behavioral, and research units** of the WNPRC during the next funding period by completing the following tasks:

- Collecting blood and various other tissues (e.g., feces, urine, hair, breast milk, etc.) from NHP for clinical, behavioral and research purposes
- Weighing and transferring conscious and sedated animals for husbandry, clinical, breeding, behavioral, and research purposes

Specific Aim 5 – The CM Unit will ensure that WNPRC core and affiliate PIs have an adequate supply of animals during the next funding period by **maintaining the existing nonhuman primate colonies** by working to achieve the following goals:

- Maintaining the SPF-4 (Herpes B-, SRV-, STLV-1-, SIV-) rhesus macaques and increasing the supply of other viral free pathogen animals (AA01, AA08, etc.) upon request.
- Ensuring the genetic diversity of the macaque colonies by following the macaque breeding management decision tree established by Redacted by agreement with the assistance of Redacted by agreement and the ONPRC genetic analysis reports
- Expand the WNPRC marmoset colony by using the breeding management decision tree established by Redacted by agreement with the assistance of Redacted by agreement and the ONPRC genetic analysis reports

COMPLIANCE AND TRAINING UNIT

Unit Head: Redacted by agreement D.V.M., D.A.C.L.A.M.

GOALS AND ACCOMPLISHMENTS

Goals

A1. Educate, train, re-train and update training records for all WNPRC staff, support personnel, and visitors who may come into contact with NHP or their tissue to ensure that they understand and follow WNPRC standard operating procedures.

- **A1.1**. Initial Training
- **A1.2.** Additional Training and Re-Training
- **A1.3.** SOP Management

A2. Ensure a safe working environment for all WNPRC staff and students and to further develop the WNPRC Occupational Health and Safety Program (OHP) to maintain compliance with new and existing standards.

- **A2.1**. Ensuring a Safe Work Environment
- **A2.2.** Further Developing the WNPRC Occupational Health and Safety Program to Maintain Compliance with New and Existing Standards

A3. Ensure that WNPRC personnel and facilities remain compliant with all institutional, state, and federal regulations governing the use of NHP in laboratory animal research.

- **A3.1.** Protocol Development
- **A3.2.** Post-Approval Compliance Monitoring
- **A3.3.** Facility Inspections
- **A3.4.** Record Reviews
- **A3.5.** Incident Reporting

Accomplishments

B1. TRAINING:
The training unit Redacted by agreement continued to train a large number of staff including animal research technicians (ARTs), research staff, veterinary staff, personnel using primate tissues, and visitors. Training module presentations and training documentation forms are used to provide consistent training points for basic and advanced husbandry. The unit continued to provide retraining as requested and are proactive in identifying and following up with deficiencies in procedures. Standard Operating Procedures (SOPs) are being reviewed and revised routinely to update changes in procedures and address incidents, with 76 SOPs reviewed, including 14 new SOPs that were developed. The Primate Orientation e-learning module continues to be developed with assistance from Research Animal Resources Center, including developing a modified in-person training module that was redesigned to better meet the initial training needs of new staff working with nonhuman primates.

B2. OCCUPATIONAL HEALTH AND SAFETY:
The Occupational Health and Safety Coordinator Redacted by agreement continued the development and enhancement of the WNPRC OHP with the assistance of the staff of the UW-Madison's Department of Environment, Health and Safety (UW Safety) and the University Health Services Occupational Medicine Department (UHS). She continued to provide occupational health and safety training to staff, ensure a safe work environment in all WNPRC facilities, follow up on all potential exposures, and update OSHA compliance plans and emergency response plans. She continued to hold monthly WNPRC Safety Committee meetings to discuss and review safety issues and ways to mitigate identified issues and conduct monthly safety inspections with members of the Safety Committee on a rotating basis. In addition, she finalized a formal Shop Safety Program which includes routine safety inspections, the development of shop specific SOPs, and "Machine Shop Safety Rules".

B3. COMPLIANCE:

The Compliance Coordinator Redacted by agreement continued to provide animal care and use protocol development and review service for all investigators utilizing NHP at the WNPRC. She performed 43 extensive IACUC protocol pre-reviews between January 1, 2018 and December 31, 2018 and developed additional templates for animal care and use protocols to assist WNPRC research staff with the online protocol submission process (ARROW). The Incident Prevention Committee continued to meet monthly to discuss NHP related errors that occurred during the previous month, make recommendations for preventing similar errors from occurring, and develop plans for instituting the recommendations. The Committee also evaluated mid-year statistics and trends that Redacted by agreement prepared and presented to determine if additional preventive measures need to be taken.

The Compliance Assistant Redacted by agreement continued to assist with numerous safety and compliance tasks, including the conduct of quarterly compliance inspections and multiple protocol audits. Redacted by agreement and Redacted by agreement continued to streamline the process for Facility Access Onboarding, which includes tracking compliance with mandatory initial training and medical clearances for new employees, students, collaborators, and visitors prior to entering any of the WNPRC facilities or having contact with nonhuman primates or nonhuman primate tissues.

The members of the Compliance and Training Unit are continuing to help with further development of the WNPRC EHR system by meeting with Informatics and Data Services staff weekly to discuss and evaluate new features and describe needed improvements.

FUTURE GOALS

Training Unit goals: The Training Unit plans to continue to provide a high level of training to new ARTs so they are able to deliver the best husbandry for the colony and be more independent following their completion of the initial training program. The Unit will utilize e-Learning software to create on-line training modules to increase the accessibility of presentations created for more complicated tasks (e.g., Primate Orientation and Animal Records and Data Entry). The Unit plans to improve documentation of training to standardize documentation, improve accessibility of information, and institute more frequent review of training records, with a large emphasis on modifying the training records in the EHR system. The Training Unit is working on creating classes for animal transport, blood draw and injection training to improve the consistency of training staff on these procedures. Classes will include training worksheets, SOPs, models, and animals as appropriate for each task.

Compliance Unit goals: The Occupational Health and Safety Coordinator plans to transition the numerous safety training modules into an e-learning format to improve accessibility of information. She also plans to explore and experiment with new PPE technology and other new engineering controls, create and implement a travel policy, and create an umbrella chemical hygiene plan as a part of a comprehensive Occupation Health and Safety Program.

The Compliance Coordinator plans to devote more time to protocol audits and fulfill the goal of completing three per month. She also plans to develop tools to assist WNPRC PIs with generating protocols, tracking protocol and procedure details, and submitting consistent data to Colony Records.

The Compliance Assistant plans to create electronic request forms, instructions, and resources for Facility Access. She will also help transition other WNPRC departments to a web-based collaborative platform to improve onboarding, manage internal communication, and increase employee engagement.

BEHAVIORAL SERVICES UNIT

Unit Head: Redacted by agreement Ph.D.

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1 (SA1): To ensure the psychological well-being of our NHP colonies. There are three sub-aims.

SA1a. To create and maintain stable social housing conditions for animals within the colony.
SA1b. To coordinate, maintain and expand upon the environmental enhancement plan (EEP).
SA1c. To maintain a surveillance program to follow behavior of potential concern.

Specific Aim 2 (SA2): To provide research support for investigators.

Specific Aim 3 (SA3): To provide NHP behavior training for personnel and NHP.

Specific Aim 4 (SA4): To disseminate BSU research results through interaction with colleagues, scientific presentations and peer-reviewed publications.

Accomplishments

To ensure the psychological well-being of our nonhuman primate (NHP) colonies (SA1). **To create and maintain stable social housing conditions for animals within the colony (SA1a).** Species-typical social behavior is essential for the healthy development and well-being (SA1a). Social groupings, however, must also harmonize with research programs and housing dynamics of the colony. In 2018, we continue to meet our objectives of providing for the social needs of the animals under our care. In brief, 100% of our marmosets are socially housed with a small number singly house for short periods as necessitated by research protocols and clinical care. Sixty-four percent (64%) our macaque colony was socially housed with an additional 16% holding IACUC approved exemptions or exceptions related to research. Approximately 8 percent of our animals are in the process of transition to research projects that require additional consideration prior to pairing or resolution of their upcoming housing status. The remaining pool of 12% were engaged in the pairing process. The animals remaining in the pairing pool are of mixed sex and age, as well as vary in other factors that preclude 1 to1 pairings or social groupings (i.e., Viral status, disease status, and historical variables). We continuously evaluate pairing relevant demographics and resources to match animals and aim to do so in a manner that optimizes pairing success and potential longevity of the pairs/groups we create.

The Behavioral Services Unit (BSU) employs several strategies to increase pairings and groupings over time and we have continued this progress in this grant period. We have developed novel housing environments to create small groups in runs, and other standard cage footprints by adding tunnels and cage extensions. The BSU also continues to mixed-age groups with the aim of building long term species-typical interactive social skills in younger animals. Finally, an area we continue to pursue includes mixed-age social breeding groups. This effort involved Operational Services: Shop Services in the further expansion of pen features by developing multiple closeable pass-throughs to chain multiple small pens to create larger areas to support these larger groups.

Currently we have 12 pen/room indoor housing environments, but have had a maximum of 17 pens groups over the project period depending upon available animals and group compositions. The groups sizes in these pens range from a minimum of 4 to a maximum of 37 over this period. We have continued to increase the number of animals socially housed in pen environments in this project period (>280) and attaining the highest number of pen-housed animals over the last 5 years.

We have also continued to use small pen or run units a as platform in the initial pairing. Some equipped with cage extensions and/or C-tunnels. These features provide additional space and structural complexity. The more complex environments allow more escape avenues in cases of aggression. The versatility we have

developed in our housing environments allows us to transition “paired or grouped” animals to standard colony housing in accordance with required cage size and maintain the animals in social pairs.

Finally, we have continued pairing animals in quarantine. Pairing in quarantine under most circumstances has now become the norm rather that an exception. We have collaborated with the Veterinary Care and Colony Management (CMU) units to increase our efforts by accumulating information on the social histories and past pair-mates prior to the animals’ arrival to our facility. Knowledge of the social histories of incoming animals and streamlining the veterinary assessment procedure has allowed our unit to pair animals as soon as possible upon arrival to our facility. For example, in this project period of the 236 arriving animals, 49% percent of our quarantine animals were paired immediately with an additional 11% paired within 30 days. The remainder of the animals single for more that 30 days required additional veterinary review and clinical testing as a required to ensure colony health. Those animals not paired in quarantine were maintained in protected or visual contact as appropriate to maintain the requirements of the veterinary quarantine procedure.

Under this aim we continue to pursue one archival study over the course of the project period. The study will describe our colony pairing efforts over time, highlight our success and identify factors that affect the pairing process. We hope to specifically characterize the dynamics that affect the transition of animals in and out of the pool of animals available for pairing.

To coordinate, maintain and expand upon the environmental enhancement plan (EEP) SA1b. The BSU has a well-developed and successful environmental enhancement plan that outlined our continued to provision of complex social and interactive environments to the animals under our care. In practice, specific strategy and practice are instantiated in WNPRC standard operating procedures (SOPs) that serve as living documents refined and updated as we “try-evaluate-and modify” our practice (SA1b). Broadly, in this project period we have updated SOPs that describe: Enrichment food lists both in variety and adjusted portion sizes, incorporated new foraging toys, upgraded our delivery of sensory enrichment employing lighting that allow varied colors and patterns and replaced and/or maintained our array of foraging and enrichment toys.

Currently the evidence-based evaluation of this aim we have 3 ongoing studies in the active data collections phase through the project period. Two projects evaluate marmosets and one macaques. The first marmoset project involves shaping the marmosets to voluntarily station on a scale to collect body weight. We are developing methods and protocols in this study that we intend to adopt for future cohorts of marmosets. Further we intend to adapt what we learn to apply broadly to other cooperative procedures involving macaques in the future. A second study in marmosets involves evaluating patterns of interaction with a common wooden toy varied by a dimension of stability.

The macaque project is a comparison of foraging toy preferences. In this project we will assess all available foraging toys by attaching an actimeter (Actical, Respironics, Inc) to each toy prior to delivery to the animal. We have piloted this work to standardize placement of the actimeter and confirm reliability of the method to capture data with simultaneous video recording. We will be cycling through all available foraging toys and perform a “head-to-head” usage analysis of each. In this manner we expect to refine our provision of foraging toys by identifying those toys that invite the most interaction and preferential select toy that engender the highest amount of interaction.

Finally, in the domain of environmental enhancement we have continued to collaborate with Operational Services: Shop Services and CMU. For example, in this project period we have continued to identify, modify and re-purpose existing caging to create enhanced structural environmental elements. For example, we recently identified 7 larger footprint cages that were in storage and modified them to connect in series and provide additional space for socialization. In past grant periods we have established the animals use often prefer the increased perspective afforded by an extended or expanded vertical spaces through the use of cage extensions and C-tunnels. We continue to provide positive pressure to increase extension use throughout the macaque colonies and use has been formalize and tracked through the EHR system since August 2018 (see CMU report).

To maintain a surveillance program to follow behavior of potential concern SA1c. The BSU employs a mixed model of behavioral surveillance integrated across Animal Services Division Units (SA1c). Daily behavior reporting begins with observations by the animal research technicians (ARTs) and veterinary technicians. Behaviors of concern are noted and BSU follow-up performed. BSU personnel intervene with appropriate behavioral treatments (e.g., increased foraging, displacement objects, relocation, etc.) and consult

with veterinary staff as needed. WNPRC's team-based surveillance approach will continue to concentrate BSU resources on animals reported for the expression of atypical behaviors. We will continue to refine our surveillance procedures in collaboration with Electronic Health Record (EHR) services to streamline behavioral reporting across units to flag and share animals' behavioral status, surveillance progress and treatment status. We hope to realize these advancements in the next project period.

In addition to our cross-unit integrated strategy, in past project periods we have performed colony-wide behavioral assessments to more broadly observe and assess welfare. The idea behind this approach was to observe the progression of untoward behavior, and thus, position the BSU to identify predictors of the development of abnormal behavior. Over time our approach has evolved from recording only "abnormal" behavior, to a holistic approach that includes species-typical behavior. This change occurred for two reasons: 1. abnormal was of low occurrence; and 2. Recording only "abnormal" behavior in absence of "normative" behavior does not inform population levels of expression. As part of this process we developed a tablet-based application to record behavior collecting observations for approximately 500 animals. From subsequent analyses of these observations we determined that a number of commonly used behavioral categories occur with low incidence and merit exclusion.

In this project period we revised our behavior ethogram, developed and implemented a 2nd generation tablet-based behavioral observation program through collaboration with a working group at Drake University and we are nearing completion of a yearly assessment of all animals in the colony. The tablet-based system outputs data in a CSV format and we are currently coding small applications to pull summary data from individual subject files create summary tables that can be uploaded to the EHR system.

Under this aim we pursued two projects: An archival analysis of the long-term behavioral adjustment outcomes following clinical nursery rearing, and a collaborative project with NPRC's Behavioral Management Consortium comparing alopecia scoring scales.

The outcomes analysis of clinical nursery rearing analysis includes both behavioral and health related measures thought to be potential indicators of welfare status. For example, duration in the nursery, abnormal behaviors, diarrhea, alopecia, and frequency of irregular observations as reported in the EHR. To date we have completed data organization for 4 of 5 "targeted" birth cohorts.

In alopecia scoring project we are comparing the "Rule of 9's" and current WNPRC scoring scales for assessment of alopecia. To date, we attended a BMC webinar describing the rule of 9's method scoring scale, achieved inter-center reliability and collected data on a pilot set of animals (n=~60).

To provide research support for investigators (SA2). Experienced BSU staff are available to assist investigators with animal transfer training, shaping techniques and positive reinforcement training (SA 2). In addition, BSU staff are available to work with scientists to develop individualized animal training plans for specific projects as needed.

As in past project periods the BSU has provided advance training in support of investigators scientific aims. We regularly interact with investigators in the process of subject selection for research projects giving input into behavioral histories of candidate animals and later work with them as experimental timelines are established if the animals experience adjustment issues.

In this project period, we continue to collaboration with the Scientific Protocol Implementation Unit (SPI) in training animals to sit in a primate chair for semen collection. Similarly, we have continued to assist a neuroscience researcher (Populin) to maintain chair training proficiency in existing animals, as well as, chair acquisition in a group of new animals.

We continued a longitudinal behavioral assessment of reactivity to a human intruder as part of a project evaluating the effects of pediatric anesthesia regimens (Ikonomidou). Over the course of this project period we have tested 11 subjects across 3 time periods (6, 12 and 18 mos.) and additional sessions remain as the animals mature to targeted testing time points. Preliminary analysis from testing completed to date suggest that suppression of behavioral activity occurs most dramatically under the stare "mild threat" condition as would be expected. There substantial inter-subject variability in the degree of this response. Analysis of individual behaviors is continuing as completed sessions are scored. Between-treatment group differences will require data from upcoming test sessions for analysis.

Two new projects requiring specific BSU support began in this project period (Sept. 18'). The will leverage archival data an ongoing project assessing adjustment outcomes of animals that have spent time in our clinical nursery. The major goals are: 1.) to determine whether emergency interventions that require clinical nursery stays in the first weeks of life affect monkey brain morphology; 2.) whether, and the degree to which, contemporary clinical nursery rearing produces changes in brain morphology relative to typically-reared monkey. To this end we will collect brain images from clinical Nursery reared (NR) animals and Mother-reared

controls (MRI) (MR/NR; 12/12; n=24) and analyze these images using machine learning, diffusion tensor imaging tractography (DTI), and region of interest (ROI) analyses ([Redacted by agreement] WNPRC pilot project). In sum, the pilot study will provide the foundation for data to be used in future grant submissions that will allow us to expand the scope of (1) brain and behavioral phenotypes and (2) to further how variation in early social rearing interacts with the genome to influence a variety of behavioral and neurological outcomes. This project is currently in the early phases of execution.

The second project began in October 2018. For this project we have been involved in identification of available dams for formation of compatible Mother-infant pairing. This involves the formation of these pairs as well as follow-up evaluation of continued compatibility. This effort requires a large multi-unit collaborative group including the investigators [Redacted by agreement] Colony Management Unit, Macaque Breeding Coordinator and veterinary staff. To date we have created 8 M-I pairs (Oct-Dec 18').

We expect the demand for BSU research support will continue to expand as the number of projects increase. For example, in a collaborative effort with Scientific Protocol Implementation (SPI) and Pathology Services Unit (PSU) we are working with an investigator to develop a behavioral test to quantify extent of neglect in a model of spinal cord injury. Another group of investigators have expressed interest in BSU support in assessment of behavioral reactivity using the human intruder test. Finally, as part of an initiative across the National Primate Centers we are going to be performing a standardized assessment of response to novelty.

To provide NHP behavior training for personnel and NHP (SA3). The BSU plays a crucial role in the campus wide laboratory animal program by providing prerequisite training in NHP behavior to all University staff that encounter NHP as a work requirement (SA3). Our unit focuses on teaching appropriate human-NHP interaction. Bi-directional "human-NHP" interactions involve both instructing humans effective handling approaches, as well as, training the NHP to adjust to the demands of the environment. These training sessions are generally available twice monthly; however, additional offerings are commonly scheduled. For the project period (1/1/18-12/31/18) we served 127 attendees for our behavioral orientation sessions. Further we provide Face-to-Face instruction to new animal care technicians as part of their initial training. This training includes guidance in animal handling and transfer, as well as, enrichment preparation and delivery. We are also involved in bringing some of this content to online modules for offsite users (see Training Unit progress report).

Another significant component of our general service aims is our role in training animals to transport for both general husbandry (CMU) and research purposes (SA2). Transport training ranges from training animals to enter and exit transport boxes or the table top restraint system to transfer training within small pen housing. We are often called upon when staff and investigators have difficulty transferring an animal. Follow up with these animals often requires retraining sessions for the animals that regress in proficient transfer. With the expansion of the number of small pen housing environments, pen transfer training sessions are required because of the unique requirements for the animals in these expanded spaces. In this project period we have developed and refined facility SOPs for transferring pen housed animals specific to type of pen housing environment. Further, we have developed SOPs for working cage extensions and C-tunnels, housing enhancements that allow increased environmental complexity. Finally, pen transfer training often requires training sessions for new staff and staff refresher presentations as these advanced behavioral training techniques are a communal effort with staff.

A final component of our training aim includes undergraduate education opportunities. We provide instruction in animal behavior and unique opportunities to work with NHP on welfare studies, while promoting peer-to-peer exchange of information about the role of NHP research in biobehavioral science. Past undergraduate students have contributed to our dissemination aims working on semi-independent project presenting results both locally at the undergraduate research forum, as well as, at regional and national scientific meetings (SA4).

Over the course of the project period 6 undergraduates contributed to our program. The student's efforts resulted a conference presentation, 2 publications and 2 pending manuscripts. The theme of two of these publications was to first develop a quantitative assessment method to compare enrichment strategies and the second an application of the metric to perform an evidence-based evaluation of enrichment programs in non-human primates across a variety of facility types housing NHPs.

The availability of qualified undergraduates is cyclical with best outcomes with recruitment at the beginning of an academic year. Student availability for an extended period of time to acquire the instruction necessary to work with primates limits our ability to accommodate large numbers. However, the placement of our facility on the campus of a research university positions use to contribute to the pipeline of future scientists with expertise in primate models. Thus, we will continue to recruit and provide undergraduates research opportunities in conjunction within this aim.

To disseminate BSU research results through interaction with colleagues, scientific presentations and peer-reviewed publications (SA4). The BSU aims to generate performance metrics to determine how our practices encourage behavioral interaction and improve overall well-being. The dissemination of our efforts through interaction and collaboration with the NPRC's Behavioral Management Consortium (BMC), the undergraduate opportunity initiative, scientific meetings and the peer-reviewed literature serve to promote the WNPRC research enterprise to the scientific community and assure the public that species-typical behavioral health is paramount for the NHP under our care.

In this project period as part of the BMC we updated the content of the NPRC behavioral welfare page adding behavioral assessment tools employed across primate centers. We also initiated an online moderated technicians' forum and webinar series on behavior related topics. At the BMC's annual meeting held jointly with the NPRC's Breeding and Colony Management Consortium (BCMC) the BSU presented cross center initiatives including: Outcomes of social housing; socialization in quarantine, updates on website and technician forum usage, enhanced cage environments, alopecia scoring, and common inspection topics.

The BSU has also been active in presenting our work and contributing to dialogues to the broader scientific community in a number of other venues. For example, 2 student presented work at conferences (SA3), the unit head presented an invited talk at the University of Wisconsin School of Veterinary Medicine entitled "In service of science and animal welfare: Behavioral management of nonhuman primate in US research facilities." The unit head Redacted by agreement serves on the Animal Welfare Committee of American Society of Primatologists (ASP), and the local planning committee for the 42nd annual ASP meeting (Madison, WI; 2019). He also serves the Midwest Psychological Society as a reviewer of the Psi Chi student presentations, and as a reviewer of the American Psychological Association (APA; Div. 6) student presentation awards.

In 2018, Redacted by was selected to a three-year term as a member of the APA Committee on Animal Research Ethics (CARE). As part of the committee Redacted by agreement participated in advocacy training, a congressional briefing and representative office visits to share both the importance of care and welfare within the context of research, and, the role of basic research in the process of scientific discoveries that directly benefit the public (2/18). Further he served as a CARE representative to the APA's board of scientific affairs which is charged with presenting the scientific goals and agenda to the governing counsel of the APA (11/18). Taken together, these activities highlight the contributions of the WNPRC BSU to a broad and wide-ranging scientific audience.

FUTURE GOALS

The primary service aims of the BSU will continue but have expanded in scope to better reflect the evolution of our unit. The opportunity provided by increased staff has allowed us to meet our expanding service to investigators. Our unit will continue to focus on socialization of single-housed animals (SA1a). Along with establishing stable pairings and groupings, the deployment of added social housing environments have continued to develop and with this opportunity our role will require more individualize animal training for those animals adapting to these environments. Overall, we have seen improvement in how we address our primary aim of providing social opportunity for the animals under our care.

We have increased staffing opportunities in the effort to continue to refine and implement efficiencies in tracking the success and progress of its pairing initiative and following behavioral treatments for cases of abnormal behavior. We will continue to make progress in efforts to use EHR to track individual animal histories and prompt "onset" and "off set" of behavioral treatments and follow-up assessments to more efficiently inform treatment strategies; however, we currently waiting in the EHR services priority cue for developing some of these features.

In the next period, the Behavioral Management Unit will continue to move forward with its projects aimed to refine strategies to ensure the psychological welfare of the NHPs (SA 1 b & c). The development of behavioral assessment tools, pairing follow-up and evidence-based analysis of our enhancement practices we will increase our ability refine our goals of providing for psychological welfare of our animals. One future goal will be to evaluation of our enrichment program by developing new strategies and interactive opportunities for the animals. We have begun this effort in our marmoset colony and will carry this forward to our macaque program. Other goals include investigating colony wide temperament assessment as a predictor of pair compatibility, expanding the use of interactive cognitive tasks and refinements to our alopecia scoring

procedure. As we move forward we will be implementing these changes, evaluating outcomes and refining our delivery the various components of our enrichment and enhancement plan.

We expect a continuing increase in requested training in support of research programs as many of the existing projects will continue in the next period and new requests continue to increase (SA2 & SA3). We also expect that our role in carrying forward our behavioral expertise in training animals and primate users in advanced techniques will continue to increase because of the ongoing upgrades in social housing and increased complex of structural environments often pose challenges for animal transfer for both daily care (CMU) and research needs (SPI). Furthermore, research scientist's requests for behavioral service have also continued to increase. Thus, we hope to expand personnel positions to accommodate the growing requests for advanced behavioral training in order to serve the entire WNPRC enterprise (CMU, SPI, PSU and individual investigators). The unit will continue as a partner in university-wide training in basic NHP behavior and enrichment (SA3) including the support of undergraduate educational opportunities. Finally, we will continue to disseminate our findings through interaction and collaboration with the NPRC's BMC, the undergraduate opportunity initiative, participation in science advocacy centered on animal care and welfare, scientific meetings and the peer-reviewed literature (SA4).

SCIENTIFIC PROTOCOL IMPLEMENTATION (SPI) UNIT

Unit Heads: Redacted by agreement Ph.D.
Redacted by agreement D.V.M.

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1: Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators.

We plan to continue to create a collaborative environment for investigators who want to perform biomedical research using NHP at the WNPRC. Both a scientist Redacted by agreement and research veterinarian Redacted by agreement will continue to head the unit. In addition, an assistant scientist (Redacted by agreement has joined the SPI unit to assist in recruitment, initiation and completion of the expanding portfolio of NHP projects. SPI will continue to coordinate with other WNPRC units to ensure that project support for WNPRC core and affiliate projects is thorough, timely, efficient, and focused on providing consistent technical expertise. Once projects are initiated, SPI will continue to execute well-organized, standardized, and compliant experimental support, arrange animal assignments, coordinate with other WNPRC units to provide needed services, and develop further expertise for new innovative projects Proprietary Info will continue to advise and have oversight on any projects related to the EMCD working group. We will continue to respond to innovative research questions by creating and/or refining technical procedures to provide the highest possible level of experimental support.

We are particularly committed to identifying new investigators that need to develop NHP projects for translational purposes. In order to continue excellent unit function, we have determined 4 goals to improve our efficiency with experimental support: (1) continue to solicit feedback from investigators as we work with them; (2) recruit and hire additional technicians to accommodate the increased demand for NHP research project support; (3) incorporate charges into procedure schedules in EHR; and (4) Utilize the EHR database to compile and provide detailed experimental summaries to PIs in a rapid, efficient fashion.

Specific Aim 2: Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities.

SPI emphasizes the importance of executing well-organized, standardized, and compliant procedures for successful research programs. Furthermore, development of new techniques for innovative experimental design requires additional training for staff. Cross training of research specialist staff is also very important to maintain flexibility for support within the unit. Equal in importance is leadership and management training so that research specialists are able to function well in teams and coordinate with investigators and WNPRC staff in effective ways as primary project management. Finally, because of the scientific aspects of the unit, we will continue to provide instructional opportunities in academic research subjects pertinent to our projects. We also plan to continue to mentor existing SPI staff in experimental design, statistical data and testing analysis.

We expect that SPI staff will continue to be prepared to take on new procedures and techniques. We recruit highly motivated individuals who actively seek further personal development. We also continue to attract animal care staff from the husbandry unit and provide a springboard for others interested in pursuing their careers in veterinary/human medicine or biomedical scientific research. Plans to continue staff development include: (1) standard operating procedures; (2) provide continuing education opportunities to augment our repertoire of services, knowledge, and expertise; (3) provide more opportunities to understand the research background of the hypothesis-driven studies we support.

Specific Aim 3: Contribute to NHP knowledge and translational models through academic output.

Excellence at the WNPRC depends upon all units having a strong academic emphasis. As co-directors of the unit, Redacted by agreement and Redacted by are experienced investigators who themselves generate and coordinate new initiatives so that they can best provide state-of-the-art collaborations for research projects that will result in publications in high-impact, peer-reviewed journals. With our unit emphasis on training research specialists on academic and scientific process, many will also contribute to these publications as co-authors. In

addition, technical reports of procedures developed or enhanced by our unit will continue to be presented at local and national consortiums.

Accomplishments

Specific Aim 1: Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators.

In Y57, there were 10 projects and 2 pilots that ended, while another 15 new projects and 2 new pilot studies were added for a net gain of 5 new projects since 1 Jan 2018. In addition, one of the projects that ended acquired successful renewal funding [Redact] PI, UW-Madison, R01 HD072077) and will begin in 2019. We are particularly committed to identifying new investigators that need to develop NHP projects for translational purposes, and in Y57, we submitted and received a fundable score for a new R01 [Redacted by] PI, University of Cincinnati) after the supplemental award for NHP translational work on desensitization of severe allergic reactions [Redacted by] PI, University of Cincinnati, R01AI113162) and are in the progress of working out NHP translational work on prevention of high-risk breast cancer for another PI [Redacted by] UW-Madison).

[Redacted by agreement] presented 19 potential new projects to the Executive Committee in the reporting time period (10 current affiliates, 5 new affiliates, and 3 core PI). All proposals were approved, though some with the condition that resources will be allocated to projects when they become available.

We had determined 4 goals to improve our efficiency with experimental support. We report 3 of those addressed so far in Y56. 1: We have solicited and received feedback from two projects where we were able to improve primary staff support by assigning new or additional staff. 2: Unit scheduling is better streamlined with the use of blood draw, and food deprive requests in our Electronic Health Records (EHR). 3: We successfully updated our chargeback rates for July 2017-June 2018 to reflect current supplies and labor costs and intend to have these incorporated in to EHR with each procedure.

Specific Aim 2: Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities.

The 3 most recent technicians added to the unit continue to grow in their positions. Each has developed in to primary project research specialists and become proficient basic and some advanced techniques. We continue to maintain at least one undergraduate student for assistance with animal procedures and will overlap students for continuity as one approaches graduation. The last 3 undergraduate students working with our unit went on to graduate school upon finishing.

Due to increased interest in Zika studies, support for reproductive techniques are required more than before. We trained several staff in ultrasound technique for pregnancy and fetal heartbeat detection. One senior staff person is proficient in oocyte collection and embryo transfer techniques and new staff are in the process of being trained on semen collection with both marmosets and macaques. With increased interest in broadly neutralizing antibody functions for vaccination targets, new requests for leukapheresis and plasmapheresis are coming in where we can utilize the Spectra Optia machine for multiple studies. As a result, we are training additional staff to the leukapheresis procedure to replace the technician who departed our unit. We are developing the SOP for this during the training process.

Training is scheduled for 1 research specialist to attend the NHP Behavioral Training Workshop in March. The research specialist applied for UW Academic Staff Development award to partially fund this training. Throughout the last year SPI staff were able to attend discussions about the research of the hypothesis-driven studies our unit supports. Two investigators presented to our SPI group at one of our staff meetings. Additionally, each of the four different scientific working groups of WNPRC provided several monthly seminar opportunities on related research.

Specific Aim 3: Contribute to NHP knowledge and translational models through academic output.

We continue to be successful in this reporting period with 7 published peer-reviewed manuscripts and 1 book chapter with SPI staff as co-authors (see SPI Unit Report Details). The journals included: 2 in PLoS One; 1 in PLoS Pathogens; 1 in Neurology Research; 1 in Psychoneuroendocrinology; 1 in NPJ Parkinson's Disease; and 1 in Comparative Medicine. The book chapter is titled Behavior and Behavioral Management and is a part of The Common Marmoset in Captivity and Biomedical Research (Eds. Marini, Wachtman,Tardif, Mansfield, and Fox). There are approximately 5 more manuscripts in preparation where SPI co-authors are involved.

FUTURE GOALS

Specific Aim 1: Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators.

1. Continue to encourage and support new investigator research by discussions of ideas, grant and budget planning, and bringing proposed research plans to the Executive Committee for resource planning.
2. Continue to solicit feedback from investigators by inquiry and following up on procedures, improvements to support, etc.
3. Work with the EHR Services to plan to include all experimental procedure and surgery requests. This will improve scheduling procedures and set up the data fields to ultimately be linked to chargeback rates. With this addition, we can free up SPI staff to have more time to perform experimental procedures and plan project timelines. Right now, we have one research specialist assigned to coordinating/ communicating schedules and two more dedicated to entering the monthly charges for our unit.

Specific Aim 2: Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities.

1. Develop plasmapheresis procedure that can also utilize column chromatography add-ins to collect antibodies in plasma, while returning not only the animal's cells, but most of the plasma fibrinogen.
2. Assess microneedle patch for mucosal and skin application of antigen for vaccination of NHPs.
3. Plan for more continuing education for staff, with more opportunities to attend research meetings or specialized training.

Specific Aim 3: Contribute to NHP knowledge and translational models through academic output.

We plan to continue to actively contribute to data compilation and manuscript preparation on projects involving our staff.

PATHOLOGY SERVICES UNIT

Unit Heads: Redacted by agreement D.V.M., D.A.C.V.P.

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1 - To continue to support NHP colony health and experimental investigations by providing rapid diagnosis of disease, characterization of current and developing NHP models, and collaborative development of experimental paradigms.

The Pathology Services Unit is essential to NHP colony health and research at the WNPRC. The Unit continued to collaborate with the clinical veterinary staff and investigators to provide rapid diagnostics and consistent monitoring of: chronic diseases, chronic metabolic conditions, and colony health.

The Unit continued to play an integral role for the vast majority of research conducted at the WNPRC through clinical pathology testing; advice concerning nonhuman primate anatomy, comparative pathology, and disease pathogenesis; development of specialized collection protocols; cytology evaluation; and surgical biopsy evaluation. Gross and histological changes and lesions were specifically evaluated to determine: if they were the consequence(s) of experimental manipulation(s); if they would confound experimental data interpretation; if they were typical of incidental findings (background lesions in model species); or if there would be an influence on colony health and management.

Specific Aim 2 - To continue to curate and expand the NIA Tissue bank and manage the NHP Biological Materials Distribution (NHPBMD) Core in cooperation with SPI.

The PSU continues to be responsible for the collection, banking, and distribution of NHP samples to numerous local, national, and international investigators through the Nonhuman Primate Biological Materials Distribution core (NHPBMD). The PSU was awarded a 5-year renewal of the NIA Aging Nonhuman Primate Tissue Bank contract Redacted by agreement, PI) during this reporting period.

Specific Aim 3 - To serve as a resource for primate research, education, and conservation through participation in pathology consortium activities, scientific meetings, serving as advisors/consultants and training of students at the WNPRC.

The Unit trains undergraduate, veterinary, and graduate students, as well as veterinarians in clinical pathology, necropsy, anatomy, disease pathogenesis, and other topics related to NHP and translational medicine and research.

Redacted by agreement regularly present at and attend monthly NPRC Virtual Slide Conferences (VSC). These meetings are regularly scheduled and provide NPRC pathologists, residents, and clinicians with a flexible forum to present “classic diseases” for the education of residents, students and NPRC staff as well as a forum for sharing and receiving advice and peer review of diagnostic conundrums.

Accomplishments

Specific Aim 1 - To continue to support NHP colony health and experimental investigations by providing rapid diagnosis of disease, characterization of current and developing NHP models, and collaborative development of experimental paradigms.

The WNPRC Pathology Services Unit provided excellent service while being fiscally responsible. This objective was met through the performance of record numbers of routine diagnostic and screening procedures as well as the development of innovative diagnostic methods and experimental techniques. During Yr. 57 PSU personnel

almost doubled the performance of on-site assays with 2921 CBCs, 1482 serum chemistries, and 994 fecal parasitology examinations for clinical diagnostic and research purposes. The unit performed biopsies and gross post mortem examinations with research and diagnostic sample collections with histology. Redacted by agreement joined the PSU part-time to ensure timely completion of histology for experimental needs.

Contract laboratories and laboratory supply resources were evaluated for quality and price biannually, or as needed. Protocols, SOPs, training and QA/QC practices were continually evaluated and revised as needed. Unit members regularly met and coordinated efforts with members of other WNPRC units to refine and improve sample and data collection, medical records, and reports generated through the electronic health record system. Unit members also reviewed selected research protocols and invited members of the investigating laboratories to present and answer questions at Morbidity and Mortality rounds.

Specific Aim 2 - To continue to curate and expand the NIA Tissue bank and manage the NHP Biological Materials Distribution (NHPBMD) Core in cooperation with SPI.

Pathology unit members continued to work with the NIA to receive samples donated to the NIA tissue bank and distributed samples as directed by the NIA. Complete aged animal collections were donated and samples were distributed as per NIA direction, during the reporting period.

The Pathology Services Unit coordinated and cooperatively distributed biological specimens to researchers and educators through the Nonhuman primate biological materials distribution (NHPBMD) core, described as an independent core.

Specific Aim 3 - To serve as a resource for primate research, education, and conservation through participation in pathology consortium activities, scientific meetings, serving as advisors/consultants and training of students at the WNPRC.

Redacted by agreement received funding from ACLAM to support short-term training opportunities for honorary fellows hosted by WNPRC to receive both laboratory animal medicine and pathology training. The fellows, to date, have included veterinary students, veterinarians, and pathology residents who have subsequently progressed to full time research, training, and diagnostic positions. One undergraduate student received training as part of the UW work-study program during the reporting period.

Redacted by agreement continued to serve as a participant and moderator for the Latin Comparative Pathology Group (Branch of the CL Davis Foundation). Redacted by agreement was coordinator for the International Mock Exam Coalition; Peer reviewer for Journal of Medical Primatology and Journal of Visualized Experiments (JoVE). Redacted by agreement was a Peer reviewer for the Journal of Medical Primatology. Both Redacted by agreement were invited reviewers for the textbook, *The Common Marmoset in Captivity and Biomedical Research* (Elsevier, pub.).

Redacted by agreement both participated in National Primate Research Center (NPRC) pathology consortium activities; primate pathology workshops; presented cases for the NPRC virtual slide conferences; and participated and presented cases at numerous rounds at the UW Medical School, UW Veterinary School and the Wisconsin Veterinary Diagnostic Laboratory.

Redacted by agreement, and Redacted by agreement published a manuscript evaluating bone marrow markers for characterization of cell types in the Journal of Leukocyte Biology - Weisgrau KL, Vosler LJ, Pomplun NL, Hayes JM, Simmons HA, et al. Neutrophil progenitor populations of rhesus macaques. J Leukoc Biol. 2019 Jan;105(1):113-121. PubMed PMID: 30395351.

FUTURE GOALS

The Pathology Services Unit will continue to refine and expand services for colony health and research. This will include ongoing work with WNPRC IDS and several other NPRCs to continue to refine the LabKey based E.H.R. (electronic health record) to more efficiently meet colony and multi-institutional research needs.

Services will be expanded in 2019 to include in-house chemistry analysis through the recent acquisition of a chemistry analyzer. A third full time pathologist will also be added to the unit to meet increasing needs.

PSU members will continue to collaborate on current and developing projects to meet specific aims as listed above. Specific projects include but are not limited to: the characterization of cervical microstructure during pregnancy, the pathogenesis of Listeria monocytogenes in pregnancy, the pathogenesis of zika virus during pregnancy, and characterization and refinement of a primate model of traumatic spinal cord injury are ongoing.

Redacted by agreement	Unpublished
Unpublished	

based on the poster presented at the 2017 ASCVP annual meeting.

Unit members will continue to support training and outreach programs for education and conservation through mentoring of undergraduate, graduate, and post-doctoral students; attendance/presentation of scientific information at national and international meetings; and organization of local meetings and seminars, and presentations at local primary and secondary schools.

NONHUMAN PRIMATE BIOLOGICAL MATERIALS DISTRIBUTION (NHBMD) CORE

Unit Heads: Redacted by agreement Ph.D.
Redacted by agreement D.V.M.

GOALS AND ACCOMPLISHMENTS

Goals

Description:
The primary goal of the Nonhuman Primate Biological Materials Distribution (NHPBMD) core is to support cutting edge research using NHP models by providing economical access to NHP biological samples and educational materials. This core goes beyond a traditional tissue distribution program by providing: samples collected at the time of necropsy, access to samples previously banked, and additionally specific minimally invasive ante-mortem manipulations prior to necropsy. The NHPBMD core has IACUC approved protocols that allow for short-term assignment of animals for minimally invasive *in vivo* sample collections. The NHPBMD core is a synergistic service making the most efficient use of SPI (Scientific Protocol Implementation) Unit and PSU (Pathology Services Unit) expertise to provide critical support for developing pilot projects and long-term research needs. This core provides a varied cadre of intellectual and service resources for investigators transitioning research paradigms from other species to NHP or from NHP to humans.

Specific Aims:

Specific Aim 1: To continue to maximize the investigative use of each animal scheduled for post-mortem examination.

The Pathology Services Unit (PSU) screens animals scheduled for necropsy for appropriate samples for investigators and educators enrolled in the NHPBMD core. WNPRC core scientists are aware of the program and suggest collaborator registration with the NHPBMD core to maximize use of experimental animals. The PSU banks samples of tissues (e.g., fresh frozen liver, spleen, kidney, plasma, serum, buffy coat, OCT frozen tissues, paraffin embedded tissues, etc.) from most clinical and some experimental necropsy cases with Systematized Nomenclature of Medicine (SNOMED) coded morphologic diagnoses; combined with electronic records of health, kinship, reproductive history, and pedigree for research purposes. This metadata combined with final medical diagnoses are integral to the efficient identification and utilization of appropriate samples for retrospective studies as well as studies involving development of unique investigative methods. Aged animal tissues are routinely donated to the NIA Aged nonhuman primate tissue bank.

Specific Aim 2: To increase the investigative usage of colony animals through minimally invasive manipulations.

SPI is responsible for requests that require sample collection from live subjects. Samples that may be collected from live animals not scheduled for necropsy may include: whole blood plasma, serum, urine, semen, CSF, bronchoalveolar lavage fluid, biopsies of skin, muscle, and superficial lymph nodes, and swabs for bacterial and viral evaluation.

Specific Aim 3: To coordinate complex collection needs through ante-mortem manipulations prior to sample collections for both *in vivo* and post-mortem sampling.

This aim has been and will continue to be, an important mechanism for the provision of affordable NHP samples to extramural investigators who need specialized tissues or organs such as embryos or fetal tissues collected at specific time points.

Specific Aim 4: To leverage and develop collaborative relationships with investigators, who may originally make simple research requests for pilot data, into projects utilizing full WNPRC research support in NHP models.

The core has the expertise and experience to mentor new investigators as well as collaborate with established individuals transferring their research to NHP models. The core serves as an initial point of contact for numerous investigators (especially those at other academic institutions lacking NHP resources) and makes use of the SPI service paradigm to support and advance NHP research from “inception to publication.” The strongest benefit in the change to a core service has been the leveraging effects for developing collaborative relationships with investigators, that have resulted in grant applications with members of both the SPI and Pathology Services units serving as co-investigators and co-authors.

Accomplishments

Specific Aim 1: To continue to maximize the investigative use of each animal scheduled for post-mortem examination.
Specific Aim 2: To increase the investigative usage of colony animals through minimally invasive manipulations.
Specific Aim 3: To coordinate complex collection needs through ante-mortem manipulations prior to sample collections for both *in vivo* and post-mortem sampling.
Specific Aim 4: To leverage and develop collaborative relationships with investigators, who may originally make simple research requests for pilot data, into projects utilizing full WNPRC research support in NHP models.

Major activities and results for all four specific aims are encompassed in the detailed core report. In summary, we continued to meet our current goals as outlined in SA1-4 which allowed for short-term assignment of animals for minimally invasive collection of biological samples, short-term experimental manipulations followed by specific post-mortem collection of tissues, traditional post-mortem sample collection, as well as access to numerous banked samples. This has resulted in peer reviewed publications and increased recognition of NHPBMD Core as a national resource.

The NHPBMD core has consistent enrollment requirements for internal and external clients. We request in our acknowledgement form a signature from both the investigator and an institutional representative the following:
1. Individuals are qualified to receive NHP biological materials “I attest that I am qualified through education and training to work with such material. I hereby assume all risk and responsibility in connection with the receipt, handling, storage, use and disposal of the material, and in accordance with this, I will ensure that all relevant parties, including my laboratory staff and collaborators, receive proper education and training to work with these materials.”
2. Any federally funded projects utilizing these NHP biological materials follow the requirements of PHS and NIH for animal use protocols and congruence with funding “I confirm that I have secured, or will secure, all the necessary institutional approvals, such as Institutional Animal Care and Use Committee (IACUC) and biosafety protocols, to receive these materials and to conduct research with them. Furthermore, I attest all approvals and protocols are congruent with any Federal funds to be used to conduct research with these materials as per National Institutes of Health (NIH) Grants Policy Statement and per the Public Health Service Policy on Humane Care and Use of Laboratory Animals.”
3. The efforts of the core can be documented by relevant publications of investigators obtaining these materials “…to facilitate the annual WNPRC P51 progress report to the National Institutes of Health, we request that each biological materials recipient send a brief annual progress report at the end of each calendar year by email to NHPBMD@primate.wisc.edu or mail to the NHPBMD core …”

The NHPBMD core continued to focus on organizing cooperative collections and processing efforts while ensuring accurate MTA agreements, and reducing questions about cost sharing. Excellent science combined with administrative support provided by the WNPRC Operational Services Division continues to be an important WNPRC resource. Finally, the NHPBMD core continued to specialize in providing resources to meet the needs of investigators transitioning research paradigms from other species such as rodents to nonhuman primate models.

FUTURE GOALS

We plan to continue with our current goals as described above which most importantly allow for short-term assignment of animals for minimally invasive collection of biological samples, short-term experimental manipulations followed by specific post-mortem collection of tissues, traditional post-mortem sample collection, as well as access to numerous banked samples.

We plan to maintain consistent enrollment of core, affiliate, and extramural investigators for NHPBMD core services to easily facilitate access to samples acutely identified for pilot projects and tangential investigations. WNPRC core investigators currently recommend enrollment of collaborators for NHPBMD core services to ensure accurate MTA agreements, and reducing questions about cost sharing in this strained funding atmosphere. These functions will be refined with emphasis placed on excellent science with administrative support provided by the WNPRC Operational Services Division.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Associate Director	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
3	Secretarial/Clerical	EFFORT			72,134.00	30,657.00	102,791.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**102,791.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**102,791.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	15,680.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**15,680.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**118,471.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	118,471.00	43,834.00
		Total Indirect Costs	**43,834.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**162,305.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Behavioral Services Unit (Animal-Resources-002)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1 (SA1): To ensure the psychological well-being of our nonhuman primate (NHP) colonies. There are three sub-aims.
SA1a. To create and maintain stable social housing conditions for animals within the colony.
SA1b. To coordinate, maintain and expand upon the environmental enhancement plan (EEP).
SA1c. To maintain a surveillance program to follow behavior of potential concern.

Specific Aim 2 (SA2): To provide research support for investigators.

Specific Aim 3 (SA3): To provide NHP behavior training for personnel and NHP.

Specific Aim 4 (SA4): To disseminate Behavioral Services Unit (BSU) research results through interaction with colleagues, scientific presentations and peer-reviewed publications.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Accomplishments_Behavioral Services.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 primary service aims of the BSU will continue but have expanded in scope to better reflect the evolution of our unit. The opportunity provided by increased staff has allowed us to meet our expanding service to investigators. Our unit will continue to focus on socialization of single-housed animals (SA1a). Along with establishing stable pairings and groupings, the deployment of added social housing environments have continued to develop and with this opportunity our role will require more individualize animal training for those animals adapting to these environments. Overall, we have seen improvement in how we address our primary aim of providing social opportunity for the animals under our care.

We have increased staffing opportunities in the effort to continue to refine and implement efficiencies in tracking the success and progress of its pairing initiative and following behavioral treatments for cases of abnormal behavior. We will continue to make progress in efforts to use EHR to track individual animal histories and prompt “onset” and “off set” of behavioral treatments and follow-up assessments to more efficiently inform treatment strategies; however, we currently waiting in the EHR services priority cue for developing some of these features.

In the next period, the Behavioral Management Unit will continue to move forward with its projects aimed to refine strategies to ensure the psychological welfare of the NHPs (SA 1 b & c). The development of behavioral assessment tools, pairing follow-up and evidence-based analysis of our enhancement practices we will increase our ability refine our goals of providing for psychological welfare of our animals. One future goal will be to evaluation of our enrichment program by developing new strategies and interactive opportunities for the animals. We have begun this effort in our marmoset colony and will carry this forward to our macaque program. Other goals include investigating colony wide temperament assessment as a predictor of pair compatibility, expanding the use of interactive cognitive tasks and refinements to our alopecia scoring procedure. As we move forward we will be implementing these changes, evaluating outcomes and refining our delivery the various components of our enrichment and enhancement plan.

We expect a continuing increase in requested training in support of research programs as many of the existing projects will continue in the next period and new requests continue to increase (SA2 & SA3). We also expect that our role in carrying forward our behavioral expertise in training animals and primate users in advanced techniques will continue to increase because of the ongoing upgrades in social housing and increased complex of structural environments often pose challenges for animal transfer for both daily care (CMU) and research needs (SPI). Furthermore, research scientist’s requests for behavioral service have also continued to increase. Thus, we hope to expand personnel positions to accommodate the growing requests for advanced behavioral training in order to serve the entire WNPRC enterprise (CMU, SPI, PSU and individual investigators). The unit will continue as a partner in university-wide training in basic NHP behavior and enrichment (SA3) including the support of undergraduate educational opportunities. Finally, we will continue to disseminate our findings through interaction and collaboration with the NPRC’s BMC, the undergraduate opportunity initiative

participation in science advocacy centered on animal care and welfare, scientific meetings and the peer-reviewed literature (SA4).

BEHAVIORAL SERVICES UNIT

Unit Head: Redacted by agreement Ph.D.

Accomplishments

To ensure the psychological well-being of our nonhuman primate (NHP) colonies (SA1). To create and maintain stable social housing conditions for animals within the colony (SA1a). Species-typical social behavior is essential for the healthy development and well-being (SA1a). Social groupings, however, must also harmonize with research programs and housing dynamics of the colony. In 2018, we continue to meet our objectives of providing for the social needs of the animals under our care. In brief, 100% of our marmosets are socially housed with a small number singly house for short periods as necessitated by research protocols and clinical care. Sixty-four percent (64%) our macaque colony was socially housed with an additional 16% holding IACUC approved exemptions or exceptions related to research. Approximately 8 percent of our animals are in the process of transition to research projects that require additional consideration prior to pairing or resolution of their upcoming housing status. The remaining pool of 12% were engaged in the pairing process. The animals remaining in the pairing pool are of mixed sex and age, as well as vary in other factors that preclude 1 to1 pairings or social groupings (i.e., Viral status, disease status, and historical variables). We continuously evaluate pairing relevant demographics and resources to match animals and aim to do so in a manner that optimizes pairing success and potential longevity of the pairs/groups we create.

The Behavioral Services Unit (BSU) employs several strategies to increase pairings and groupings over time and we have continued this progress in this grant period. We have developed novel housing environments to create small groups in runs, and other standard cage footprints by adding tunnels and cage extensions. The BSU also continues to mixed-age groups with the aim of building long term species-typical interactive social skills in younger animals. Finally, an area we continue to pursue includes mixed-age social breeding groups. This effort involved Operational Services: Shop Services in the further expansion of pen features by developing multiple closeable pass-throughs to chain multiple small pens to create larger areas to support these larger groups.

Currently we have 12 pen/room indoor housing environments, but have had a maximum of 17 pens groups over the project period depending upon available animals and group compositions. The groups sizes in these pens range from a minimum of 4 to a maximum of 37 over this period. We have continued to increase the number of animals socially housed in pen environments in this project period (>280) and attaining the highest number of pen-housed animals over the last 5 years.

We have also continued to use small pen or run units a as platform in the initial pairing. Some equipped with cage extensions and/or C-tunnels. These features provide additional space and structural complexity. The more complex environments allow more escape avenues in cases of aggression. The versatility we have developed in our housing environments allows us to transition “paired or grouped” animals to standard colony housing in accordance with required cage size and maintain the animals in social pairs.

Finally, we have continued pairing animals in quarantine. Pairing in quarantine under most circumstances has now become the norm rather that an exception. We have collaborated with the Veterinary Care and Colony Management (CMU) units to increase our efforts by accumulating information on the social histories and past pair-mates prior to the animals’ arrival to our facility. Knowledge of the social histories of incoming animals and streamlining the veterinary assessment procedure has allowed our unit to pair animals as soon as possible upon arrival to our facility. For example, in this project period of the 236 arriving animals, 49% percent of our quarantine animals were paired immediately with an additional 11% paired within 30 days. The remainder of the animals single for more that 30 days required additional veterinary review and clinical testing as a required to ensure colony health. Those animals not paired in quarantine were maintained in protected or visual contact as appropriate to maintain the requirements of the veterinary quarantine procedure.

Under this aim we continue to pursue one archival study over the course of the project period. The study will describe our colony pairing efforts over time, highlight our success and identify factors that affect the pairing process. We hope to specifically characterize the dynamics that affect the transition of animals in and out of the pool of animals available for pairing.

To coordinate, maintain and expand upon the environmental enhancement plan (EEP) SA1b. The BSU has a well-developed and successful environmental enhancement plan that outlined our continued to provision of complex social and interactive environments to the animals under our care. In practice, specific strategy and practice are instantiated in WNPRC standard operating procedures (SOPs) that serve as living documents refined and updated as we "try-evaluate-and modify" our practice (SA1b). Broadly, in this project period we have updated SOPs that describe: Enrichment food lists both in variety and adjusted portion sizes, incorporated new foraging toys, upgraded our delivery of sensory enrichment employing lighting that allow varied colors and patterns and replaced and/or maintained our array of foraging and enrichment toys.

Currently the evidence-based evaluation of this aim we have 3 ongoing studies in the active data collections phase through the project period. Two projects evaluate marmosets and one macaques. The first marmoset project involves shaping the marmosets to voluntarily station on a scale to collect body weight. We are developing methods and protocols in this study that we intend to adopt for future cohorts of marmosets. Further we intend to adapt what we learn to apply broadly to other cooperative procedures involving macaques in the future. A second study in marmosets involves evaluating patterns of interaction with a common wooden toy varied by a dimension of stability.

The macaque project is a comparison of foraging toy preferences. In this project we will assess all available foraging toys by attaching an actimeter (Actical, Respironics, Inc) to each toy prior to delivery to the animal. We have piloted this work to standardize placement of the actimeter and confirm reliability of the method to capture data with simultaneous video recording. We will be cycling through all available foraging toys and perform a "head-to-head" usage analysis of each. In this manner we expect to refine our provision of foraging toys by identifying those toys that invite the most interaction and preferential select toy that engender the highest amount of interaction.

Finally, in the domain of environmental enhancement we have continued to collaborate with Operational Services: Shop Services and CMU. For example, in this project period we have continued to identify, modify and re-purpose existing caging to create enhanced structural environmental elements. For example, we recently identified 7 larger footprint cages that were in storage and modified them to connect in series and provide additional space for socialization. In past grant periods we have established the animals use often prefer the increased perspective afforded by an extended or expanded vertical spaces through the use of cage extensions and C-tunnels. We continue to provide positive pressure to increase extension use throughout the macaque colonies and use has been formalize and tracked through the EHR system since August 2018 (see CMU report).

To maintain a surveillance program to follow behavior of potential concern SA1c. The BSU employs a mixed model of behavioral surveillance integrated across Animal Services Division Units (SA1c). Daily behavior reporting begins with observations by the animal research technicians (ARTs) and veterinary technicians. Behaviors of concern are noted and BSU follow-up performed. BSU personnel intervene with appropriate behavioral treatments (e.g., increased foraging, displacement objects, relocation, etc.) and consult with veterinary staff as needed. WNPRC's team-based surveillance approach will continue to concentrate BSU resources on animals reported for the expression of atypical behaviors. We will continue to refine our surveillance procedures in collaboration with Electronic Health Record (EHR) services to streamline behavioral reporting across units to flag and share animals' behavioral status, surveillance progress and treatment status. We hope to realize these advancements in the next project period.

In addition to our cross-unit integrated strategy, in past project periods we have performed colony-wide behavioral assessments to more broadly observe and assess welfare. The idea behind this approach was to observe the progression of untoward behavior, and thus, position the BSU to identify predictors of the development of abnormal behavior. Over time our approach has evolved from recording only "abnormal" behavior, to a holistic approach that includes species-typical behavior. This change occurred for two reasons: 1. abnormal was of low occurrence; and 2. Recording only "abnormal" behavior in absence of "normative" behavior does not inform population levels of expression. As part of this process we developed a tablet-based application to record behavior collecting observations for approximately 500 animals. From subsequent analyses of these observations we determined that a number of commonly used behavioral categories occur with low incidence and merit exclusion.

In this project period we revised our behavior ethogram, developed and implemented a 2nd generation tablet-based behavioral observation program through collaboration with a working group at Drake University and we are nearing completion of a yearly assessment of all animals in the colony. The tablet-based system outputs data in a CSV format and we are currently coding small applications to pull summary data from individual subject files create summary tables that can be uploaded to the EHR system.

Under this aim we pursued two projects: An archival analysis of the long-term behavioral adjustment outcomes following clinical nursery rearing, and a collaborative project with NPRC's Behavioral Management Consortium comparing alopecia scoring scales.

The outcomes analysis of clinical nursery rearing analysis includes both behavioral and health related measures thought to be potential indicators of welfare status. For example, duration in the nursery, abnormal behaviors, diarrhea, alopecia, and frequency of irregular observations as reported in the EHR. To date we have completed data organization for 4 of 5 "targeted" birth cohorts.

In alopecia scoring project we are comparing the "Rule of 9's" and current WNPRC scoring scales for assessment of alopecia. To date, we attended a BMC webinar describing the rule of 9's method scoring scale, achieved inter-center reliability and collected data on a pilot set of animals (n=~60).

To provide research support for investigators (SA2). Experienced BSU staff are available to assist investigators with animal transfer training, shaping techniques and positive reinforcement training (SA 2). In addition, BSU staff are available to work with scientists to develop individualized animal training plans for specific projects as needed.

As in past project periods the BSU has provided advance training in support of investigators scientific aims. We regularly interact with investigators in the process of subject selection for research projects giving input into behavioral histories of candidate animals and later work with them as experimental timelines are established if the animals experience adjustment issues.

In this project period, we continue to collaboration with the Scientific Protocol Implementation Unit (SPI) in training animals to sit in a primate chair for semen collection. Similarly, we have continued to assist a neuroscience researcher Redacted by agreement to maintain chair training proficiency in existing animals, as well as, chair acquisition in a group of new animals.

We continued a longitudinal behavioral assessment of reactivity to a human intruder as part of a project evaluating the effects of pediatric anesthesia regimens (Ikonomidou). Over the course of this project period we have tested 11 subjects across 3 time periods (6, 12 and 18 mos.) and additional sessions remain as the animals mature to targeted testing time points. Preliminary analysis from testing completed to date suggest that suppression of behavioral activity occurs most dramatically under the stare "mild threat" condition as would be expected. There substantial inter-subject variability in the degree of this response. Analysis of individual behaviors is continuing as completed sessions are scored. Between-treatment group differences will require data from upcoming test sessions for analysis.

Two new projects requiring specific BSU support began in this project period (Sept. 18'). The will leverage archival data an ongoing project assessing adjustment outcomes of animals that have spent time in our clinical

nursery. The major goals are: 1.) to determine whether emergency interventions that require clinical nursery stays in the first weeks of life affect monkey brain morphology; 2.) whether, and the degree to which, contemporary clinical nursery rearing produces changes in brain morphology relative to typically-reared monkey. To this end we will collect brain images from clinical Nursery reared (NR) animals and Mother-reared controls (MRI) (MR/NR; 12/12; n=24) and analyze these images using machine learning, diffusion tensor imaging tractography (DTI), and region of interest (ROI) analyses (Redacted by agreement WNPRC pilot project). In sum, the pilot study will provide the foundation for data to be used in future grant submissions that will allow us to expand the scope of (1) brain and behavioral phenotypes and (2) to further how variation in early social rearing interacts with the genome to influence a variety of behavioral and neurological outcomes. This project is currently in the early phases of execution.

The second project began in October 2018. For this project we have been involved in identification of available dams for formation of compatible Mother-infant pairing. This involves the formation of these pairs as well as follow-up evaluation of continued compatibility. This effort requires a large multi-unit collaborative group including the investigators Redacted by Colony Management Unit, Macaque Breeding Coordinator and veterinary staff. To date we have created 8 M-I pairs (Oct-Dec 18').

We expect the demand for BSU research support will continue to expand as the number of projects increase. For example, in a collaborative effort with Scientific Protocol Implementation (SPI) and Pathology Services Unit (PSU) we are working with an investigator to develop a behavioral test to quantify extent of neglect in a model of spinal cord injury. Another group of investigators have expressed interest in BSU support in assessment of behavioral reactivity using the human intruder test. Finally, as part of an initiative across the National Primate Centers we are going to be performing a standardized assessment of response to novelty.

To provide NHP behavior training for personnel and NHP (SA3). The BSU plays a crucial role in the campus wide laboratory animal program by providing prerequisite training in NHP behavior to all University staff that encounter NHP as a work requirement (SA3). Our unit focuses on teaching appropriate human-NHP interaction. Bi-directional "human-NHP" interactions involve both instructing humans effective handling approaches, as well as, training the NHP to adjust to the demands of the environment. These training sessions are generally available twice monthly; however, additional offerings are commonly scheduled. For the project period (1/1/18-12/31/18) we served 127 attendees for our behavioral orientation sessions. Further we provide Face-to-Face instruction to new animal care technicians as part of their initial training. This training includes guidance in animal handling and transfer, as well as, enrichment preparation and delivery. We are also involved in bringing some of this content to online modules for offsite users (see Training Unit progress report).

Another significant component of our general service aims is our role in training animals to transport for both general husbandry (CMU) and research purposes (SA2). Transport training ranges from training animals to enter and exit transport boxes or the table top restraint system to transfer training within small pen housing. We are often called upon when staff and investigators have difficulty transferring an animal. Follow up with these animals often requires retraining sessions for the animals that regress in proficient transfer. With the expansion of the number of small pen housing environments, pen transfer training sessions are required because of the unique requirements for the animals in these expanded spaces. In this project period we have developed and refined facility SOPs for transferring pen housed animals specific to type of pen housing environment. Further, we have developed SOPs for working cage extensions and C-tunnels, housing enhancements that allow increased environmental complexity. Finally, pen transfer training often requires training sessions for new staff and staff refresher presentations as these advanced behavioral training techniques are a communal effort with staff.

A final component of our training aim includes undergraduate education opportunities. We provide instruction in animal behavior and unique opportunities to work with NHP on welfare studies, while promoting peer-to-peer exchange of information about the role of NHP research in biobehavioral science. Past undergraduate students have contributed to our dissemination aims working on semi-independent project presenting results both locally at the undergraduate research forum, as well as, at regional and national scientific meetings (SA4).

Over the course of the project period 6 undergraduates contributed to our program. The student's efforts resulted a conference presentation, 2 publications and 2 pending manuscripts. The theme of two of these

publications was to first develop a quantitative assessment method to compare enrichment strategies and the second an application of the metric to perform an evidence-based evaluation of enrichment programs in non-human primates across a variety of facility types housing NHPs.

The availability of qualified undergraduates is cyclical with best outcomes with recruitment at the beginning of an academic year. Student availability for an extended period of time to acquire the instruction necessary to work with primates limits our ability to accommodate large numbers. However, the placement of our facility on the campus of a research university positions use to contribute to the pipeline of future scientists with expertise in primate models. Thus, we will continue to recruit and provide undergraduates research opportunities in conjunction within this aim.

To disseminate BSU research results through interaction with colleagues, scientific presentations and peer-reviewed publications (SA4). The BSU aims to generate performance metrics to determine how our practices encourage behavioral interaction and improve overall well-being. The dissemination of our efforts through interaction and collaboration with the NPRC's Behavioral Management Consortium (BMC), the undergraduate opportunity initiative, scientific meetings and the peer-reviewed literature serve to promote the WNPRC research enterprise to the scientific community and assure the public that species-typical behavioral health is paramount for the NHP under our care.

In this project period as part of the BMC we updated the content of the NPRC behavioral welfare page adding behavioral assessment tools employed across primate centers. We also initiated an online moderated technicians' forum and webinar series on behavior related topics. At the BMC's annual meeting held jointly with the NPRC's Breeding and Colony Management Consortium (BCMC) the BSU presented cross center initiatives including: Outcomes of social housing; socialization in quarantine, updates on website and technician forum usage, enhanced cage environments, alopecia scoring, and common inspection topics.

The BSU has also been active in presenting our work and contributing to dialogues to the broader scientific community in a number of other venues. For example, 2 student presented work at conferences (SA3), the unit head presented an invited talk at the University of Wisconsin School of Veterinary Medicine entitled "In service of science and animal welfare: Behavioral management of nonhuman primate in US research facilities." The unit head, Redacted by agreement serves on the Animal Welfare Committee of American Society of Primatologists (ASP), and the local planning committee for the 42nd annual ASP meeting (Madison, WI; 2019). He also serves the Midwest Psychological Society as a reviewer of the Psi Chi student presentations, and as a reviewer of the American Psychological Association (APA; Div. 6) student presentation awards.

In 2018, Dr. Pierre was selected to a three-year term as a member of the APA Committee on Animal Research Ethics (CARE). As part of the committee Redacted by agreement participated in advocacy training, a congressional briefing and representative office visits to share both the importance of care and welfare within the context of research, and, the role of basic research in the process of scientific discoveries that directly benefit the public (2/18). Further he served as a CARE representative to the APA's board of scientific affairs which is charged with presenting the scientific goals and agenda to the governing counsel of the APA (11/18). Taken together, these activities highlight the contributions of the WNPRC BSU to a broad and wide-ranging scientific audience.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Unit Head	Redacted by agreement	EFFORT			58,505.00	19,482.00	77,987.00
2.					PhD	Core Investigator					17,829.00	5,937.00	23,766.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **101,753.00**

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						
4	Research Specialist	EFFORT			49,318.00	16,423.00	65,741.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**65,741.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**167,494.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	116,545.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**116,545.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**284,039.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	284,039.00	105,094.00
		Total Indirect Costs	**105,094.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**389,133.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Colony Management Unit (Animal-Resources-003)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1 - To provide a consistent and excellent husbandry program compliant with all laws, regulations, and guidelines governing the care of captive NHP utilized in research
The primary goal of the Colony Management Unit (CM) of the WNPRC is to provide the highest quality animal husbandry program for the NHP colonies of the Center. The main components of the husbandry program include the provision of food and water, consistent and thorough sanitation of the NHP enclosures and support areas, and the implementation of a rigorous pest management program in collaboration with a commercial vendor. The husbandry program is supervised by a colony manager and five animal care supervisors with extensive NHP husbandry experience.

Specific Aim 2 - To perform, document, and communicate daily health observations for the NHP colonies
An Animal Research Technician (ART) of the CM evaluates each animal in the WNPRC's NHP colony a minimum of two times per day for evidence of disease or injury. This information is crucial to the well-being of the colony as it is used by the WNPRC Veterinary Staff to triage animals that may require clinical treatment. Each ART undergoes intensive instruction from WNPRC supervisors, Compliance and Training, and Behavioral Services Unit (BSU) personnel to ensure that they are able to identify common and abnormal behaviors exhibited by captive NHP.

Specific Aim 3 - To execute the delivery of environmental enrichment (food treats and manipulanda) to the NHP colonies
The staff of CM play a pivotal role in assisting the BSU with implementing the WNPRC Environmental Enhancement Plan (EEP) by delivering a majority of the edible and inanimate enrichment objects to the NHP colonies of the center. The ARTs also execute the remainder of the food-based portion of the EEP by offering fruit or vegetable pieces to the NHPs each day and by preparing and delivering a majority of the foraging opportunities offered to the colonies each week.

Specific Aim 4 - To support the clinical, behavioral, and research initiatives of the WNPRC by providing personnel to administer medical and experimental treatments, collect biological samples, transport animals and biological samples, and collect behavioral and scientific data in collaboration with the WNPRC SPI unit
Colony Management personnel play a critical support role for the clinical, behavioral, and research units of the WNPRC. The ARTs administer a majority of the clinical treatments prescribed by veterinary staff and, in collaboration with the Scientific Protocol Implementation (SPI) and Veterinary Services Units (VS), ARTs are also responsible for weighing animals, administering experimental agents, collecting tissue samples, and collecting data for various experimental protocols and clinical evaluation.

Specific Aim 5 - To meet the animal subject requirements of investigators by managing the NHP breeding and stock colonies of the WNPRC
In collaboration with the other units of the Animal Services Division, CM personnel are responsible for maintaining the NHP colonies of the Center by utilizing contemporary methods to track and maintain the genetic integrity of breeding populations and by breeding or purchasing animals to fulfill the needs of investigators.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Accomplishments_Colony Managment.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?

During the next funding period, the personnel of the Colony Management Unit will continue to provide an excellent and compliant standard of NHP husbandry, assist the other units within the Animal Services Division, and support the ongoing and new projects of the Center's core and affiliate PIs.

Specific Aim 1 – To provide an excellent and compliant standard of animal husbandry, the Colony Manager and the animal care supervisors will continue to nurture and motivate the existing animal care staff through close evaluation of their daily performance, positive feedback, and advice on how to improve their skill sets and efficiency. With the assistance of the WNPRC Human Relations Unit, the Colony Manager and supervisors will ensure that deserving Animal Research Technicians (ART) receive merit raises and

promotions. Similarly, ARTs who are underperforming will receive retraining from the supervisors and personnel of the Compliance and Training Unit to ensure that their performance improves. The WNPRC continually supports the career development of our ARTs by providing continuing education opportunities to attend leadership lecture series offered by the UW, becoming certified through the American Association of Laboratory Animal Research, and successfully obtaining positions as colony management supervisors, research associate positions, veterinary technician positions, and attending veterinary and post-graduate school.

In collaboration with the Attending Veterinarian and BSU personnel, CM personnel will continue to play a crucial role in the WNPRC's commitment to socializing NHPs. ARTs immediately report any evidence of aggression or wounding between pairs and groups of animals to Behavioral and Veterinary Services personnel to ensure timely intervention. CM personnel will work in unison with BSU and the WNPRC shop personnel to identifying any structural modifications that are required in animal housing to promote wellbeing and investigate innovative social enclosures to help enhance animal housing.

Specific Aim 2 – CM personnel will continue to perform daily health observations that are crucial to ensuring that animal needs are addressed in a timely fashion by both VS and BSU. CM personnel will work closely with Informatics and Data Services (IDS) personnel to continue to hone the electronic health record (EHR) system to improve data entry and to further reduce the need of hardcopy forms.

In addition, CM will continue working with IDS to streamline the newly added pregnancy and breeding module in EHR.

Specific Aim 3 – CM personnel will continue to support the EEP by providing edible and destructible enrichment, foraging opportunities, and audio and visual stimulation. ARTs will assist Behavioral Services in improving the plan by reporting on which components of the EEP are most well used by the animals and which components need to be altered or eliminated from the plan. The positive psychological bond build between the ARTs and the animals will continue to be emphasized as an important part of the EEP.

Specific Aim 4 – CM personnel will provide support to the clinical, behavioral, and research units of the WNPRC during the next funding period by completing the following tasks:
• Collecting blood and various other tissues (e.g., feces, urine, hair, breast milk, etc.) from NHP for clinical, behavioral and research purposes
• . Weighing and transferring conscious and sedated animals for husbandry, clinical, breeding, behavioral, and research purposes

Specific Aim 5 – The CM Unit will ensure that WNPRC core and affiliate PIs have an adequate supply of animals during the next funding period by maintaining the existing nonhuman primate colonies by working to achieve the following goals:

• Maintaining the SPF-4 (Herpes B-, SRV-, STLV-1-, SIV-) rhesus macaques and increasing the supply of other viral free pathogen animals (AA01, AA08, etc.) upon request.
• Ensuring the genetic diversity of the macaque colonies by following the macaque breeding management decision tree established by Redacted by with the assistance of Redacted by and the ONPRC genetic analysis reports
• Expand the WNPRC marmoset colony by using the breeding management decision tree established by Redacted by agreement with the assistance of Redacted by agreement and the ONPRC genetic analysis reports

COLONY MANAGEMENT UNIT

Unit Head: Redacted by agreement

Accomplisments

Specific Aim 1 - To provide a consistent and excellent husbandry program compliant with all laws, regulations, and guidelines governing the care of captive NHP utilized in research

- CM personnel performed daily cleaning, feeding, and bi-weekly cage sanitation for the entire WNPRC population of nonhuman primates, which consists of, on average, 1120 rhesus macaques, 188 cynomolgus macaques, and 258 marmosets during the reporting period.
- In collaboration with the Behavioral Services Unit (BSU), CM has helped introduce 122 animals into social breeding groups during the reporting period.
- To help support the Environmental Enhancement Plan (EEP), CM has placed 131 c-tunnels and 298 cage extensions to enhance the housing environment for the macaque colonies in Building 2 and BMQ during the reporting period.

Specific Aim 2 - To perform, document, and communicate daily health observations for the NHP colonies

- CM submitted 755,164 daily observation reports on individual animals that needed to be addressed by the WNPRC veterinary and/or Behavioral Management staff. These morning and afternoon health observations are pivotal to ensuring that clinically compromised animals receive rapid and appropriate care during this reporting period.
- During this same time period, CM personnel performed 121,629 menses checks on female macaques. Data from these menstrual checks is used to populate monthly menstruation tables for each female animal in the macaque colony. This information is extensively used by the rhesus breeding coordinator to determine the most appropriate time to breed an animal and to increase the possibility of conception. In addition, the data on stock animals is used by investigative groups for reproductive, neurological, and infectious disease research.

Specific Aim 3 - To execute the delivery of environmental enrichment (food treats and manipulanda) to the NHP colonies

- CM personnel continue to support, up to six days per week whenever possible, foraging opportunities for the entire colony at the WNPRC.
- In addition to the foraging opportunities listed above, CM personnel delivered 958 additional foraging opportunities to animals exhibiting self-injurious behavior or recovering from surgery/injuries to assist in the improvement of their psychological wellbeing and physical recovery.

Specific Aim 4 - To support the clinical, behavioral, and research initiatives of the WNPRC by providing personnel to administer medical and experimental treatments, collect biological samples, transport animals and biological samples, and collect behavioral and scientific data in collaboration with the WNPRC SPI unit

- CM personnel performed 9056 blood collections for experimental and clinical purposes during this reporting period.

- CM personnel performed 2614 ART therapy applications for experimental support during this reporting period.
- CM personnel performed 331,273 clinical and experimental treatments that were prescribed during this reporting period.
- CM personnel performed daily observations on newly formed social groups and reported any evidence of incompatibility to BSU.
- Starting August 2018, CM personnel has performed 5677 vaginal swabs for various research projects.
- CM personnel collected 293 urine and 50 fecal samples to support the Zika and Listeria research projects during this reporting period.

Specific Aim 5 - To meet the animal subject requirements of investigators by managing the NHP breeding and stock colonies of the WNPRC

- The SPF macaque-breeding colony produced 106 offspring and the marmoset-breeding colony produced 52 offspring.
- CM personnel assisted in acquiring 235 macaques (150 rhesus, 85 cynomolgus) to fulfill PI needs that could not be fulfilled by animals from the existing WNPRC colonies.
- The WNPRC acquired two established Mauritius cynomolgus breeding colonies (n=34, n=16) to support infectious disease research.
- In collaboration with the WNPRC Genetic Services Unit and the NPRC Genetics Consortium, the CM unit continues to obtain samples that have been utilized to identify the MHC type of each new offspring of the macaque-breeding colonies.
- In collaboration with the VS and in response to the needs of multiple investigators, the CM continues to collect samples that are used to identify SPF macaques that are also negative for Adeno-Associated virus (AAV) and/or Rhesus Rhadinovirus (RRV).

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Unit Head	Institutional Base Salary:	EFFORT			37,182.00	12,382.00	49,564.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **49,564.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
3	Undergraduate Students	EFFORT			8,927.00	276.00	9,203.00
	Secretarial/Clerical						
48	Research Prog Mgr / Lab Tech Supv / Animal Research Tech				659,506.00	274,506.00	934,012.00
51	**Total Number Other Personnel**					**Total Other Personnel**	**943,215.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**992,779.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	625,767.00
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	**625,767.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**1,618,546.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	1,618,546.00	598,862.00
		Total Indirect Costs	**598,862.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**2,217,408.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Compliance and Training Unit (Animal-Resources-004)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

A1. Educate, train, re-train and update training records for all WNPRC staff, support personnel, and visitors who may come into contact with NHP or their tissue to ensure that they understand and follow
WNPRC standard operating procedures.
A1.1. Initial Training
A1.2. Additional Training and Re-Training
A1.3. SOP Management

A2. Ensure a safe working environment for all WNPRC staff and students and to further develop the WNPRC Occupational Health and Safety Program (OHP) to maintain compliance with new and existing standards.
A2.1. Ensuring a Safe Work Environment
A2.2. Further Developing the WNPRC Occupational Health and Safety Program to Maintain
Compliance with New and Existing Standards

A3. Ensure that WNPRC personnel and facilities remain compliant with all institutional, state, and federal regulations governing the use of NHP in laboratory animal research.
A3.1. Protocol Development
A3.2. Post-Approval Compliance Monitoring
A3.3. Facility Inspections
A3.4. Record Reviews
A3.5. Incident Reporting

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: B.2 Accomplishments_Compliance and Training.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?

Training Unit goals: The Training Unit plans to continue to provide a high level of training to new ARTs so they are able to deliver the best husbandry for the colony and be more independent following their completion of the initial training program. The Unit will utilize e-Learning software to create on-line training modules to increase the accessibility of presentations created for more complicated tasks (e.g., Primate Orientation and Animal Records and Data Entry). The Unit plans to improve documentation of training to standardize documentation, improve accessibility of information, and institute more frequent review of training records, with a large emphasis on modifying the training records in the EHR system. The Training Unit is working on creating classes for animal transport, blood draw and injection training to improve the consistency of training staff on these procedures. Classes will include training worksheets, SOPs, models, and animals as appropriate for each task.

Compliance Unit goals: The Occupational Health and Safety Coordinator plans to transition the numerous safety training modules into an e-learning format to improve accessibility of information. She also plans to explore and experiment with new PPE technology and other new engineering controls, create and implement a travel policy, and create an umbrella chemical hygiene plan as a part of a comprehensive Occupation Health and Safety Program.

The Compliance Coordinator plans to devote more time to protocol audits and fulfill the goal of completing three per month. She also plans to develop tools to assist WNPRC PIs with generating protocols, tracking protocol and procedure details, and submitting consistent data to Colony Records.

The Compliance Assistant plans to create electronic request forms, instructions, and resources for Facility Access. She will also help transition other WNPRC departments to a web-based collaborative platform to improve onboarding, manage internal communication, and increase employee engagement.

COMPLIANCE AND TRAINING UNIT

Unit Head: Redacted by agreement

Accomplishments

TRAINING:
The training unit Redacted by agreement continued to train a large number of staff including animal research technicians (ARTs), research staff, veterinary staff, personnel using primate tissues, and visitors. Training module presentations and training documentation forms are used to provide consistent training points for basic and advanced husbandry. The unit continued to provide retraining as requested and are proactive in identifying and following up with deficiencies in procedures. Standard Operating Procedures (SOPs) are being reviewed and revised routinely to update changes in procedures and address incidents, with 76 SOPs reviewed, including 14 new SOPs that were developed. The Primate Orientation e-learning module continues to be developed with assistance from Research Animal Resources Center, including developing a modified in-person training module that was redesigned to better meet the initial training needs of new staff working with nonhuman primates.

OCCUPATIONAL HEALTH AND SAFETY:
The Occupational Health and Safety Coordinator Redacted by agreement continued the development and enhancement of the WNPRC OHP with the assistance of the staff of the UW-Madison's Department of Environment, Health and Safety (UW Safety) and the University Health Services Occupational Medicine Department (UHS). She continued to provide occupational health and safety training to staff, ensure a safe work environment in all WNPRC facilities, follow up on all potential exposures, and update OSHA compliance plans and emergency response plans. She continued to hold monthly WNPRC Safety Committee meetings to discuss and review safety issues and ways to mitigate identified issues and conduct monthly safety inspections with members of the Safety Committee on a rotating basis. In addition, she finalized a formal Shop Safety Program which includes routine safety inspections, the development of shop specific SOPs, and "Machine Shop Safety Rules".

COMPLIANCE:
The Compliance Coordinator Redacted by agreement continued to provide animal care and use protocol development and review service for all investigators utilizing NHP at the WNPRC. She performed 43 extensive IACUC protocol pre-reviews between January 1, 2018 and December 31, 2018 and developed additional templates for animal care and use protocols to assist WNPRC research staff with the online protocol submission process (ARROW). The Incident Prevention Committee continued to meet monthly to discuss NHP related errors that occurred during the previous month, make recommendations for preventing similar errors from occurring, and develop plans for instituting the recommendations. The Committee also evaluated mid-year statistics and trends that Redacted by agreement prepared and presented to determine if additional preventive measures need to be taken.

The Compliance Assistant Redacted by agreement continued to assist with numerous safety and compliance tasks, including the conduct of quarterly compliance inspections and multiple protocol audits. Redacted by agreement Redacted by continued to streamline the process for Facility Access Onboarding, which includes tracking compliance with mandatory initial training and medical clearances for new employees, students, collaborators, and visitors prior to entering any of the WNPRC facilities or having contact with nonhuman primates or nonhuman primate tissues.

The members of the Compliance and Training Unit are continuing to help with further development of the WNPRC EHR system by meeting with Informatics and Data Services staff weekly to discuss and evaluate new features and describe needed improvements.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Co-Unit Head	Institutional Base Salary	EFFORT			42,231.00	14,063.00	56,294.00
2.						Co-Unit Head					11,144.00	3,711.00	14,855.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **71,149.00**

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						
4	Secretarial/Clerical	EFFORT			73,624.00	25,977.00	99,601.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**99,601.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**170,750.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	8,809.00
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. Keller Online Subscription	680.00
Total Other Direct Costs	**9,489.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**180,239.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	180,239.00	66,688.00
		Total Indirect Costs	**66,688.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**246,927.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Pathology Services (Animal-Resources-005)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1 - To continue to support nonhuman primate (NHP) colony health and experimental investigations by providing rapid diagnosis of disease, characterization of current and developing NHP models, and collaborative development of experimental paradigms.

The Pathology Services Unit (PSU) is essential to NHP colony health and research at the WNPRC. The Unit continued to collaborate with the clinical veterinary staff and investigators to provide rapid diagnostics and consistent monitoring of: chronic diseases, chronic metabolic conditions, and colony health.

The Unit continued to play an integral role for the vast majority of research conducted at the WNPRC through clinical pathology testing; advice concerning nonhuman primate anatomy, comparative pathology, and disease pathogenesis; development of specialized collection protocols; cytology evaluation; and surgical biopsy evaluation. Gross and histological changes and lesions were specifically evaluated to determine: if they were the consequence(s) of experimental manipulation(s); if they would confound experimental data interpretation; if they were typical of incidental findings (background lesions in model species); or if there would be an influence on colony health and management.

Specific Aim 2 - To continue to curate and expand the NIA Tissue bank and manage the NHP Biological Materials Distribution (NHPBMD) Core in cooperation with SPI.

The PSU continues to be responsible for the collection, banking, and distribution of NHP samples to numerous local, national, and international investigators through the Nonhuman Primate Biological Materials Distribution core (NHPBMD). The PSU was awarded a 5-year renewal of the NIA Aging Nonhuman Primate Tissue Bank contract Redacted by PI) during this reporting period.

Specific Aim 3 - To serve as a resource for primate research, education, and conservation through participation in pathology consortium activities, scientific meetings, serving as advisors/consultants and training of students at the WNPRC.

The Unit trains undergraduate, veterinary, and graduate students, as well as veterinarians in clinical pathology, necropsy, anatomy, disease pathogenesis, and other topics related to NHP and translational medicine and research.

Redacted by agreement regularly present at and attend monthly NPRC Virtual Slide Conferences (VSC). These meetings are regularly scheduled and provide NPRC pathologists, residents, and clinicians with a flexible forum to present “classic diseases” for the education of residents, students and NPRC staff as well as a forum for sharing and receiving advice and peer review of diagnostic conundrums.

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: B.2 Accomplishments_Pathology.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 Pathology Services Unit will continue to refine and expand services for colony health and research. This will include ongoing work with WNPRC IDS and several other NPRCs to continue to refine the LabKey based EHR (electronic health record) to more efficiently meet colony and multi-institutional research needs. Services will be expanded in 2019 to include in-house chemistry analysis through the recent acquisition of a chemistry analyzer. A third full time pathologist will also be added to the unit to meet increasing needs.

PSU members will continue to collaborate on current and developing projects to meet specific aims as listed above. Specific projects include but are not limited to: the characterization of cervical microstructure during pregnancy, the pathogenesis of Listeria monocytogenes in pregnancy, the pathogenesis of zika virus during pregnancy, and characterization and refinement of a primate model of traumatic spinal cord injury are ongoing.

Redacted by agreement Pending Support Pending Support based on the poster presented at the 2017 ASCVP annual

meeting.

Unit members will continue to support training and outreach programs for education and conservation through mentoring of undergraduate, graduate, and post-doctoral students; attendance/presentation of scientific information at national and international meetings; and organization of local meetings and seminars, and presentations at local primary and secondary schools.

Pathology Services Unit

Unit Head: Redacted by agreement D.V.M.

Accomplishments

Specific Aim 1 - To continue to support NHP colony health and experimental investigations by providing rapid diagnosis of disease, characterization of current and developing NHP models, and collaborative development of experimental paradigms.

The WNPRC Pathology Services Unit provided excellent service while being fiscally responsible. This objective was met through the performance of record numbers of routine diagnostic and screening procedures as well as the development of innovative diagnostic methods and experimental techniques. During Yr. 57 PSU personnel almost doubled the performance of on-site assays with 2921 CBCs, 1482 serum chemistries, and 994 fecal parasitology examinations for clinical diagnostic and research purposes. The unit performed biopsies and gross post mortem examinations with research and diagnostic sample collections with histology. Redacted by agreement Redacted by joined the PSU part-time to ensure timely completion of histology for experimental needs.

Contract laboratories and laboratory supply resources were evaluated for quality and price biannually, or as needed. Protocols, SOPs, training and QA/QC practices were continually evaluated and revised as needed. Unit members regularly met and coordinated efforts with members of other WNPRC units to refine and improve sample and data collection, medical records, and reports generated through the electronic health record system. Unit members also reviewed selected research protocols and invited members of the investigating laboratories to present and answer questions at Morbidity and Mortality rounds.

Specific Aim 2 - To continue to curate and expand the NIA Tissue bank and manage the NHP Biological Materials Distribution (NHPBMD) Core in cooperation with SPI.

Pathology unit members continued to work with the NIA to receive samples donated to the NIA tissue bank and distributed samples as directed by the NIA. Complete aged animal collections were donated and samples were distributed as per NIA direction, during the reporting period.

The Pathology Services Unit coordinated and cooperatively distributed biological specimens to researchers and educators through the Nonhuman primate biological materials distribution (NHPBMD) core, described as an independent core.

Specific Aim 3 - To serve as a resource for primate research, education, and conservation through participation in pathology consortium activities, scientific meetings, serving as advisors/consultants and training of students at the WNPRC.

Redacted by agreement received funding from ACLAM to support short-term training opportunities for honorary fellows hosted by WNPRC to receive both laboratory animal medicine and pathology training. The fellows, to date, have included veterinary students, veterinarians, and pathology residents who have subsequently progressed to full time research, training, and diagnostic positions. One undergraduate student received training as part of the UW work-study program during the reporting period.

Redacted by agreement continued to serve as a participant and moderator for the Latin Comparative Pathology Group (Branch of the CL Davis Foundation) Redacted by was coordinator for the International Mock Exam Coalition; Peer reviewer for Journal of Medical Primatology and Journal of Visualized Experiments (JoVE). Redacted by agreement

was a Peer reviewer for the Journal of Medical Primatology. Both Redacted by agreement were invited reviewers for the textbook, *The Common Marmoset in Captivity and Biomedical Research* (Elsevier, pub.).

Redacted by agreement both participated in National Primate Research Center (NPRC) pathology consortium activities; primate pathology workshops; presented cases for the NPRC virtual slide conferences; and

participated and presented cases at numerous rounds at the UW Medical School, UW Veterinary School and the Wisconsin Veterinary Diagnostic Laboratory.

Ms. Hayes, Dr. Friedrichs, Dr. Simmons, and Dr. Rakasz published a manuscript evaluating bone marrow markers for characterization of cell types in the Journal of Leukocyte Biology - Weisgrau KL, Vosler LJ, Pomplun NL, Hayes JM, Simmons HA, et al. Neutrophil progenitor populations of rhesus macaques. J Leukoc Biol. 2019 Jan;105(1):113-121. PubMed PMID: 30395351.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Unit Head	Institutional Base Salary	EFFORT			53,312.00	17,753.00	71,065.00
2.					MD	Core Investigator					8,767.00	2,919.00	11,686.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **82,751.00**

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						
2	Undergraduate Students	EFFORT			10,100.00	314.00	10,414.00
	Secretarial/Clerical						
7	Veterinary Pathologist / Research Specialist				109,213.00	37,134.00	146,347.00
9	**Total Number Other Personnel**					**Total Other Personnel**	**156,761.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**239,512.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	21,823.00
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. Histology Services	23,262.00
Total Other Direct Costs	**45,085.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**284,597.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	284,597.00	105,301.00
		Total Indirect Costs	**105,301.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**389,898.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Scientific Protocol Implementation (SPI) Unit (Animal-Resources-006)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1: Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators.

We plan to continue to create a collaborative environment for investigators who want to perform biomedical research using NHP at the WNPRC. Both a scientist Redacted by agreement and research veterinarian Redacted by will continue to head the unit. In addition, an assistant scientist Redacted by has joined the SPI unit to assist in recruitment, initiation and completion of the expanding portfolio of NHP projects. SPI will continue to coordinate with other WNPRC units to ensure that project support for WNPRC core and affiliate projects is thorough, timely, efficient, and focused on providing consistent technical expertise. Once projects are initiated, SPI will continue to execute well-organized, standardized, and compliant experimental support, arrange animal assignments, coordinate with other WNPRC units to provide needed services, and develop further expertise for new innovative projects. Redacted by will continue to advise and have oversight on any projects related to the EMCD working group. We will continue to respond to innovative research questions by creating and/or refining technical procedures to provide the highest possible level of experimental support.

We are particularly committed to identifying new investigators that need to develop NHP projects for translational purposes. In order to continue excellent unit function, we have determined 4 goals to improve our efficiency with experimental support: (1) continue to solicit feedback from investigators as we work with them; (2) recruit and hire additional technicians to accommodate the increased demand for NHP research project support; (3) incorporate charges into procedure schedules in EHR; and (4) Utilize the EHR database to compile and provide detailed experimental summaries to PIs in a rapid, efficient fashion.

Specific Aim 2: Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities.

SPI emphasizes the importance of executing well-organized, standardized, and compliant procedures for successful research programs. Furthermore, development of new techniques for innovative experimental design requires additional training for staff. Cross training of research specialist staff is also very important to maintain flexibility for support within the unit. Equal in importance is leadership and management training so that research specialists are able to function well in teams and coordinate with investigators and WNPRC staff in effective ways as primary project management. Finally, because of the scientific aspects of the unit, we will continue to provide instructional opportunities in academic research subjects pertinent to our projects. We also plan to continue to mentor existing SPI staff in experimental design, statistical data and testing analysis.

We expect that SPI staff will continue to be prepared to take on new procedures and techniques. We recruit highly motivated individuals who actively seek further personal development. We also continue to attract animal care staff from the husbandry unit and provide a springboard for others interested in pursuing their careers in veterinary/human medicine or biomedical scientific research. Plans to continue staff development include: (1) standard operating procedures; (2) provide continuing education opportunities to augment our repertoire of services, knowledge, and expertise; (3) provide more opportunities to understand the research background of the hypothesis-driven studies we support.

Specific Aim 3: Contribute to NHP knowledge and translational models through academic output.

Excellence at the WNPRC depends upon all units having a strong academic emphasis. As co-directors of the unit Redacted by agreement and Redacted are experienced investigators who themselves generate and coordinate new initiatives so that they can best provide state-of-the-art collaborations for research projects that will result in publications in high-impact, peer-reviewed journals. With our unit emphasis on training research specialists on academic and scientific process, many will also contribute to these publications as co-authors. In addition, technical reports of procedures developed or enhanced by our unit will continue to be presented at local and national consortiums.

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: B.2 Accomplishments_SPI.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: Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators.
1. Continue to encourage and support new investigator research by discussions of ideas, grant and budget planning, and bringing proposed research plans to the Executive Committee for resource planning.
2. Continue to solicit feedback from investigators by inquiry and following up on procedures, improvements to support, etc.
3. Work with the EHR Services to plan to include all experimental procedure and surgery requests. This will improve scheduling procedures and set up the data fields to ultimately be linked to chargeback rates. With this addition, we can free up SPI staff to have more time to perform experimental procedures and plan project timelines. Right now, we have one research specialist assigned to coordinating/ communicating schedules and two more dedicated to entering the monthly charges for our unit.

Specific Aim 2: Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities.
1. Develop plasmapheresis procedure that can also utilize column chromatography add-ins to collect antibodies in plasma, while returning not only the animal's cells, but most of the plasma fibrinogen.
2. Assess microneedle patch for mucosal and skin application of antigen for vaccination of NHPs.
3. Plan for more continuing education for staff, with more opportunities to attend research meetings or specialized training.

Specific Aim 3: Contribute to NHP knowledge and translational models through academic output.

We plan to continue to actively contribute to data compilation and manuscript preparation on projects involving our staff

SCIENTIFIC PROTOCOL IMPLEMENTATION (SPI)

Unit Head: Redacted by agreement Ph.D.

Accomplishments

Specific Aim 1: Engender NHP research success by providing scientific input, experienced research staff, experimental protocol support, and new techniques for all investigators.

In Y57, there were 10 projects and 2 pilots that ended, while another 15 new projects and 2 new pilot studies were added for a net gain of 5 new projects since 1 Jan 2018. In addition, one of the projects that ended acquired successful renewal funding Redact PI, UW-Madison, R01 HD072077) and will begin in 2019. We are particularly committed to identifying new investigators that need to develop NHP projects for translational purposes, and in Y57, we submitted and received a fundable score for a new R01 (Redacted by PI, University of Cincinnati) after the supplemental award for NHP translational work on desensitization of severe allergic reactions Redacted by PI, University of Cincinnati, R01AI113162) and are in the progress of working out NHP translational work on prevention of high-risk breast cancer for another PI Redacted UW-Madison).

Redacted by agreement presented 19 potential new projects to the Executive Committee in the reporting time period (10 current affiliates, 5 new affiliates, and 3 core PI). All proposals were approved, though some with the condition that resources will be allocated to projects when they become available.

We had determined 4 goals to improve our efficiency with experimental support. We report 3 of those addressed so far in Y56. 1: We have solicited and received feedback from two projects where we were able to improve primary staff support by assigning new or additional staff. 2: Unit scheduling is better streamlined with the use of blood draw, and food deprive requests in our Electronic Health Records (EHR). 3: We successfully updated our chargeback rates for July 2017-June 2018 to reflect current supplies and labor costs and intend to have these incorporated in to EHR with each procedure.

Specific Aim 2: Provide SPI research staff with the opportunity to improve their skills in emerging technologies, research design, and data analysis as well as fostering their leadership abilities.

The 3 most recent technicians added to the unit continue to grow in their positions. Each has developed in to primary project research specialists and become proficient basic and some advanced techniques. We continue to maintain at least one undergraduate student for assistance with animal procedures and will overlap students for continuity as one approaches graduation. The last 3 undergraduate students working with our unit went on to graduate school upon finishing.

Due to increased interest in Zika studies, support for reproductive techniques are required more than before. We trained several staff in ultrasound technique for pregnancy and fetal heartbeat detection. One senior staff person is proficient in oocyte collection and embryo transfer techniques and new staff are in the process of being trained on semen collection with both marmosets and macaques. With increased interest in broadly neutralizing antibody functions for vaccination targets, new requests for leukapheresis and plasmapheresis are coming in where we can utilize the Spectra Optia machine for multiple studies. As a result, we are training additional staff to the leukapheresis procedure to replace the technician who departed our unit. We are developing the SOP for this during the training process.

Training is scheduled for 1 research specialist to attend the NHP Behavioral Training Workshop in March. The research specialist applied for UW Academic Staff Development award to partially fund this training. Throughout the last year SPI staff were able to attend discussions about the research of the hypothesis-driven studies our unit supports. Two investigators presented to our SPI group at one of our staff meetings. Additionally, each of the four different scientific working groups of WNPRC provided several monthly seminar opportunities on related research.

Specific Aim 3: Contribute to NHP knowledge and translational models through academic output.

We continue to be successful in this reporting period with 7 published peer-reviewed manuscripts and 1 book chapter with SPI staff as co-authors (see SPI Unit Report Details). The journals included: 2 in PLoS One; 1 in PLoS Pathogens; 1 in Neurology Research; 1 in Psychoneuroendocrinology; 1 in NPJ Parkinson's Disease; and 1 in Comparative Medicine. The book chapter is titled Behavior and Behavioral Management and is a part of The Common Marmoset in Captivity and Biomedical Research (Eds. Marini, Wachtman,Tardif, Mansfield, and Fox). There are approximately 5 more manuscripts in preparation where SPI co-authors are involved.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5899

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Co-Unit Head	Institutional Base Salary		EFFORT		42,319.00	14,092.00	56,411.00
2.						Co-Unit Head					26,445.00	8,806.00	35,251.00
3.					PhD	Core Investigato					14,482.00	4,823.00	19,305.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **110,967.00**

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						
1	Undergraduate Students	EFFORT			4,208.00	130.00	4,338.00
1	Secretarial/Clerical				8,616.00	3,662.00	12,278.00
11	Asst Scientist / Research Specialist				132,779.00	44,215.00	176,994.00
13	**Total Number Other Personnel**					**Total Other Personnel**	**193,610.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**304,577.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	7,798.00
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	**7,798.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**312,375.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	312,375.00	115,579.00
		Total Indirect Costs	**115,579.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**427,954.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Veterinary Services Unit (Animal-Resources-007)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1- To provide consistent and exemplary clinical care to the nonhuman primate (NHP) colonies housed at the WNPRC

To achieve this aim, the well-trained and experienced veterinarians and veterinary technicians of the Veterinary Services unit utilize a rigorous preventative medicine program, an intensive daily health evaluation system, aggressive clinical and surgical practices, modern equipment, and a state-of-the-art electronic health records system to ensure that each NHP housed at the WNPRC receives excellent clinical care. The multifaceted health care program implemented by the unit ensures WNPRC investigators have access to healthy animals for their projects and that these animals' health is maintained once they are enrolled in experimental studies.

Specific Aim 2 – To provide excellent technical support for the investigators performing research at the WNPRC

The veterinarians and veterinary technicians of the Veterinary Services Unit provide intellectual and experienced-based pre-project input and technical project support to WNPRC investigators to achieve this aim. Prior to the initiation of a project (and often prior to the submission of a grant proposal), personnel from each unit of the Animal Services Division (including the Veterinary Services unit) meet with an investigator to discuss important aspects of experimental design such as species choice, equipment needs, specialized procedure requests, and experimental timelines to ensure that all aspects of the proposed study are feasible and will be executed properly. Once a project has been initiated, Veterinary Services unit personnel provide all the clinical care required for experimental animals (as outlined in Specific Aim 1), technical support for research procedures, and virtually all anesthesia support for experimental procedures (e.g., imaging, surgical procedures).

Specific Aim 3 - To provide training for personnel working with NHPs at the WNPRC and at other institutions

Through didactic and applied instruction, the unit provides training to residents, veterinary students and veterinary technical students, visiting veterinarians and veterinary technicians, WNPRC and visiting investigators, and scientific support staff to achieve this aim. Training ranges from a two- to three-year laboratory animal medicine residency program that prepares residents to sit for ACLAM boards to short externships that teach basic NHP medical techniques and research procedures to students and WNPRC research staff. Veterinary Services personnel also participate in various training teleconferences established by the National Primate Research Center consortia (i.e., NPRC Training Consortium Virtual Grand Rounds, Clinical and Surgical Techniques Working Group)

Specific Aim 4 - To maintain continuous academic output

To maintain the academic production of the unit, veterinary personnel strive to:
- Utilize clinical and research data collected at the WNPRC to disseminate information to their veterinary colleagues pertaining to novel techniques and treatments through the presentation of clinical case reports at national meetings and NPRC consortium teleconferences.
- Utilize clinical and research data collected at the WNPRC to publish case reports, retrospective studies, and hypothesis-based clinical research in peer-reviewed veterinary journals or collaborate with WNPRC investigators and contribute as co-authors on hypothesis-based studies published in peer-reviewed, high-impact journals.
- Determine the feasibility and their desire to gain accreditation in a veterinary specialty of his/her choosing.

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: B.2 Accomplishments_Vet.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?

WNPRC Animal Health Program (Specific Aim 1)

The Veterinary Services Unit will continue to implement and hone each component of the PMP to ensure the ongoing health of all breeding colony, stock colony, and research assigned animals at the WNPRC. In collaboration with the EHR Services Unit, Veterinary Services personnel will continue to improve the capabilities of the EHR system to further reduce the need for paper records and to

improve the ease and quickness of tracking clinical data.

Research Support (Specific Aim 2)

Over the next funding period, the Veterinary Services Unit will continue to work closely with the other units of the Animal Services Division and all other WNPRC Divisions to provide the Center's PIs with excellent research support to ensure the health of all experimental animals and the success of all experimental protocols.

Training (Specific Aim 3)

The Veterinary Services Unit will continue to advertise the externship-training program with the AVMA and AALAS to continue to recruit students interested in obtaining NHP experience. The unit will also continue to offer paid veterinary student assistant positions to UW veterinary students who can make a multi-year commitment.

Academic Output (Specific Aim 4)

Redacted by will continue to expect each veterinarian employed by the unit to present at one national conference per year. In addition, Redacted by will also expect and encourage the veterinary technicians employed by the unit to attend and present at appropriate meetings. With the assistance of Redacted by and in collaboration with Redacted by of the SPI unit and the core and affiliate PIs of the Center, Redacted by will ensure that WNPRC veterinary personnel have continuing opportunities to hone their skills as pivotal research collaborators which should increase their opportunities to be first author or co-authors on peer-reviewed manuscripts over the next grant cycle. Redacted by will provide ample opportunity for Redacted to complete his research project and will allow Redacted and Redacted to study for the ACLAM Boards over the next funding period to ensure they becomes board certified.

VETERINARY SERVICES UNIT

Unit Head: Redacted by agreement D.V.M., D.A.C.L.A.M.

Accomplishments

To fulfill the primary aim of the unit, (i.e., **providing consistent and exemplary clinical care to the WNPRC's NHP colonies**), the Veterinary Services unit employs a group of well-trained and experienced veterinarians and veterinary technicians to implement a multifaceted animal health program consisting of a rigorous preventative medicine program, an intensive daily health evaluation system, aggressive clinical and surgical practices, modern equipment, and a state-of-the-art electronic health records system. The animal health care program implemented by the unit also ensures WNPRC investigators have access to healthy animals for their projects and that these animals' health is maintained once they are enrolled in experimental studies.

The WNPRC maintains a veterinary staff consisting of 6 full-time veterinarians, 1 part-time veterinarian 10 full-time veterinary technicians, 2 part-time veterinary technicians, and 6 veterinary student assistants. Two full-time veterinary technicians were added to the unit and 1 full-time veterinarian left the unit during the current reporting period.

As part of the WNPRC's preventative medicine program, NHP obtained from domestic sources are held in quarantine for a minimum period of 30 days and newly imported foreign source animals or foreign source animals housed in the U.S. for less than one year are held for at least 90 days as outlined in WNPRC SOP 3.06 (Quarantine of Newly Arrived Nonhuman Primates). During the current reporting period, **210** newly acquired nonhuman primates underwent quarantine at the WNPRC's Blue Mounds Quarantine facility including **85** cynomolgus macaques and **125** rhesus macaques.

The Veterinary Services Unit currently maintains five functional operating rooms Specific Animal Location Specific Animal Location to support clinical and research procedures performed at the WNPRC. Maintaining surgical suites in three separate buildings virtually eliminates the need to transport an animal out of the building it is housed in to perform a major clinical or research surgical procedure, thus reducing the level of distress an animal may experience associated with the procedure. During the current reporting period, Veterinary Services personnel performed or provided support for **21** clinical surgeries (20 macaque, 1 marmoset) and **222** research surgical procedures (197 macaque, 25 marmoset). Veterinary personnel also provide support for a variety of research imaging procedures (e.g., MRI, CT, PET scans During the current reporting period, the unit provided anesthetic support for **227** research imaging procedures (CT- 11, PET – 38, MRI – 178).

The Veterinary Services Unit uses contemporary diagnostic modalities (e.g. ultrasonography and digital radiology) to perform clinical and experimental evaluations of NHP housed at the WNPRC. During the current reporting period, Animal Services personnel performed radiographic procedures on 248 animals and **4,143** ultrasound procedures (2,455 macaque, 1,688 marmoset).

The Veterinary Services Unit continues to maintain a multi-faceted training program for undergraduates, veterinary technician students, veterinary students, and veterinarians. The program, which consists of externships, paid student positions, and an ACLAM accredited Laboratory Animal Medicine Residency Training Program, provides training opportunities for individuals interested in an introduction to, or extensive experience with NHP medicine and husbandry. During the current reporting period, the WNPRC veterinary staff hosted two veterinary students through the externship program.

During the current reporting period, Veterinary Services personnel presented **11** presentations at national/international meetings in 2017, presented on **2** national teleconferences, and co-authored **7** manuscripts in peer-reviewed journals.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5900

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Unit Head	Institutional Base	EFFORT			45,790.00	15,248.00	61,038.00

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

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **61,038.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
2	Graduate Students	EFFORT			5,050.00	156.00	5,206.00
	Undergraduate Students						
	Secretarial/Clerical						
24	Res Animal Vet / Vet Tech				347,802.00	129,791.00	477,593.00
26	**Total Number Other Personnel**					**Total Other Personnel**	**482,799.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**543,837.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	16,795.00
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	**16,795.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**560,632.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	560,632.00	207,434.00
		Total Indirect Costs	**207,434.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**768,066.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Non-Human Primate Biological Materials Distribution Core

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Description:
The primary goal of the Nonhuman Primate Biological Materials Distribution (NHPBMD) core is to support cutting edge research using NHP models by providing economical access to NHP biological samples and educational materials. This core goes beyond a traditional tissue distribution program by providing: samples collected at the time of necropsy, access to samples previously banked, and additionally specific minimally invasive ante-mortem manipulations prior to necropsy. The NHPBMD core has IACUC approved protocols that allow for short-term assignment of animals for minimally invasive in vivo sample collections. The NHPBMD core is a synergistic service making the most efficient use of SPI (Scientific Protocol Implementation) Unit and PSU (Pathology Services Unit) expertise to provide critical support for developing pilot projects and long-term research needs. This core provides a varied cadre of intellectual and service resources for investigators transitioning research paradigms from other species to NHP or from NHP to humans.

Specific Aims:

Specific Aim 1: To continue to maximize the investigative use of each animal scheduled for post-mortem examination.

The Pathology Services Unit (PSU) screens animals scheduled for necropsy for appropriate samples for investigators and educators enrolled in the NHPBMD core. WNPRC core scientists are aware of the program and suggest collaborator registration with the NHPBMD core to maximize use of experimental animals. The PSU banks samples of tissues (e.g., fresh frozen liver, spleen, kidney, plasma, serum, buffy coat, OCT frozen tissues, paraffin embedded tissues, etc.) from most clinical and some experimental necropsy cases with Systematized Nomenclature of Medicine (SNOMED) coded morphologic diagnoses; combined with electronic records of health, kinship, reproductive history, and pedigree for research purposes. This metadata combined with final medical diagnoses are integral to the efficient identification and utilization of appropriate samples for retrospective studies as well as studies involving development of unique investigative methods. Aged animal tissues are routinely donated to the NIA Aged nonhuman primate tissue bank.

Specific Aim 2: To increase the investigative usage of colony animals through minimally invasive manipulations.

SPI is responsible for requests that require sample collection from live subjects. Samples that may be collected from live animals not scheduled for necropsy may include: whole blood plasma, serum, urine, semen, CSF, bronchoalveolar lavage fluid, biopsies of skin, muscle, and superficial lymph nodes, and swabs for bacterial and viral evaluation.

Specific Aim 3: To coordinate complex collection needs through ante-mortem manipulations prior to sample collections for both in vivo and post-mortem sampling.

This aim has been and will continue to be, an important mechanism for the provision of affordable NHP samples to extramural investigators who need specialized tissues or organs such as embryos or fetal tissues collected at specific time points.

Specific Aim 4: To leverage and develop collaborative relationships with investigators, who may originally make simple research requests for pilot data, into projects utilizing full WNPRC research support in NHP models.

The core has the expertise and experience to mentor new investigators as well as collaborate with established individuals transferring their research to NHP models. The core serves as an initial point of contact for numerous investigators (especially those at other academic institutions lacking NHP resources) and makes use of the SPI service paradigm to support and advance NHP research from “inception to publication.” The strongest benefit in the change to a core service has been the leveraging effects for developing collaborative relationships with investigators, that have resulted in grant applications with members of both the SPI and Pathology Services units serving as co-investigators and co-authors.

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: B.2 Accomplishments_NHPBMD.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 plan to continue with our current goals as described above which most importantly allow for short-term assignment of animals for minimally invasive collection of biological samples, short-term experimental manipulations followed by specific post-mortem collection of tissues, traditional post-mortem sample collection, as well as access to numerous banked samples.

We plan to maintain consistent enrollment of core, affiliate, and extramural investigators for NHPBMD core services to easily facilitate access to samples acutely identified for pilot projects and tangential investigations. WNPRC core investigators currently recommend enrollment of collaborators for NHPBMD core services to ensure accurate MTA agreements, and reducing questions about cost sharing in this strained funding atmosphere. These functions will be refined with emphasis placed on excellent science with administrative support provided by the WNPRC Operational Services Division.

NONHUMAN PRIMATE BIOLOGICAL MATERIALS DISTRIBUTION (NHPBMD) CORE

Unit Heads: Redacted by agreement Ph.D.
Redacted by agreement Ph.D.

Accomplishments

Specific Aim 1: To continue to maximize the investigative use of each animal scheduled for post-mortem examination.
Specific Aim 2: To increase the investigative usage of colony animals through minimally invasive manipulations.
Specific Aim 3: To coordinate complex collection needs through ante-mortem manipulations prior to sample collections for both *in vivo* and post-mortem sampling.
Specific Aim 4: To leverage and develop collaborative relationships with investigators, who may originally make simple research requests for pilot data, into projects utilizing full WNPRC research support in NHP models.

Major activities and results for all four specific aims are encompassed in the detailed core report. In summary, we continued to meet our current goals as outlined in SA1-4 which allowed for short-term assignment of animals for minimally invasive collection of biological samples, short-term experimental manipulations followed by specific post-mortem collection of tissues, traditional post-mortem sample collection, as well as access to numerous banked samples. This has resulted in peer reviewed publications and increased recognition of NHPBMD Core as a national resource.

The NHPBMD core has consistent enrollment requirements for internal and external clients. We request in our acknowledgement form a signature from both the investigator and an institutional representative the following:
1. Individuals are qualified to receive NHP biological materials "I attest that I am qualified through education and training to work with such material. I hereby assume all risk and responsibility in connection with the receipt, handling, storage, use and disposal of the material, and in accordance with this, I will ensure that all relevant parties, including my laboratory staff and collaborators, receive proper education and training to work with these materials."
2. Any federally funded projects utilizing these NHP biological materials follow the requirements of PHS and NIH for animal use protocols and congruence with funding "I confirm that I have secured, or will secure, all the necessary institutional approvals, such as Institutional Animal Care and Use Committee (IACUC) and biosafety protocols, to receive these materials and to conduct research with them. Furthermore, I attest all approvals and protocols are congruent with any Federal funds to be used to conduct research with these materials as per National Institutes of Health (NIH) Grants Policy Statement and per the Public Health Service Policy on Humane Care and Use of Laboratory Animals."
3. The efforts of the core can be documented by relevant publications of investigators obtaining these materials "…to facilitate the annual WNPRC P51 progress report to the National Institutes of Health, we request that each biological materials recipient send a brief annual progress report at the end of each calendar year by email to NHPBMD@primate.wisc.edu or mail to the NHPBMD core …"

The NHPBMD core continued to focus on organizing cooperative collections and processing efforts while ensuring accurate MTA agreements, and reducing questions about cost sharing. Excellent science combined with administrative support provided by the WNPRC Operational Services Division continues to be an important WNPRC resource. Finally, the NHPBMD core continued to specialize in providing resources to meet the needs of investigators transitioning research paradigms from other species such as rodents to nonhuman primate models.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Core-5901

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Co-Administrator	Institutional Base Salary	EFFORT			1,016.00	338.00	1,354.00
2.						Co-Administrator					1,599.00	532.00	2,131.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **3,485.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	**0.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**3,485.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**3,485.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	3,485.00	1,289.00
		Total Indirect Costs	**1,289.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**4,774.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Consortium (NPRC-Consortium-001)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The goal of the Nonhuman Primate Research Center Consortium (NHPRCC) is to strengthen communications, leverage system--wide resources, and facilitate sharing of information and best practices across the seven National Primate Research Centers (NPRCs). To meet these objectives, the Wisconsin National Primate Research Center (WNPRC) proposes the following Specific Aims for the project period of the competing continuation application:

Specific Aim 1: Continue to participate actively in all NHPRCC working groups, including the Behavioral Management Consortium (BMC), the Breeding Colony Management Consortium (BCMC), the Clinical and Surgical Techniques (CAST) Working Group, the Educational Outreach Working Group, the Genetics/Genomics Working Group, the Integrity and Compliance Working Group, the Marmoset Colony Management Group, the Occupational Health and Safety Working Group, the Pathology Working Group, and the Training Consortium.

Specific Aim 2: Utilize the shared expertise of the NHPRCC members to enhance and improve best practices across the WNRPC units as relevant.

Specific Aim 3: Initiate a new Electronic Health Records (EHR) Working Group, called Project MergEHR, to facilitate knowledge sharing between current users of the LabKey platform—the WNPRC, the Oregon National Primate Research Center (ONPRC), and the Southwest National Primate Research Center (SNPRC)—and the other NPRCs who are implementing the LabKey platform—the California National Primate Research Center (CNPRC)—or who are considering its implementation—Tulane National Primate Research Center (Tulane).

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: B2_Accomplishments_Consortium_02212019.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?

Behavioral Management Consortium (BMC):
• Continue to develop “Primate Behavioral Management” webinar series for vetted primatological community. Topic slate full through 2020.
• Survey the use of social housing for animals assigned to infectious disease research projects. Initial conference call and presentation occurred in 2018. Next steps, begin dialoging with researchers to identify any areas of incongruity that could be resolved in such way as to increase the use of social housing on such projects.
• Continue the collaboration with the Breeding Colony Management Consortium (BCMC). Some action items include, (1) Continued discussion of an exchange program for primate trainers at the centers, and consider electronic discussions or a workshop format for their continued education; (2) Continued enhancement of social housing for monkeys; (3) conduct annual cross-facility survey for identifying common topics of interest in regulation, care and welfare of the animals under our care.
• Continue collaborative research across the BMC through (e.g. self-injurious behavior and alopecia; male introduction strategies to stabilize groups;), grant applications, publications, presentations, symposia, and workshops (e.g., pair housing).

Breeding Colony Management Consortium (BCMC):
• Continue discussion and consideration of best practices related to infection control
• Limb fractures subgroup to continue their investigation into causes and best practices to minimize and manage limb fractures in outdoor, group housed NHPs.
• Colony Health Benchmarks subgroup to continue their work to define metrics that are comparable across the NPRCs
• Continue discussions regarding NPRC and national NHP supply and demand
• Consider marmoset supply and demand as a specific priority NHP supply and demand issue
• Population modeling subgroup will continue to refine current models and consider new approaches as appropriate
• The Pathogen Detection Working Group will continue to work closely with the BCMC to refine assays pertinent to colony health including refinement of the TB GIFT assay
• Continued discussion of Center approaches ensuring that personnel working with NHPs have immunity to Measles infection

• Support expansion of the animal locator system to additional external institutions
• Budget request justification: We request support for an annual BCMC Face to Face meeting to take pace in late 2019 or early 2020. Ideally, this will be in conjunction with one or more other NPRC working groups to maximize efficiency and shared knowledge. Potential outcomes include shared presentations, survey results, meeting minutes and any guidelines developed by the group.

Clinical and Surgical Techniques (CAST) Working Group:
• Improve the frequency and effectiveness of communications across the NHP pathology community including monthly virtual slide conferences.
• Position pathology data associated with NHP models for use in translational research.
• Enable direct quantitative comparisons between NHP and human pathologies.
• Advance the use of common vocabularies and ontologies, i.e., SNOMED CT.
• Preserve critical knowledge and archival collections.
• Establish a comprehensive pathology resource supporting NHP research and education - the primatepathology image database (PPID)

Educational Outreach Working Group:
• Continue regular contributions to nprc.org and its Twitter feed.
• Continue discussing appropriate scientific meetings and public events for the NPRCs to attend to disseminate NPRC resources, capabilities and successes to increase awareness, knowledge and use of the resource.
• Continue sharing news releases, issue-driven public responses, best communications practices, and new tools and techniques for reaching our many audiences.
• Continue notifying NIH ORIP Program Officer Sheri Hild monthly about new high-profile publications.
• Produce new exhibit booth panels, brochures, giveaways and other outreach materials that incorporate our new NPRC branding and messaging.

Electronic Health Records (EHR) Working Group:
• The Informatics and Data Services unit will continue to meet with the other National Primate Research Centers to discuss plans for moving towards the use of more mobile friendly front-end web frameworks.
• Implement a new financial module.

Genetics / Genomics Working Group:
• Will have quarterly conference calls and take turns presenting on a compliance topic of interest or concern.

Integrity and Compliance Working Group:
• Will have quarterly conference calls and take turns presenting on a compliance topic of interest or concern.

Marmoset Colony Management Working Group:
• The major focus of this working group will be to facilitate contact and collaboration between common marmoset colony managers, behaviorists, veterinarians, and those scientists utilizing this species in biomedical research studies to share best practices, support research, and to promote animal welfare.
• Strive to establish ties with all viable suppliers of common marmosets across the world, support an animal locator mechanism similar to the one already employed by the NPRCs, and work to ensure that genetic diversity is established and maintained within the US colonies.

Occupational Health and Safety Working Group:
• Working with Center Directors and Redacted by o reconvene the B-virus Working Group to update the 2002 recommendations, develop common indicators to bench mark between NPRCs and post face-to-face meeting presentations to the working group's shared drive, continue to focus on implementing needle-safe systems and practices.

Pathology Working Group:
• Improve the effectiveness of communication and learning across the NHP pathology community through monthly virtual slide conferences.
• Position pathology data associated with NHP models for use in translational research.
• Enable direct quantitative comparisons between NHP and human pathologies.
• Advance the use of common vocabularies and ontologies
• Preserve critical knowledge and archival collections.
• Establish a comprehensive pathology resource supporting NHP research and education - the primate pathology image database (PPID)

Training Consortium:
• Members of the WNPRC Training Consortium will continue to participate in monthly teleconference lectures.
• Plans to reenergize the Laboratory Animal Medicine Training program with increased participation.

WNPRC CONSORTIUM

Unit Head: Redacted by agreement Ph.D.

Accomplishments

From January 1, 2018 through December 31, 2018, WNPRC personnel participated in, and contributed to, the following working groups:

WNPRC Year 57 Consortium Activity	Participants
Behavioral Management Consortium (BMC)	Redacted by agreement
Breeding Colony Management Consortium (BCMC)	
Clinical and Surgical Techniques (CAST) Working Group	
Educational Outreach Working Group	
Electronic Health Records (EHR) Working Group	
Genetics/Genomics Working Group	
Integrity and Compliance Working Group	
Marmoset Colony Management Group	
Occupational Health and Safety Working Group	
Pathology Working Group	
Training Consortium	

Behavioral Management Consortium (BMC)

The Behavioral Management Consortium (BMC) was established in 2007 and serves the NPRCs, as well as the broader research community, by sharing expertise of nonhuman primate behavior to ensure the psychological well-being and adjustment needs of the animals. The BMC is comprised of expert representatives from each NPRC, as well as the National Centers for Disease Control and the Caribbean Primate Research Center. The BMC leverages the collective expertise gained from working with multiple primate species to develop behavioral methods and tools that can inform practice across facilities, each of which serves unique research portfolios and operates under different husbandry environments. The BMC meets monthly via online conference and once yearly in a face-to-face meeting.

- Collaborative Outreach to Primate Research Community:
  - Completed BMC section of the NPRC external website with content currently consisting of common tools for behavioral management: (scoring systems, record-keeping templates, common definitions), introduction and overview of techniques associated with important behavioral management topics (e.g. social housing and positive reinforcement training), reference libraries, key BMC-authored papers, and position statements
  - Other collaborative outreach activities included workshop and symposia: two workshops, one symposium, and five collaborative publications.
- Progressed with the New Model Development initiative (cross-center project). This project aims to identify animals with extreme levels of behavioral inhibition/anxiety. We have begun piloting all aspects of the procedure and are modifying the protocol as a result of these pilot tests.
- Joint annual meeting with the Breeding Colony Management Consortium (BCMC). (January 16 & 17, 2019). Aim: Synchronize goals associated with behavioral management and breeding colony management, identify common tools, and collaborate to identify best practices. Discussed survey concerning topics raised during external site visits and IACUC inspections, cross-facility exchange on information, novel enclosure types successes and challenges. Discussed progress on cross-center alopecia assessments. Continued discussion of social housing in quarantine, and the development of animal training programs.
- Face-to-Face BMC meeting (January 16th, 2019).
- Discussed social pairing expectations, strategies, success and longevity of pairs within the context of indoor housing at multi-use research facilities.
- Discussed success and future of quarterly “Primate Behavioral Management” webinar series for vetted primatological community. Presented data on interest from web attendance, discussed comparison series to further define audience and future presentations.
- Discussed “Technicians forum” presented data on interest from web attendance, topics and use. Potential for continued use and archiving discussion content.
- Alopecia scoring: Discussed progress on cross-center reliably on scoring alopecia using the “rule of 9’s” method. Two centers remain to perform training and reliability analysis. WNPRC finished reliability analysis in 2018.

Breeding Colony Management Consortium (BCMC)

The BCMC was established in early 2008 to strengthen existing communication between individual NHP breeding colony management teams in order to collectively improve processes and maximize use of system-wide resources. Members of the BCMC work with ORIP program staff to meet the NHP needs of the biomedical research community and to ensure that these invaluable resources are used efficiently and effectively in support of the NIH mission. The BCMC is comprised of colony managers from each of the seven National Primate Research Centers and the Caribbean Primate Research Center, the directors of the OAR/ORIP supported national macaque SPF breeding programs, and representatives from ORIP. Members include veterinarians, colony managers, administrators, technology professionals, and epidemiologists. The BCMC conducts monthly web-meetings and meets face-to-face once per year to hold a two-day workshop covering topics of interest to the consortium. Redacted by agreement (WNPRC Attending Veterinarian) and Bonnie Friscino (WNPRC Colony Manager) actively participate in the BCMC teleconferences and face-to-face meetings. During the current reporting period, the BCMC held 10 monthly teleconferences. Due to scheduling conflicts precluding a 2018 meeting date the 2018 BCMC/BMC Face to Face Meeting took place January 17, 2019 in Mesa, AZ. Examples of topics discussed include breeding group social management, NHP housing

innovations, sanitation of outdoor enclosures, positive reinforcement training, compassion fatigue, social housing in quarantine, the development of a wound scoring system, making the most of animal records systems, common queries noted during inspections of animal care and use programs at NPRCs and optimizing the use of medical records system. The BCMC also conducted the 2018 Nonhuman Primate Management Webinar – "The Practical Management of Nonhuman Primate Well-Being" hosted by the NPRC Associate Directors in Bethesda, MD. Webinar attendees included USDA Veterinary Medical Officers and administrative staff, faculty and staff from the NPRCs, and faculty and staff from other nonhuman primate research institutions that receive NIH support. The seminar included presentations on different Center approaches to preventing and managing unanticipated adverse events. The webinar was well attended, including the in-person attendance of Redacted by agreement Deputy Administrator USDA/APHIS/AC for the third year in a row.

Clinical and Surgical Techniques (CAST) Working Group

- The purpose of this working group is to cultivate open discussions and critical thinking about surgical and clinical procedures performed at the National Primate Research Centers (NPRCs). Target members include veterinarians and veterinary technicians as well as scientific staff. The direct, tangible goal of this working group is the development of a reference library that consists of procedure descriptions (written narratives and PowerPoint presentations) as well as transcripts from discussions about various procedures. During the current reporting period, monthly webinars continued to be well-attended by representatives from each of the NPRCs and external institutions. CAST currently has 132 active members. Presentations are assigned on a rotating basis so that each organization has an opportunity to present at one meeting per year. Topics included NHP dentistry, Clinical Management of Graft-vs-Host Disease, and Epidural Anesthesia in NHPs.
  - The topics provided training opportunities for novice veterinary staff as well as a point-of-reference for those more experienced in these procedures.
  - Ideas and tips for improving common procedures have been discussed in a group setting, resulting in the adoption of multiple procedural refinements among the NPRCs.
  - Expanded participation to include 3 additional external institutions (28 external institutions in total).

WNPRC veterinarian Redacted by agreement continues to be a driving force for this group and many WNPRC Veterinary Services and SPI members participate in the monthly teleconferences. Due to scheduling conflicts, no WNPRC personnel were able to present in 2018.

Educational Outreach Working Group

The mission of the NPRCs Outreach Working Group is increase and improve outreach communication and collaboration among the NPRCs and to the public, ensuring that information about NPRC resources and advances is readily available and communicated broadly, and sharing information focusing specifically on the value and importance of nonhuman primate research to advance human health.

Activities and Accomplishments:

- Participated in the Basel Declaration Society's "Openness and Transparency: Building Trust in Animal Research" February 2018 workshop in San Francisco to advance better communications strategies for reaching the public and gaining their support for biomedical research.

- Presented a large NPRCs booth full of informative, engaging information and hands-on activities at the April 2018 USA Science and Engineering Festival, the largest public STEM event in North America, occurring every two years in Washington, D.C.

- Worked with the NPRC Directors and our professional public relations firm to launch NPRC.org, a new NPRCs website for the public, in May 2018. The site features a new NPRCs logo and branding messages, as well as a linked Twitter account.

- Continued to assist the NPRC Directors and Nytech Strategic Planning, LLC, with maintaining NPRCresearch.org, the research, capabilities and educational website for the scientific community.

- Recruited scientists and staff to represent all seven centers at the Society for Neuroscience annual meeting in November 2018, to help advertise the NPRCs' research support capabilities and services to more scientists. In addition to the booth, the NPRCs sponsored an Animals in Research Panel, with ~200 people attending. SfN is a key opportunity to reach the scientific community, allowing us to inform scientists and trainees about NPRC-based research, available resources and NPRC contributions to human health.

- Participated in monthly conference calls to share center updates, progress on consortium activities, responses to animal rights allegations and other communications strategies.

- Coordinated presentations and other outreach events to educate the public, students and scientists about the use of nonhuman primates in research, and progress and translational benefits in biomedical research. In 2018, NPRC face-to-face outreach programs – including visits, lectures, Biomedical Research Awareness Day events, school family science nights, classroom visits, science festivals and more – reached more than 50,000 people.

Electronic Health Records (EHR) Working Group

The Informatics and Data Services (IDS) unit has continued to meet with the other National Primate Research Centers on an ongoing basis. It was decided earlier this year to shorten the length of each meeting, but increase the frequency from bimonthly to monthly. This allows for all of the centers to remain more up to date on what the others are working on. One of the main points of focus in these meetings has been discussing plans for moving towards the use of more mobile friendly front-end web frameworks. If multiple centers can settle on the same solution there will be more opportunity for sharing of source code in the future, benefiting everyone. Aside from these regular meetings, IDS staff has met with our counterparts at Oregon and Southwest. WNPRC is implementing a new financial module originally developed by Oregon; therefore, we have been working with Oregon and relying on their previous experiences to develop and implement Wisconsin's financial module. With Southwest, there are a couple of research projects that the IDS unit is involved in. IDS unit staff also attended an in-person EHR collaborative meeting with members of all of the other National Primate Research Centers in October 2018. This meeting is a way for the centers to talk about what new projects they are working on, what they are having issues with, and to get input and feedback from the other centers. Discussion included topics such as calendaring and scheduling approaches, LIMS integration, server configurations, and mobile data entry.

Genetics / Genomics Working Group

The Genetics and Genomics Working Group within the NPRC Consortium was established to provide a forum for discussion and collaboration among NPRC faculty and staff involved in the genetic analysis of nonhuman primates. The group works to develop and distribute new molecular and software tools that facilitate the genetic analysis of primate models of disease. The members also share their knowledge and experience, with the goal of increasing the application of primate genetic data in research concerning human health, and increasing the value of genetic information for the long-term management and improvement of primate animal resources. This database of genetic variation in rhesus macaques is made available by the Genetics and Genomics Working Group to the wider research community in order to assist researchers using this species to address research questions related to human health and primate biology.

Formed in 2012, 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 NPRCs. During every call, members are encouraged to share problems, ideas, solutions and approaches to challenges common to the centers. From December 2012 until September 2016 the group had a formal conference call quarterly, however since the chair of the committee retired in 2016 the working group has only had one call each year (March 2017, March 2018, and January 2019). During the January 2019 conference call, the working group decided to return to having quarterly conference calls and taking turns presenting on a compliance topic of interest or concern. Redacted by agreement (Compliance Coordinator) presented on "Best Practices for Ensuring

Compliance" in March 2019. Redacted by agreement has been a member of the working group since its inception and has participated in all conference calls.

Integrity and Compliance Working Group

Formed in 2012, 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 NPRCs. During every call, members are encouraged to share problems, ideas, solutions and approaches to challenges common to the centers. From December 2012 until September 2016 the group had a formal conference call quarterly, however since the chair of the committee retired in 2016 the working group has only had one call each year (March 2017, March 2018, and January 2019). During the January 2019 conference call, the working group decided to return to having quarterly conference calls and taking turns presenting on a compliance topic of interest or concern. Redacted by agreement (Compliance Coordinator) is presenting on "Best Practices for Ensuring Compliance" in March 2019. In addition, during the last conference call the working group discussed how helpful it would be if we could meet face-to-face to discuss the sensitive compliance issues that arise at our facilities, and the many strategies that have been or could be used to resolve them Redacted by agreement has been a member of the working group since its inception and has participated in all conference calls.

Marmoset Colony Management Working Group

As a result of the Marmoset PI Meeting held in Boulder, Colorado on September 26-27, 2018 and the ILAR Roundtable Workshop held in Washington, DC on October 22-23, 2018 many new working groups have been created across the United States to focus on the care, use, and acquisition of common marmosets.

In collaboration with Redacted by agreement of the Salk Institute, Redacted by agreement will co-lead the Marmoset Working Group. This working group will consist of veterinarians, behaviorists, colony managers, and investigators who are interested in strengthening communications, leveraging system-wide resources, and facilitating sharing of information and best practices across US institutions housing common marmosets.

The consortium overview is provided below:

> The common marmoset (*Callithrix jacchus*) is a small, highly fecund New World monkey that has been employed as a model organism for a variety of biomedical research studies including basic neuroscience, neurodegenerative disease, infectious disease, aging, and behavior for several decades. The recent development of powerful, new genomic editing techniques (e.g., Zinc Finger nuclease [ZFN], Transcription Activator-Like Effector Nuclease [TALEN] and clustered regularly interspaced short palindromic repeats [CRISPR]) has fueled a significant increase in the demand for common marmosets as biomedical research subjects.
>
> Despite the relatively long-term use of this species in biomedical research, crucial data is still lacking regarding the daily husbandry, behavioral, and veterinary care of the common marmoset when compared to other common laboratory-utilized Old World monkeys such as the rhesus and cynomolgus macaques. ***The major focus of this working group will be to facilitate contact and collaboration between common marmoset colony managers, behaviorists, veterinarians, and those scientists utilizing this species in biomedical research studies to share best practices, support research, and to promote animal welfare.***
>
> Additionally, the current supply of common marmosets from established breeding colonies at national primate research centers (NPRCs), academic institutions, and commercial suppliers cannot meet the present or predicted future national and worldwide demand for this species. The consortium will also strive to establish ties with all viable suppliers of common marmosets across the world, support an animal locator mechanism similar to the one already employed by the NPRCs, and work to ensure that genetic diversity is established and maintained within the US colonies.

Redacted by agreement will provide organizational assistance to this consortium. The Marmoset Working Group will also merge with the already existing Marmoset Focus Group and will work closely with the Marmoset PI Group

and Mamroshub.org to share information. The first true meeting of the working group will be held in February or March of 2019.

Occupational Health and Safety Working Group

Formed in 2011, the mission of the working group is to develop a forum to share ideas, expertise, and experience to improve and support stronger and more efficient Occupational Health and Safety programs and to identify opportunities to work together on shared programs, materials, and training. During conference calls held every other month, and during annual face-to-face meetings, the Occupational Health and Safety Program representatives are encouraged to share problems, ideas, solutions and approaches to challenges common to the centers. Redacted by agreement (Compliance Coordinator) has been a member of the working group since its inception. Redacted by agreement (Occupational Health and Safety Coordinator) has been a member since October 2016. Redacted by agreement participate in all conference calls and attended the annual meeting at the Tulane National Primate Research Center in April 2018. The following topics were discussed during the past year: Occupational Health and Safety requirements when working with select agents and new research pathogens (such as Zika virus, Anthrax, and Malaria); PPE risk assessments; routine Tb testing and immunization policies; visitor and contractor safety orientation; health and safety training, Dangerous Goods Shipping Requirements; laboratory acquired infections; the decision to stop collecting samples from macaques following possible B-virus exposure; costs associated with B-virus testing; updates from the B-virus Lab and new information related to B-virus exposures and infections; a formal request for the reconvening of the B-virus Working Group; development of tools to collect, analyze and compare injury and exposure data; root causes of exposures; post exposure procedure differences between centers; needle safe systems; serum banking; compassion fatigue programs; annual health assessments; the use of CRISPRcas9; tissue distribution programs; disaster planning; disaster drills; work force anxiety; creating a culture of safety; and medical surveillance services (cost and who is included). The group is planning to meet at the Yerkes National Primate Research Center in April 2019, and while in Atlanta meet with the staff of the B-Virus Lab at Georgia State University. Other plans for the upcoming year include working with Center Directors and Redacted by agreement to reconvene the B-virus Working Group to update the 2002 recommendations, develop common indicators to bench mark between NPRCs and post face-to-face meeting presentations to the working group's shared drive, continue to focus on implementing needle-safe systems and practices.

Pathology Working Group

The Pathology working group is comprised of pathologists from each of the National Primate Research Centers (NPRCs) and also includes colleagues from other NHP research institutions. Goals of the working group are as follows:

- Improve the effectiveness of communication and learning across the NHP pathology community through monthly virtual slide conferences.
- Position pathology data associated with NHP models for use in translational research.
- Enable direct quantitative comparisons between NHP and human pathologies.
- Advance the use of common vocabularies and ontologies
- Preserve critical knowledge and archival collections.
- Establish a comprehensive pathology resource supporting NHP research and education - the primate pathology image database (PPID)

The PPID incorporates gross and histologic images and is derived from archival and ongoing contributions from each of the primate centers. Images are organized for easy and rapid retrieval via the Web. The creation of this shared resource facilitates collaborations among the primate centers, enhances productivity of the pathologists and provides an invaluable resource to the veterinary and research community. Members review monthly communications with cases of interest.

During the current reporting period, the PWG held 10 virtual slide conferences sharing information about diagnostic conundrums and classic NHP pathologies. Redacted by agreement presented cases for two of the PWG virtual slide conferences. All materials from the VSC are entered into the PPID for both archive and future teaching purposes.

PWG members met in Washington, DC at the Primate Pathology workshop which focused on both diagnostic and experimental methods with case presentations.

Redacted by agreement is a member of the Phenotype Mining Committee and helped identified left ventricular hypertrophy (LVH) as one phenotype to be investigated as a resource for NHP investigations. Members of the PWG submitted data, images, and samples of NHP tissues for LVH surveillance as part of a multi NPRC collaborative investigation that also includes Baylor University Redacted by agreement for genotyping NPRC macaque populations relevant to the LVH/cardiomyopathy phenotype. Samples submitted from participating NPRCs comprise a dataset of affected and unaffected individuals as defined by methods developed by the California NPRC. Initial analysis of this collaborative multi-NPRC dataset is in progress.

Redacted by agreement is an invited speaker for the Primate Pathology workshop which will take place in San Antonio Texas in November 2019.

Training Consortium

The Mission Statement of this consortium is as follows: The care and use of nonhuman primates in the research setting requires specialized training and expertise. The Training Consortium in Primate Medicine and Surgery (initially formed in support of the R25 training grants) is designed to serve as a forum for cross-center exchange of “best practices” and to facilitate dissemination of clinical information to both new and seasoned members in the field.

Over the last year, the consortium Convened 12 monthly Virtual Grand Rounds (VGR) sessions which covered the following topics:

- Planning for the Unexpected”
- "Weight loss and lethargy and anemia, oh my!"
- "It's Gotta Be a Tumor.....or Maybe Not"
- “Red, White, and Blue: The Science Behind Vervet Romance”
- “Calcinosis Circumscripta in a Rhesus Macaque”
- "Failure to Thrive in a Cynomolgus Macaque"
- "A Rare Abdominal Neoplasm in a Sooty Mangabey" and “Abdominal Mass in a Young Rhesus Macaque”
- “Regional Anesthesia for Dental Procedures in Rhesus Macaques”
- "Renal Disease in Two Gray Mouse Lemurs (Microcebus murinus)"
- “Allergic contact dermatitis in rhesus macaques”
- “A Case of Dilated Cardiomyopathy”

The WNRC participants in this consortium include Redacted by agreement Redacted by agreement Our participation in this consortium may increase extensively in 2019 as we plan to reenergize our Laboratory Animal Medicine Training program.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5902

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Project Lead	Institutional Base	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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	7,679.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**7,679.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**7,679.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	7,676.00	2,841.00
		Total Indirect Costs	**2,841.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-797-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**10,520.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Outreach (Outreach-001)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1: Engage and inform the public through numerous professional communications partners and strategies on the value of research with nonhuman primates, emphasizing its translational importance.

Specific Aim 2: Identify appropriate scientific meetings for the NPRCs to disseminate NPRC resources, capabilities and successes, with the goal of increasing awareness, knowledge and use of the resource.

Specific Aim 3: Work with the NPRC directors, communications managers and the NPRCs' professional public relations (PR) firm to produce effective public information branding and messages representing all seven NPRCs: Streamline communications efforts, messages and timely responses at the national level on behalf of all the NRPCs. Actively participate in the NPRC Outreach Consortium (monthly conference calls) and the NPRC PR Working Group.

Specific Aim 4: Continue to work with all NPRCs to develop, expand and improve the program websites and social media: NPRC.org (public site) and NPRCresearch.org (capabilities and research inventory site).

Specific Aim 5: Train scientists, students and staff to volunteer for and lead public outreach events.

Specific Aim 6: Train scientists, students and staff in news media relations.

Specific Aim 7: Advise and mentor University of Wisconsin–Madison (UW–Madison) students, who are the next generation of scientists, physicians, veterinarians, business people, teachers and science communicators, on the critical importance of humane, lifesaving biomedical research with nonhuman primates, and promote careers in this area.

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: B.2. Accomplishments_Outreach.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

In the next funding period, Lenon will continue to perform the foregoing PIO and outreach activities and inform the public, news media, scientific and medical communities, teachers, politicians, patients and other citizens about the importance of lifesaving research with nonhuman primates.

OUTREACH

Unit Head: Redacted by agreement

Accomplishments

Major Activities

The Public Information and Outreach (PIO) activities of the Wisconsin National Primate Research Center (WNPRC) are conducted by Redacted by agreement who staffs the WNPRC PIO and Outreach office in the Director's Office at % effort, while expending % effort in the University of Wisconsin Madison (UW–Madison) Stem Cell and Regenerative Medicine Center. The two centers attract a great deal of public interest and help increase science news media and outreach visitor attention to one another, providing many opportunities to convey a strong UW–Madison biomedical research communications message. Through Redacted by agreement initiatives, especially with continuing promotion through the UW–Madison Campus Visit Program, as well as new WNPRC and NPRC public relations channels, the WNPRC's overall audiences continue to grow.

Redacted by agreement works closely on disseminating timely and accurate stories to the public with the WNPRC Director, staff, scientists, students, the UW–Madison Communications Office and the NPRCs. She writes original content on WNPRC published research and provides story tips for UW Communications staff writers. She also assists with fielding news media queries throughout the year. Redacted by agreement works closely with UW–Madison Director of Research Communications Redacted by agreement Senior University Relations Specialist Redacted by agreement UW–Madison Animal Research Program Director Redacted by agreement Strategic Communications Manager Redacted by agreement in the UW Research Office, communicators with Americans for Medical Progress and Foundation for Biomedical Research, and the NPRC liaison to NPRC.org Redacted by agreement (and the other NPRCs) to coordinate public responses from the university concerning the WNPRC.

Working with these and other communications partners Redacted by agreement publicized weekly – sometimes daily – stories and announcements about the WNPRC in 2018, reaching millions of people through the national and international professional news media, WNPRC and NPRC websites and social media. (Source: Google searches of story placement in news media outlets: too many to list.) She also reached nearly 13,000 people through WNPRC in-person outreach events.

WNPRC PIO and outreach activities are successful thanks to strong collaborations with the UW–Madison Chancellor's and Communications Office, Campus Visit Program, Discovery Building, Stem Cell & Regenerative Medicine Center (SCRMC), Wisconsin Alumni Association (WAA), Biotechnology–Genetics Center's Biotrek outreach program, UW Animal Research Program, UW Science Alliance, Student Society for Stem Cell Research, Wisconsin Stem Cell Roundtable, Speaking for Research, the Foundation for Biomedical Research, School of Medicine and Public Health, College of Engineering, School of Veterinary Medicine, Science Expeditions, and the Wisconsin Science Festival.

Redacted by agreement and the WNPRC's audiences include students, teachers, the news media, campus affiliates, WNPRC, NPRC, Office of Research Infrastructure Programs (ORIP) and National Institutes of Health (NIH) staffs, other national, state and local government officials, patients and biomedical research advocacy groups, and other citizens at the state, national and international levels.

The Public Information Officer and Outreach Specialist reports to the WNPRC Director and does not have a dedicated staff, but rather one paid part-time student hourly undergraduate outreach assistant. She partners with many scientists, staff, students and external partners to implement center outreach activities. (Please refer to the WNPRC Organizational Chart in the Overall component.)

Specific Objectives

Specific objectives relate to the production and distribution of informative and engaging content for all audiences and include the following:

Provide first-response, direct-response emails and telephone callbacks containing answers, information and updates, website links, referrals and other resources for those requesting information about the WNPRC and NPRCs.

Write and edit news stories, pitch ideas and resources to reporters and other communicators, disseminate relevant news media and university articles via email, websites and social media.

Produce WNPRC web and social media content. The WNPRC website receives about 20 million hits per year (mostly to Primate Info Net). The website serves as the main portal for scientists seeking to conduct research through the center, as well as for the public, including many teachers, students and reporters who follow up with emails or phone calls seeking additional information, visits and interviews. The WNPRC Facebook page is now over a year old and its audience continues to grow.

Contribute content to NPRC.org and NPRC Twitter for the public, as well as to NPRCresearch.org for scientists.

Produce materials for scientific meetings to publicize the WNPRC's services and capabilities, as well as those of the NPRCs Program.

Produce outreach materials for the public, including displays, hands-on activities, movies, brochures, discoveries bookmarks, educational stickers and other items.

Write guest posts on speakingofresearch.com in coordination with the other NPRCs.

Provide photography and video services for scientists, staff and the news media.

Publish a year-in-review newsletter for staff, stakeholders and the public.

Significant Results (Key Outcomes)

Public outreach events: The WNPRC boasts a strong community and statewide outreach program. The program involves many scientific, staff and student volunteers, who help educate the public about the importance of biomedical research and humane animal care at the WNPRC and the NPRCs, and the critical link between animal research and improvements in human health. Near weekly outreach visits, presentations, science fairs and other events engage teachers, civic leaders, students and families from preschool age through lifelong learners. WNPRC and NPRCs public outreach also extends nationally to participation in the USA Science and Engineering Festival in Washington, D.C., every other year.

The PIO and Outreach Specialist coordinated, recruited volunteers for, and presented public outreach events for 66 school and community audiences in 2018. These included field trips, school family science nights, lectures, and several regional, state and national events in 2018. *(See Table 1: Outreach Event History.)*

In 2018, Lenon coordinated the seven NPRCs' presence at the USA Science & Engineering Festival (USASEF) in Washington, D.C. The WNPRC also participated in Biomedical Research Awareness Day in April, as well as in several campus and community events throughout the year to celebrate the 20th anniversary of the successful derivation and culture of human embryonic stem cells. The stem cell anniversary was an excellent opportunity to promote the WNPRC's pioneering role in this discovery and its continuing research in this area. WNPRC outreach events highlighted humane animal care and scientific and translational discoveries including research on aging and calorie restriction, HIV, Ebola, Zika, menopause, Parkinson's disease, glaucoma, parent-to-infant bond, protecting kidneys from transplant rejection, pluripotent stem cells, gene editing in brain cells, anxiety and depression, and other studies in regenerative and reproductive medicine, neuroscience, global infectious disease and energy metabolism.

Outreach satisfaction metrics compiled by the UW–Madison Campus Visit Program for January through June 2018 (July-Dec not yet compiled) showed that, out of 25 visiting groups to our on-site programs, 11

returned surveys, 10 replied "very satisfied" and 1 replied "satisfied." (Surveys are not taken at larger events such as science fairs and festivals.)

News media relations and direct editorial content to the public: News releases, blogs and other content written by the PIO and her communications partners for 2018 are included in *Table 2: News Stories* after the outreach table. The Center's public information officer, with support from the WNPRC Director, the other NPRCs, University Communications, UW Animal Program Director, center staff and scientists writes news releases, fields reporters' queries and facilitates interviews with news media. Working with these and other communications partners, Redacted publicized stories and announcements about the WNPRC several times per week in 2018, reaching millions of people through the national and international professional news media, WNPRC and NPRC websites, social media, and in-person outreach events. The WNRPC Facebook page enjoyed a growing public audience in 2018 and now appears second in Google searches for the WNPRC, right after the website. Both sites are updated weekly, sometimes daily. The WNPRC began contributing content for the NPRCs Twitter feed in 2018. The PIO also works with the UW–Madison's Vice-Chancellor's Office for Community Relations, the Office of the Vice Chancellor for Research and Graduate Education, Office of Corporate Relations, the School of Medicine and Public Health, UW Health, the Research Animal Resources Center and others to help coordinate accurate, consistent and supportive messages representing the WNPRC and the University.

Training and professional development: With 22 years of experience in her position with the WNPRC, Redacted continues to train and support staff members and students to be skilled outreach partners in delivering truthful and positive research and animal care messages to the public. She also trains staff members and students in news media relations. Redacted by agreement UW–Madison students have all worked with her from their freshmen or sophomore years all the way through to their graduations, and then either gone on to graduate school, medical school, or were hired by biotech or other companies. In Spring 2018, Redacted graduated to pursue her nursing career. Redacted in turn, helped train her successor, Redacted by agreement, who is now in her second year working for Redacted and is majoring in life sciences communications and integrative biology. Redacted is also the outreach advisor to both the Student Society for Stem Cell Research, UW–Madison Chapter, and the Wisconsin Stem Cell Roundtable, the organization for graduate students and post-doctoral trainees conducting or interested in stem cell research on campus. She trains several students each year from these organizations on public outreach as well. Many of these students work in WNPRC labs, as several of our Primate Center PIs are very active in stem cell and regenerative medicine research, including exploring new gene editing techniques — such as Redacted by agreement Redacted by agreement UW–Madison's nonhuman primate, stem cell and regenerative medicine – in fact, all of its biomedical research – is continually at the forefront of the great accomplishments the university can be proud to share with the public. As far as professional development, Redacted did not take any courses, herself, in 2018, but continued to be invited as a guest-lecturer for UW–Madison courses instead. She has lectured for courses in Life Science Communications, Bioethics, Psychology, Veterinary Medicine and was asked at the end of 2018 to guest lecture for a Pathobiological Sciences course (Path-Bio 370) for spring semester 2019: Addressing Controversy, the Science, Ethics and Public Discussion of Animal Research. Redacted by agreement Redacted also worked with teachers and scientists in 2018 to update high school lesson plans for teaching about stem cells.

Advertising NPRC capabilities to potential collaborators outside of the grantee institution: The WNPRC publicizes its capabilities on a global level by reaching out to potential collaborators and affiliates through its website, the new NPRCresearch.org website, scientific meetings and awards programs:

Website: The WNPRC's *Our Services* main website portal serves as the main resource for scientists seeking to conduct research through the center. In 2018, Lenon greatly benefited from the assistance of Redacted by agreement Ph.D., research program manager in WNRPC Research Services to help keep the center's service pages up to date. Redacted by agreement met several times in 2018 to discuss and improve the services information on the website. Maher now updates most of the *Our Services* pages with help from center staff.

Scientific Meetings: The WNPRC each year publicizes its capabilities by providing scientific and staff expertise and information at national and international meetings to prospective researchers. These meetings include the American Society of Primatologists, International Primatological Society, Society for

Neuroscience, Society of Behavioral Neuroendocrinology, Nonhuman Primate Models for AIDS, International Society for Stem Cell Research, Endocrine Society and many other scientific meetings, to make the nonhuman primate research community aware of our services, resources and expertise. In 2018, Lenon joined the planning committee for the American Society of Primatologists meeting in 2019.

Research Awards Programs: The WNPRC has an outreach and collaborative presence on the UW-Madison Institute of Clinical & Translational Research (ICTR) website (part of the National Institutes of Health's Clinical and Translational Science Awards) where institute members can access WNPRC services and information. WNPRC staff members provide consultation on methodology, species, and sample matrix. We also receive clients from recommendations by previous clients. This information is provided to all interested investigators, not just core and affiliate scientists. The WNPRC also awards Pilot Research Project awards to competing investigators.

Inseparable from supporting and promoting research is supporting and promoting public outreach, to help ensure the future of research and the NPRCs. The WNPRC supports in-person outreach to local, county, state and Great Lakes Region communities. Weekly and often daily in-person outreach activities with school and community groups educate the public about research at the WNPRC, NPRCs, UW-Madison, and the critical link between animal research and improvements in human and animal health. It is especially important to note that scientists, too, are the public. We continually work to reach people working across various scientific fields and educate them about what *we* do and also how to better talk to the public about what *they* do. We need the scientific community as a whole to support us as fellow scientists upholding the highest standards in conducting controlled scientific research.

Stated Goals Not Met

All goals and objectives have been met and most have been met quite successfully. If the PIO and Outreach Specialist had more time, she could expand her social media efforts to other platforms besides WNPRC Facebook and NPRC Twitter. Unfortunately, this is not practical at this time with a EFFORT appointment at the WNPRC and a EFFORT appointment with the SCRMC. Her responsibilities already include editorial duties, daily public correspondence, administrative meetings, social media and face-to-face outreach for *each center*. Redacted by fills *two* academic staff positions that are typically separate at UW–Madison — Senior Editor and University Relations Specialist — for *two* high-profile research centers on campus.

Plans for the Next Grant Period

In the next funding period, Redacted by will continue to perform the foregoing PIO and outreach activities and inform the public, news media, scientific and medical communities, teachers, politicians, patients and other citizens about the importance of lifesaving research with nonhuman primates.

Table 1: Outreach Event History

Outreach Event History for 1/1/2018 – 12/31/2018

Audience	# Groups	# Engaged	Topic(s) Discussed
K-12 school field trips & family science nights	52	1,712	Research areas, research discoveries, research ethics, animal care, human and animal biology, college majors, careers.
Public science festivals	3	10,550	" "
College students (clubs, lectures)	5	135	" "
Adult: Civic and business groups, seniors, patients, others	6	564	" "
TOTALS	66	12,961	" "

Table 2: News Stories

News Stories for 1/1/2018 – 12/31/2018

Date of Story	Method of Release *(professional and social news media, websites, TV, other video, newsletter)*	Topic or Story Title and WNPRC Scientists Included	Hyperlink (if available)
Dec. 2, 2018	Sisters pioneer new kidney transplant surgery at UW that includes immune system	Includes reference to WNPRC rhesus monkey research. By Redacted by agreement for Wisconsin State Journal; features Redacted by agreement	All stories and their links are listed from newest to oldest at www.primate.wisc.edu, under the WNPRC News column

Dec. 1, 2018	World AIDS Day: National Primate Research Centers Saving Lives	By J. Lenon for NPRC.org and Twitter	
Nov. 6, 2018	The cells that changed the world	By J. Lenon for NPRC.org and Twitter; NPRCs stem cell discovery anniversary piece; features James Thomson	
Oct. 24, 2018	Why are U.S. neuroscientists clamoring for marmosets?	In *Science Magazine;* incudes WNPRC Director Redacted by agreement	
Oct. 11, 2018	UW–Madison Researchers Developing Methods to Edit Genes in Brain Cells	Wisconsin Institute for Discovery news; includes Redacted by Redacted by agreement	
Sept. 28, 2018	New macaque model to study pathology of TB in AIDS patients	By Redacted by agreement for WNPRC; includes Redacted by agreement	
Sept. 11, 2018	Why does menopause increase the risk for diabetes?	By J. Lenon for NPRC.org and Twitter; features Marissa Kraynak and Ricki Colman	
Sept. 11, 2018	A starring role for nonhuman primates in the stem cell story	By N. Kassulke for UW–Madison News; features James Thomson, Marina Emborg, Jon Levine, Ted Golos, Igor Slukvin, Su-Chun Zhang, Dixon Kaufman	
July 30, 2018	Inherited brain pathway underlies the risk for anxiety and depression	By UW–Madison School of Medicine and Public Health; features Ned Kalin	
July 13, 2018	Researchers trace Parkinson's damage in the heart	By Chris Barncard for UW–Madison News; features Marina Emborg and graduate student Jeanette Metzger	
July 2, 2018	Zika virus infection may multiply risk of miscarriage, stillbirth	By Chris Barncard for UW–Madison News; features Dawn Dudley, David O'Connor	

May 30, 2018	National Primate Research Centers Launch Educational Resources about Research with Animals	NPRC news release; features NPRC.org and NPRC Twitter	
May 16, 2018	UW Researchers identify arterial hemogenic endothelial cells that can function as lymphoid precursors	By UW–Madison School of Medicine and Public Health; features Igor Slukvin	
April 11, 2018	Ned Kalin named editor in chief of leading psychiatric journal	By UW–Madison School of Medicine and Public Health; features Ned Kalin	
April 1, 2018	Applications for 2018 WNPRC Pilot Project grants now accepted	WNPRC announcement	
March 20, 2018	Nature News Feature: How human embryonic stem cells sparked a revolution	In Nature News; includes James Thomson	
March 6, 2018	Researchers one step closer to learning how calorie restriction extends lifespan in animals	By UW–Madison School of Medicine and Public Health; features Rozalyn Anderson and Ricki Colman	
Jan. 17, 2018	Study advances gene therapy for glaucoma	By David Tenenbaum for UW–Madison News; features Paul Kaufman	
Throughout 2018	54 posts on WNPRC Facebook page: (https://www.facebook.com/WNPRC)	WNPRC original content and relevant posts from other sites	

Also, the Primate Center's year in review newsletter (https://www.primate.wisc.edu/?page_id=5305 featured additional news, such as our number of research journal articles published (67), an announcement of our hosting the 2019 American Society of Primatologists meeting, and our staff volunteers who helped restore Cayo Santiago, devasted by Hurricane Maria in 2017, through Project Monkey Island. (https://www.projectmonkeyisland.org)

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5903

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement				Editor	Institutional Base	EFFORT			38,742.00	12,901.00	51,643.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **51,643.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
0	**Total Number Other Personnel**					**Total Other Personnel**	**0.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**51,643.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	1,025.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**1,025.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**52,668.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	52,668.00	19,487.00
		Total Indirect Costs	**19,487.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**72,155.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Pilot Program (Pilot-Research-001)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The Wisconsin National Primate Research Center (WNPRC) proposes a continuation of its revitalized Pilot Project Research Program (PPRP), which is designed to facilitate the use of non--human primates (NHPs) in new, high--impact biomedical research studies as well as investigations leading to development of new NHP models of disease, or significant enhancements in NHP welfare or husbandry. The PPRP will continue to solicit and review high--risk or developmental proposals, and select for funding only those with the highest potential to progress towards subsequent successful grant applications to the NIH, other federal agencies, or foundations. Priority will be given to those proposals that align with the broadly defined interests of the WNPRC Working Groups, and the technical capabilities of the WNPRC Scientific Protocol Implementation unit (SPI). The WNPRC will also continue to partner with the Institute for Clinical and Translational Research (ICTR), the Clinical and Translational Science Award (CTSA) program at the University of Wisconsin, to provide opportunities for jointly--funded projects that synergistically address the objectives of the PPRP and the ICTR Pilot Project programs.

The PPRP will continue to fund a minimum of two and a maximum of five $50,000 awards per year, each to be utilized as required by awardees over 1--2 years. Core--PIs, UW investigators, and national investigators are equally eligible to compete for these awards. Proposals that request additional or interim funding for existing research projects will not be considered. The WNPRC will continue to encourage external applications, for which the PPRP requires that proposed studies are to be conducted at the WNPRC, utilizing the Center's animal resources and in collaboration with a Core--PI or local WNPRC Affiliate PI.

The major objectives of the PPRP are summarized in the following Specific Aims:

Specific Aim 1. To provide the opportunity for both local and national investigators to propose high--risk, high--benefit pilot studies utilizing NHPs at the WNPRC.

Specific Aim 2. To provide the opportunity for investigators without significant previous NHP research experience to partner with Core staff scientists in developing experimental approaches with NHP models.

Specific Aim 3. In partnership with the UW ICTR, to provide the opportunity for pilot project support for investigators who focus on translational research projects involving NHP models.

Specific Aim 4. To provide opportunities for junior investigators to obtain preliminary data for grant applications to support their new independent research programs.
In pursuing these PPRP aims, we will continue to foster development of exciting new avenues of research in NHPs, maximize the utility of the NPRC resources in the service of high--impact science, and newly engage investigators in translational research with 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: WNPRC Pilot Program_02222019.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 WNPRC Pilot Project Research Program (PPRP) will release a Request for Proposals (RFP) in April 2019 to solicit new Pilot Award applications. The RFP will be publicized through a description on the WNPRC web site, via an email announcement to investigators who had previously contacted the WNPRC, as well as by direct contact of prospective collaborators by Core scientists. The PPRP will continue to fund a minimum of two and a maximum of five $50,000 awards per year, each to be utilized as required by awardees over 1-2 years. The number of awards per year may vary according to the depth of the pool of outstanding applications, and the support available from university sources to supplement the overall pool of available funds each year.

WNPRC PILOT PROGRAM

PILOT PROJECTS FUNDED IN 2015

PERIOD OF SUPPORT: JANUARY 1, 2015 – APRIL 30, 2019

Project Title	Principal Investigator(s)	Dates of funding	Amount of funding (Direct Costs	Co-funded?
A Radiometabolism Study of Hair Hormones in Rhesus Macaques	Redacted by agreement	07/21/17 – 04/30/19	$42,376	WNPRC only
Towards KSHV VLP-based Vaccine Development		07/21/17 – 04/30/19	$50,000	WNPRC only
Priming Protective CD8 T-Cell Memory in the Lung		07/21/17 – 04/30/19	$50,000	WNPRC only

PILOT PROJECTS FUNDED IN 2017

PERIOD OF SUPPORT: SEPTEMBER 1, 2017 – APRIL 30, 2019

Project Title	Principal Investigator(s)	Dates of funding	Amount of funding (Direct costs)	Co-funded?
Optical Imaging of Functional Maps in the Dorsal Visual Pathway of Marmosets	Redacted by agreement	09/01/2017 – 04/30/2019	$50,000	WNPRC only
ZIKV Infection on Male Macaque Reproductive Health		09/01/2017 – 04/30/2019	$27,274	WNPRC only
Manipulating the Initial Size of the SIV Reservoir in Macaques		09/01/2017 – 04/30/2019	$50,000	WNPRC only
Chemogenetic Manipulation of Thalamo-cortical Dynamics		09/01/2017 – 04/30/2019	$50,000	WNPRC only
Vaccine to Induce Ab Production in Cervicovaginal Mucosa		09/01/2017 – 04/30/2019	$50,000	WNPRC only

PILOT PROJECT PROGRESS OR FINAL REPORTS

Project Title: A Radiometabolism Study of Hair Hormones in Rhesus Macaques

Name, Title, Institutional Affiliation: Redacted by agreement Assistant Scientist, Wisconsin National Primate Research Center, University of Wisconsin-Madison Redacted by agreement Distinguished Scientist, Wisconsin National Primate Research Center, University of Wisconsin-Madison

Years Funded: 07/21/17 – 04/30/19

Project Abstract:

Analysis of long-term endocrine activity can be challenging since traditional methods require repeated specimen collection, are sensitive to acute changes in hormone levels and sample collection can be invasive and difficult to obtain. Analysis of hormones in hair has become an increasingly widespread tool for assessment of long-term endocrine function as it circumvents many of these issues. While there are clear benefits of hair hormone analysis there have only been a handful of studies addressing the biological significance of hair hormones. In order to meaningfully interpret hair hormone results, validation studies for each steroid hormone measured in hair, in a species in which the data can be translated to humans, is required. Rhesus macaques are the ideal model for a validation study of hair hormones as they are closely related to humans and their hair growth and metabolism of steroid hormones are similar to those in the human. Assay Services at the Wisconsin National Primate Research Center (WNPRC) is at the forefront of hair hormone analysis. Recently, we have developed the methodology for state-of-the-art hair hormone analysis to measure a panel of steroid hormones from one hair sample using liquid chromatography-tandem mass spectrometry (LC/MS/MS). In order to continue to lead this rapidly expanding field, we need to conduct the fundamental validation studies to understand the biological significance of the hair hormones in rhesus macaques. The WNPRC is uniquely positioned for this project, as the animals, the equipment and the expertise are available. Therefore, the overall aim of this pilot project is to conduct radiometabolism studies to provide basic data on hormone incorporation into hair in the rhesus macaque. We will fulfill the following specific aims: (1) Determine the time course of 3H-or 14C-labeled hormone incorporation, and the proportion of radiolabeled hormone and metabolites in hair of rhesus macaques. We will inject a precise amount of either 3H-cortisol, 14Ctestosterone, 14C-progesterone or 3H-estradiol to rhesus macaques and collect urine, feces and hair samples to determine when the radiolabeled hormone can been found in the hair, and the proportion of the radiolabeled that is incorporated into hair. This will inform us on how much hormone in circulation is actually, integrated into the hair shaft, and precisely when this occurs. (2) Determine the characteristics of the major hormone (parent and/or metabolites) in the hair. We will use the hair that was collected from the monkeys in Specific Aim 1 to determine in which form each of the radiolabeled hormones is integrated in the hair shaft. For this we will use high-pressure liquid chromatography (HPLC) separation to visualize the radioactive peak(s), and compare them to authentic standards. This will provide us with the knowledge of which parent hormone or its metabolite to measure in hair that is relevant to the hormone in circulation. The results of this pilot study will be highly informative for interpretation of hair hormone data. We will provide information about the biological significance of important steroid hormones in hair, in a species that is closely related to humans.

Progress to Date:

The aims of the study were to determine when, how much and in what form radiolabeled hormones were incorporated into hair. We have conducted two experiments in which monkeys were injected with radiolabeled cortisol. We determined that the majority of the radioactivity (98%) was excreted in the urine and feces by 5 days post injection and we were able to measure the radiolabel in hair by 10 days post injection and it corresponded to about 1% of the total administered dose. Using high-pressure liquid chromatography (HPLC) separation we were able to show that the radiolabel was incorporated into the hair as cortisol and cortisone and some was incorporated as a third yet unidentified metabolite. A secondary, unanticipated result of this first study was that we found that there was a great deal of variability in the growth rate of the hair between monkeys. Work is continuing to identify the unknown metabolite of cortisol in the hair with the UW Biotechnology Center and the UWCCC Small Molecule Screening Facility. The radiolabeled studies for

testosterone and progesterone are complete and data analysis is underway. The intent is to combine the progesterone and testosterone data for a manuscript.

Full bibliographic materials on each paper published, in press, or submitted:

Kapoor A, Schultz-Darken N & Ziegler TE. Radiolabel validation of cortisol in the hair of rhesus monkeys. Psychoneuroendocrinology. 2018 Nov; 97:190-195.

Kapoor A & Ziegler T, A validation study of hair cortisol in rhesus monkeys. American Society of Primatologists 2017 conference, Washington D.C.

Kapoor A, Post J & Zieger TE, Validation of hair cortisol in rhesus monkeys: A radiometabolism study. Society for Behavorial Neuroendocrinology 2016 conference, Montreal Canada.

Kapoor A & Ziegler TE, A radiometabolism study of hair cortisol in rhesus monkeys. Psychoneuroendocrinology. 2015 Nov;61:69-70. Presentation at International Society for Psychoneuroendocrinology 2015 conference, Edinburgh, Scotland.

Grant applications and funded grants resulting from this project:

Kapoor A & Ziegler T, Validating the use of hair glucocorticoids as a marker of central hypothalamic-pituitary-adrenal axis activity. 1R03HD093999-01 NICHD 07/01/18-06/30/20

Project Title: Towards KSHV VLP-based Vaccine Development

Name, Title, Institutional Affiliation: Redacted by agreement Assistant Professor, Department of Medicine, University of Massachusetts Medical School; Redacted by agreement Scientific Unit Head, Scientific Protocol Implementation, Wisconsin National Primate Research Center, University of Wisconsin-Madison

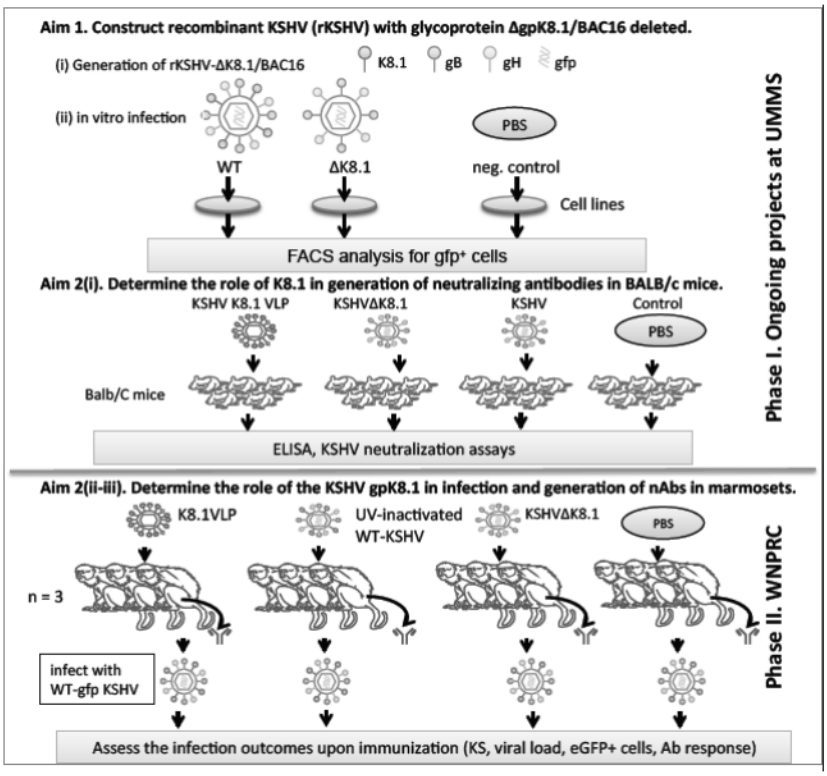
Years Funded: 07/21/17 – 04/30/19

Project Abstract:

Efforts to develop Kaposi's sarcoma-associated herpesvirus (KSHV) vaccines are limited due to lack of animal models to test potential vaccine candidates. Recently, the successful transmission of KSHV into common marmosets (Callithrix jacchus) was reported. In this exciting new model, marmosets infected with recombinant KSHV (rKSHV) rapidly seroconverted and maintained a strong anti-KSHV antibody response, opening a new frontier for the study of KSHV infection in vivo and vaccine development.

The overall goal of this application is to define the role of KSHV glycoprotein (gp)K8.1 in mediating virus entry in vivo, a prerequisite step in designing vaccines that stimulate humoral immunity and evoke potent T-cell responses, thereby preventing infection. We hypothesize that immunization of marmosets, a recently developed non-human primate model susceptible to KSHV infection and disease with KSHV gpK8.1 incorporated into virus-like particles (VLPs), will be the ideal candidate for preventing KSHV infection. To begin to address our hypothesis, we propose two specific aims:

(1) Construct recombinant KSHV (rKSHV) with ΔgpK8.1/BAC16 deleted. To achieve this goal, Dr. Ogembo at UMMS is currently at an advanced stage of deleting K8.1 from a bacterial artificial chromosome (BAC) system carrying the whole KSHV genome (BAC16wt-KSHV-JSC1). The infectivity of rKSHVΔK8.1 will be tested both in vitro and in the common marmoset. We anticipate to complete the project (Phase-I) as illustrated above before the end of 2014.



(2) Determine the role of the KSHV gpK8.1 in generation of neutralizing antibody (nAbs) in BALB/c mice and in marmosets. First, we provide preliminary data on the construction and characterization of KSHVgpK8. 1VLPs, the viral ligand most consistently implicated as the major target of nAbs response in vivo. To determine whether gpK8.1 VLPs are capable of eliciting nAbs response, a group of five 6-8 weeks old BALB/c mice were immunized with either gpK8.1 VLPs, purified UV-inactivated KSHV or phosphate buffered saline (PBS). All animals received boost immunizations at day 43, 173 and 183 and sacrificed at day 228. Serum samples were obtained from immunized mice every two weeks post immunization. Experiments are underway in Dr. Ogembo's lab to determine the presence of anti-K8.1 antibody titers and in vitro neutralization of KSHV by the sera from immunized mice. VLPs lack viral nucleic acids, and thus have no oncogenic potential.

After validating that antibodies against gpK8.1 VLPs can block infection, a group of three marmosets (3–4 years old) at WNPRC will be immunized with either 20μg of VLPs in 1 ml PBS, UV-inactivated KSHV particles, KSHVΔgpK8.1 or 1 ml PBS alone at week 0, 4 and 24. These animals will be challenged with wild-type

KSHVexpressing green fluorescent protein to test the ability of K8.1-VLP to block viral infection and Kaposi's sarcoma (KS). The funds requested would be used primarily on proposed activities implemented at WNPRC (Phase-II) led by Redacted by agreement

Progress to Date: Nothing to report.

Full bibliographic materials on each paper published, in press, or submitted: Nothing to report.

Grant applications and funded grants resulting from this project: Nothing to report.

Project Title: Priming Protective CD8 T-Cell Memory in the Lung
Name, Title, Institutional Affiliation: Redacted by agreement Professor, Department of Pathobiological Sciences, University of Wisconsin-Madison; Redacted by agreement Associate Professor, Department of Pathobiological Sciences, University of Wisconsin-Madison

Years Funded: 07/21/17 – 04/30/19 (FINAL)

Project Abstract:

Acute infections of the respiratory tract (RT) with viruses such as influenza A virus (IAV), respiratory syncytial virus, adenovirus, parainfluenza virus, and rhinovirus are the leading cause of morbidity and mortality in the US. In addition, emerging pathogens including avian influenza virus, Middle-East respiratory syndrome coronavirus and severe acute respiratory syndrome coronavirus cause severe lung disease and mortality. Except for IAV, there is neither a vaccine nor an effective therapy to treat acute viral infections of the RT. Moreover, vaccines for IAV are far from optimally effective and confer protection in only <60% of the vaccinees that are under 65 years of age. There is emerging consensus that defense against respiratory viruses will require both antibodies and CD8 T cells and induction of memory CD8 T cells in the lung airways might be crucial for maintaining broad protective immunity to IAV in the RT. However, a daunting challenge is the development of safe adjuvants that can stimulate potent and durable CD8 T cell responses to non-replicating antigens in the RT mucosa.

Carbomers (polymers of acrylic acid) have been used extensively to achieve controlled release of medications in tablets and as a bioadhesive in mucosal applications. We have strong preliminary data that similar to a live attenuated virus, intranasal (IN) or subcutaneous (SQ) immunization of mice with a carbomer-based adjuvant, Adjuplex® (ADJ) stimulated potent CD8 T cell memory to ovalbumin, a model soluble antigen. Intriguingly, memory CD8 T cells induced by immunization via the IN but not SQ route potently suppressed replication of IAV in the RT. While these findings are novel and promising, ADJ's efficacy in mice may not accurately predict its ability to induce protective CD8 T cell memory in the RT of humans. We therefore propose to investigate the T cell immunogenicity, protective efficacy and mechanism of protection of ADJ using an authentic pathogen-derived protein in macaques, a biologically relevant translational model of influenza immunity. The central hypothesis is that, "a carbomeradjuvanted viral protein-based IN vaccine will induce potent CD8 T cell memory in lung and blood, and protect macaques against influenza". The specific aims of this proposal are to: (1) test whether the programming of protective memory CD8 T cells in the lung airways of macaques requires mucosal delivery of a carbomer-based vaccine; (2) determine the extent to which an IN carbomer-based vaccine confers superior protection for macaques against IAV in the RT over a SQ vaccine. This project forges new collaboration between investigators with expertise in basic cellular immunology and in nonhuman primate models of influenza infection and immunity. The objective of this pilot project is to establish a novel subunit vaccine platform that elicits potent humoral and CD8 T cell immunity in the mucosa against respiratory viruses. If successful, we envision to leverage the data from this study in macaques to attract support for future projects aimed at translating basic immunology to preclinical applications and probe the molecular and cellular mechanisms of protective immunity in the respiratory mucosa.

Progress to Date:

The objective of the project was to assess the comparative efficacy of a influenza vaccine upon administered by the subcutaneous and intranasal routes to rhesus macaques. Rhesus macaques were vaccinated and challenged with an influenza virus strain that is known to replicate in monkeys. Monkeys responded to the vaccines, and the results were promising but variability between monkeys in terms of viral titers precluded us from making any conclusions about the experiment. In summary, we found that the experimental vaccine is mildly immunogenic and would need the addition of another adjuvant to enhance the overall immunogenicity and protective ability.

Full bibliographic materials on each paper published, in press, or submitted: Nothing to report.

Grant applications and funded grants resulting from this project: Nothing to report.

Project Title: Optical Imaging of Functional Maps in the Dorsal Visual Pathway of Marmosets

Name, Title, Institutional Affiliation: Redacted by agreement Associate Professor, Department of Neuroscience, University of Wisconsin-Madison Redacted by agreement Assistant Professor, Department of Neuroscience, University of Wisconsin-Madison; Redacted by agreement Assistant Professor, Department of Psychology, University of Wisconsin-Madison; Redacted by agreement Professor, Department of Neuroscience, University of Wisconsin-Madison

Years Funded: 09/01/17 – 04/30/19

Project Abstract:

In the cerebral cortex, neurons that share similar preference for a sensory feature tend to cluster together and form a functional map. Some intrinsic changes in optical properties such as the reflectance of light are dependent on electrical or metabolic activity. Optical imaging of the intrinsic signals has become an important tool to study the functional architecture of the sensory cortex. In primates, the visual areas can be divided into the ventral and dorsal visual streams. The ventral stream is important for object recognition and processing form and color information, whereas the dorsal stream is important for spatial vision and visual motion processing. A great deal of knowledge about the visual system has been learned from studying macaque monkeys. However, several cortical areas in the dorsal visual pathway of macaques are hidden inside the sulci, making it difficult to study their functional architecture. These areas include the middle temporal (MT) cortex, which is crucial for processing visual motion and depth information, and the medial superior temporal (MST) cortex, which is important for processing more complex visual motion patterns that are associated with self-motion. The common marmoset, a new world monkey, is emerging as a valuable animal model for systems neuroscience research. Since the marmoset brain is lissencephalic, most of the cortical regions, including areas MT and MST, are accessible for optical imaging. It is also viable to train marmosets to perform behavioral tasks. In the proposed research, we will measure intrinsic optical signals from awake common marmosets. In Aim 1, we will set up an intrinsic optical imaging system and develop the necessary apparatus and procedure. In Aim 2a, we will determine the functional maps of binocular disparity and motion direction in area MT, and the relationship between the two maps. In Aim 2b, we will determine how the maps of binocular disparity and motion direction vary with eccentricity. In Aim 2c, we will test a novel hypothesis that area MST contains functional maps for various types of optical-flow information generated by self-motion. The functional maps determined in the proposed research will help to provide an accurate and thorough view of the cortical architecture in the dorsal visual pathway, filling in a critical gap in our knowledge. The results will also provide insights on how a stimulus feature is processed in the neural network and the principle of representing multiple stimulus features (i.e. multiplexing) in the brain. Determining the functional map of optical-flow fields in area MST will shed light on how complex motion patterns are processed by the visual system and the neural transformation occurring as information flows along the visual hierarchy. Moreover, the functional maps obtained in areas MT and MST will guide future investigations of neural circuits within and between these areas, and other brain regions, using the combined methods of optical imaging, electrophysiology, and optogenetics. The WNPRC has the largest research colony of captive marmosets in the Midwest. The proposed research leverages this valuable resource and will help to build an imaging core at the WNPRC.

Progress to Date:

In 2018, we constructed a primate chair specially designed for conducting behavioral training and the proposed physiological experiments using awake behaving marmosets. We have also built a head holder and several head posts designed to stabilize the head position of marmoset subjects during experiments of visual stimulations and physiological recordings. We have been setting up a new experimental equipment rig that is capable of controlling for the experimental trials, delivering visual stimuli for animals to view, monitoring animal's behavior, delivering reward, and acquiring electrophysiological data. This equipment rig will be used to conduct experiments involving marmosets. The rig set up is near completion.

Full bibliographic materials on each paper published, in press, or submitted: Nothing to report.

Grant applications and funded grants resulting from this project: Nothing to report.

Project Title: ZIKV Infection on Male Macaque Reproductive Health

Name, Title, Institutional Affiliation Redacted by agreement Assistant Scientist, Wisconsin National Primate Research Center, University of Wisconsin-Madison; Redacted by agreement Professor, Department of Comparative Biosciences, University of Wisconsin-Madison; Redacted by agreement Associate Professor, Department of Pathobiological Sciences, University of Wisconsin-Madison; Redacted by agreement Clinical Assistant Professor, Department of Comparative Biosciences, University of Wisconsin-Madison

Years Funded: 09/01/17 – 04/30/19 (FINAL)

Project Abstract:

The recent Zika virus (ZIKV) epidemic has become a global concern as it has been linked to adverse pregnancy outcomes, including pregnancy loss, microcephaly and other neurological defects. Zika virus is primarily transmitted via mosquitos; however, sexual transmission has also been demonstrated. Recent reports of ZIKV shedding in bodily fluids have revealed that ZIKV persists longer in semen compared to serum or urine. As prospective studies are still ongoing, the duration and extent to which ZIKV persists in semen has not been well characterized. Moreover, it is unknown whether ZIKV is present and actively replicates in the human male reproductive tract. Thus, our overall goals are to evaluate the duration of ZIKV shedding in seminal fluid, the impact of infection on sperm quality, and to define ZIKV tropism of the male reproductive tract within our non-human primate model. **We hypothesize that ZIKV will replicate in tissues of the male reproductive tract, persist in macaque semen, and have a negative impact on sperm function.** To test this hypothesis we will execute the following Specific Aims:

Specific Aim 1. To assess the duration and persistence of ZIKV shedding in semen, and evaluate semen quality parameters following ZIKV infection. *This aim will test the hypothesis that ZIKV is shed in semen for an extended duration in macaques beyond clearance in other bodily fluids. Additionally, this aim will address impact of infection on sperm function.*

Specific Aim 2. To determine macaque male reproductive tract histopathology and ZIKV replication. *This experiment will address the impact of ZIKV on structural integrity of the male reproductive tract as well as identify tissues of the male reproductive tract that serve as a reservoir for ZIKV replication.*

This study will define the presence of ZIKV within the male reproductive tract in terms of the duration of ZIKV shedding following infection, and establish which tissues may support virus replication. Modeling infection in the non-human primate will also systematically identify the tissue(s) from which ZIKV is shed into semen. It is unknown if ZIKV infection negatively impacts the male reproductive tract or poses a risk to male fertility. Semen quality parameters can also be evaluated in this model to elucidate the effect of ZIKV infection on male fertility. Therefore the preliminary results of these experiments have implications in better informing guidelines to prevent sexual transmission, and also to provide insight into the impact of infection on male fertility.

Progress to Date:

Objectives: Our overall goals are to evaluate the duration of ZIKV shedding in seminal fluid, the impact of infection on sperm quality, and to define ZIKV tropism of the male reproductive tract within our non-human primate model. The first aim was to assess the duration and persistence of ZIKV shedding in semen, and evaluate semen quality parameters following ZIKV infection, and the second aim was to determine macaque male reproductive tract histopathology and ZIKV replication.

Methods: We evaluated the persistence of virus in semen in 3 rhesus macaque males infected with 10^5 PFU PR strain (PRVABC59) ZIKV. Bodily fluids including semen, urine and blood were collected weekly until day 63 post-infection for 1 male, and through day 9 and day 21 for the other 2 males. Two additional rhesus macaque males that were not infected with Zika served as control specimens and underwent semen collection and blood draws in parallel to the infected males. Semen quality parameters, including motility and viability, were measured by computer assisted semen analysis (CASA). Sperm cells and seminal plasma were separated and ZIKA viral RNA was measured by quantitative real-time PCR (qRT-PCR). In addition, testosterone levels were measured to determine the impact on male reproductive hormones. To define ZIKV tropism, male reproductive

tract tissues were collected at day 9, 21, and 42 days post infection and tissues were subjected to viral RNA analysis by qRT-PCR. Histopathology was also assessed.

Results: Data analysis is currently ongoing. Data was collected through fall of 2018 to assess persistence of virus and semen quality parameters. Virus was present in seminal fluid of one male on day 21 post-infection, while all other samples have been negative. One male is scheduled to undergo infection on 10/22/18 to assess persistence of virus in semen for an extended duration as only one male was collected through day 63 post-infection. Tissue analysis of viral RNA and histopathology analysis are also currently ongoing.

Conclusions: Awaiting completion of data analysis before conclusion can be drawn. We can provide an update once analysis is complete.

Full bibliographic materials on each paper published, in press, or submitted: TBD

Grant applications and funded grants resulting from this project: TBD

Project Title: Manipulating the Initial Size of the SIV Reservoir in Macaques

Name, Title, Institutional Affiliation: Redacted by agreement, Assistant Professor, Department of Pathobiological Sciences, University of Wisconsin-Madison

Years Funded: 09/01/17 – 04/30/19

Project Abstract:

A major impediment to curing human immunodeficiency virus (HIV) infection is eradicating long-lived latently infected cells. Targeted therapeutic approaches are being designed to eliminate the latent reservoir. However, it is difficult to assess the effectiveness of treatment regimens *in vivo* due to sensitivity limitations of *ex vivo* assays measuring the size of the latent reservoir. Therefore, clinical trials rely on removing HIV patients from antiretroviral drug therapy (ART) and measuring time to viral rebound as a direct measurement of treatment efficacy. However, this approach is problematic due to ethical concerns of removing patients from ART and the low statistical power of using time-to-viremia alone as an approximation for reservoir size. Developing new methods with increased sensitivity to detect reductions in reservoir size will aid in identifying effective HIV cure therapies.

Simian immunodeficiency virus (SIV) infections of non-human primates (NHP) are useful models for evaluating the size and tissue distribution of the latent reservoir. An advantage of these models is that the virus inoculum and the size of the latent reservoir can be manipulated in a manner that is impossible to replicate in humans. Additionally, the recent development of a “barcoded” strain of SIV provides a targeted method for estimating the number of reactivating latently infected cells. After ART interruption the barcoded region of plasma virus can be analyzed by deep sequencing to identify the unique variants present. Even with these advantages, though, it is impossible to know the absolute size of the latent reservoir in SIV infected NHP.

HIV latency is thought to be established by the transition of a small population of activated CD4+ T cells to a resting-memory state. This process can be modeled *in vitro* by infecting activated CD4+ cells with HIV and culturing them under conditions that transition them into a quiescent state. Importantly, latently infected CD4+ T cells can be generated from uninfected individuals. These methods, therefore, offer a unique opportunity to define the size of the SIV latent reservoir by transferring specific numbers of *in vitro* generated latently infected cells to SIV-negative macaques. Controlling the size of the latent reservoir will aid in identifying treatments that significantly reduce the size of the latent reservoir in macaques.

We, therefore, hypothesize that CD4+ T cells latently infected *in vitro* with barcoded SIV can be transferred back into SIV-negative macaques to establish a defined latent reservoir. We will test this hypothesis in two Specific Aims.

Specific AIM I: Generate SIV latently infected cells in vitro.

Specific AIM II: Adoptively transfer autologous SIV latently infected CD4+ cells to rhesus macaques

Progress to Date:

The overall goal of this project is to manipulate the initial size of the SIV reservoir in rhesus macaques through autologous transfer of latently infected cells. We first focused on finding the best method to obtain the highest frequency of latently infected cells *in vitro*. We tested two different models of *in vitro* latency in rhesus macaques: post-activation latency and direct infection. For the post-activation latency model, CD4+ T cells are activated, infected, and returned to a resting state. However, in our hands, the major limitation of this approach is extensive cell death prior to reaching a resting state. In contrast, the direct infection model involves infecting CD4+ cells without prior activation. Despite a low frequency of infected cells, this model yields a consistent number of viable latently infected cells. Moving forward, this method will be to generate latently infected cells *in vitro*.

In order to assess the frequency of latently infected cells, we reactivated the cells using αCD3/CD28 activation beads and examined expression of CD4 and the SIV core protein p27 with flow cytometry. The panels below (Figure 1) represent the rate of p27 expression and CD4 downregulation on cells infected by direct infection before (top) and after (bottom) stimulation. The right panels serve as fluorescence minus one (FMO) controls.

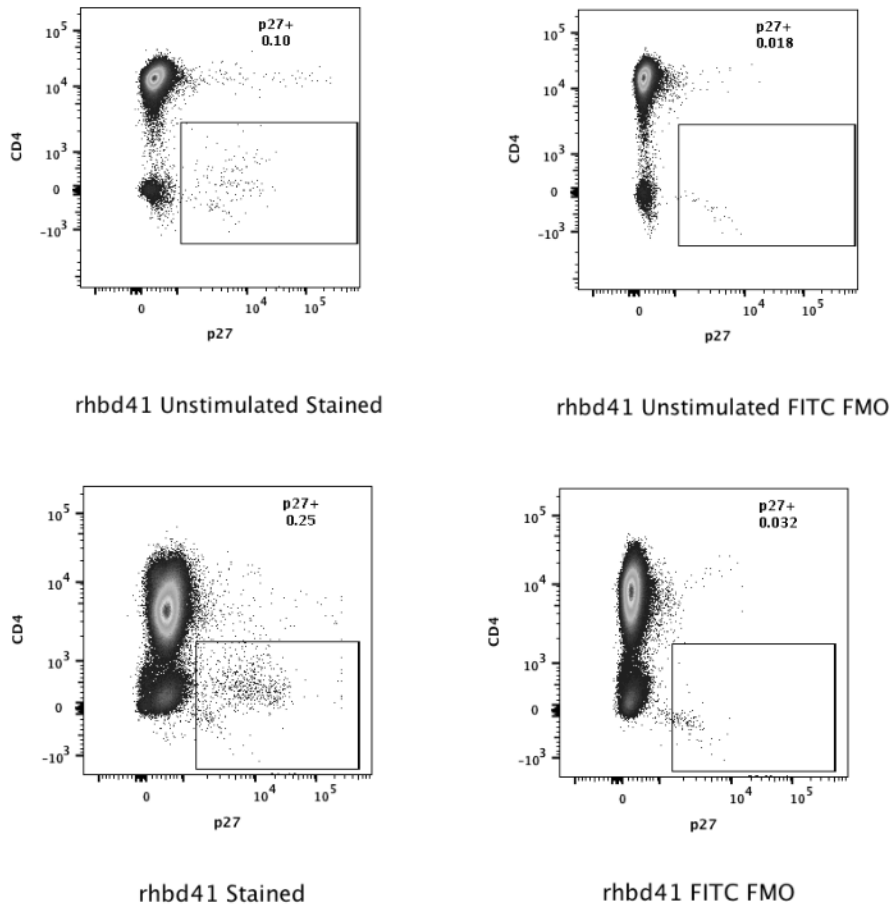
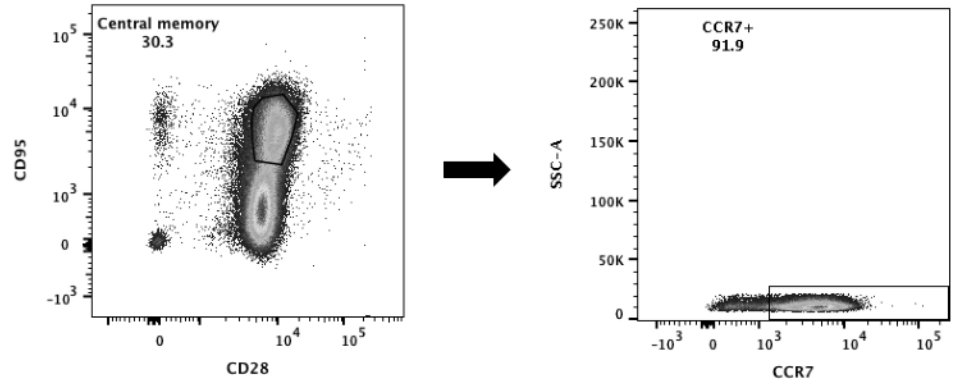


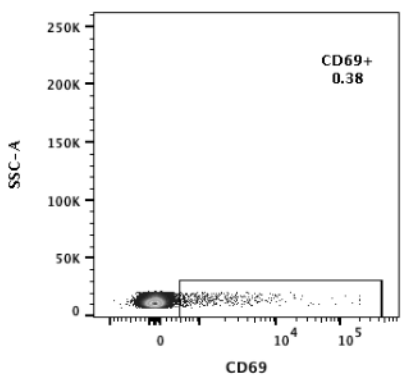
Figure 1.
Throughout this process, we collected unstimulated cells from independent experiments to quantify the amount of cell-associated viral DNA (CA-vDNA) in each sample. We will compare CA-vDNA to the frequencies of p27+ cells obtained by flow cytometry to provide an additional method for quantifying the number of latently infected cells.

Furthermore, we determined the memory phenotype and the activation state of the *in vitro* generated SIV latently infected cells using flow cytometry. Memory CD4+ T cells express the co-stimulatory molecule CD28, the apoptosis-associated molecule CD95, and the secondary lymphoid tissue migration marker CCR7. Dependent on the animal, memory CD4+ T cells ($CD4^+/CD28^+/CD95^+/CCR7^+$) comprised 28%-40% of the population. A representative panel of this is shown below (Figure 2) with the right panel showing CCR7 expression of $CD28^+/CD95^+$ cells in the left panel.

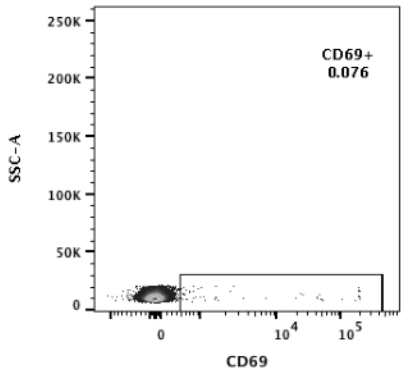


rhbd41

Figure 2.
To assess activation state, we stained the cells for CD69, an early activation marker, and CD25, a late activation marker. Throughout our experiments, we found that CD69 expression was consistently low (Figure 3).

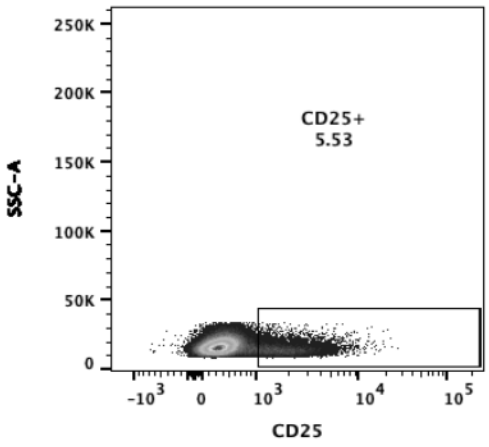


Stained - 5 Days Post-Infection

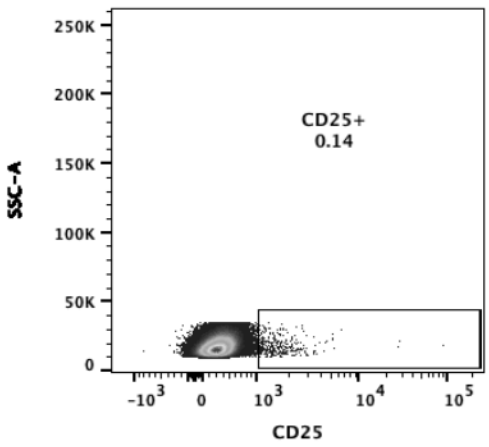


PE/Dazzle 594 FMO - 5 Days Post-Infection

Figure 3.
Conversely, we detected CD25 expression in 3-8% of the cells in each experiment (Figure 4). To eliminate this population, CD25 microbeads were used to magnetically deplete CD25+ cells. Based on initial experiments, the frequency of latently infected cells is not significantly decreased after CD25 depletion, but the frequency of CD25-expressing cells is reduced to 0.1%-0.7% (Figure 4). However, we are repeating this experiment to confirm these results. We anticipate that depleting CD25+ cells from the population will give us a final population of resting memory CD4+ T cells with a known frequency of latent SIV infection.



rhbd41 Non-depleted



rhbd41 Depleted

Figure 4.
Based on the consistency of our flow cytometry data and the congruence of our data with previously published literature, we are confident that we have successfully produced latently infected cells *in vitro*. Prior to starting the animal studies involved with AIM II, we will be (1) repeating the experiment involving CD25 depletion that was described above, (2) correlating the amount of cell-associated viral DNA to the frequency of infection determined by flow cytometry, (3) testing a second anti-p27 antibody to allow for a more defined positive population when staining for p27, and (4) conducting an *in vitro* experiment to confirm that the number of latently infected cells can be correlated to the number of molecular barcodes found in viral RNA after stimulation. Once we have completed these objectives, we will begin the adoptive transfer of autologous SIV latently infected CD4+ T cells into rhesus macaques (AIM II).

Full bibliographic materials on each paper published, in press, or submitted: Nothing to report.

Grant applications and funded grants resulting from this project: Nothing to report.

Project Title: Chemogenetic Manipulation of Thalamo-cortical Dynamics

Name, Title, Institutional Affiliation: Redacted by agreement Assistant Professor, Department of Psychology, University of Wisconsin-Madison Redacted by agreement Professor, Department of Psychology, University of Wisconsin-Madison; Redacted by agreement Professor, Department of Neuroscience, University of Wisconsin-Madison; Redacted by agreement Assistant Professor, Department of Anesthesiology, University of Wisconsin-Madison; Redacted by agreement Associate Professor, Department of Neuroscience, University of Wisconsin-Madison; Redacted by agreement Assistant Professor, Department of Neuroscience, University of Wisconsin-Madison

Years Funded: 09/01/17 – 04/30/19

Project Abstract:

The neural correlates of consciousness (NCC) are the minimal brain mechanisms sufficient to produce a conscious state. Two prominent models of consciousness, Integrated Information Theory (IIT) and Predictive Coding Theory (PCT), have proposed key mechanisms forming the NCC. IIT holds that consciousness depends on the information generated by the brain above that of its parts. This integration is supported by reciprocal interactions between neurons in cortical and thalamo-cortical circuits. In comparison, PCT holds that the brain models conscious experience via top-down processes, with predictive information transmitted along feedback pathways from frontal cortex to sensory cortex. Neuroimaging, electrophysiology and lesion evidence points to the frontal and parietal lobes, as well as the thalamus, as vital brain structures contributing to the NCC. However, experimental evidence is lacking on how information is transmitted through neural circuits in these structures to support consciousness.

The higher-order thalamus forms indirect pathways between directly connected cortical areas (in contrast to the first-order thalamus, which relays information from the sensory organs to the cortex) and is thus well-suited to influencing cortico-cortical information transmission. Neurons in the higher-order central thalamus modulate their activity across the sleep-wake cycle, and central thalamic lesions can produce disorders of consciousness such as coma. **We hypothesize that the central thalamus regulates information flow between cortical neurons, including feedback, thereby supporting conscious states**. To test our hypothesis and key predictions of IIT and PCT, first, we will implant linear electrode arrays at interconnected thalamic (central lateral nucleus), frontal (frontal eye field) and parietal (lateral intraparietal area) sites in macaques, and measure information flow through this thalamo-cortical network. Next, we will manipulate information flow through the thalamo-cortical network, by chemogenetically deactivating the central thalamus (using inhibitory designer receptors exclusively activated by designer drugs), to regulate the level of consciousness. This unique combination of neuroimaging, chemogenetics and multi-site multi-electrode electrophysiology in thalamo-cortical circuits of behaving macaques allows us to respectively target, manipulate and measure activity in a distributed network important for maintaining consciousness.

Our two specific aims are to (1) **investigate the behavioral effects of chemogenetically deactivating the central thalamus**, and (2) **investigate how central thalamic deactivation influences cortico-cortical interactions**. We expect central thalamic deactivation to reversibly perturb information transmission between groups of cortical neurons as well as impair or cause loss of consciousness. In support of our hypothesis, we have collected preliminary data suggesting that information transmission across the cortex is reduced during unconsciousness and that electrical stimulation of the central thalamus can restore consciousness in macaques receiving anesthetic-doses of propofol or isoflurane. This project is not only a vital step towards resolving the NCC, but also reducing anesthetic complications, such as awareness under anesthesia, as well as improving the diagnosis and treatment of disorders of consciousness like coma.

Progress to Date:

This project probes the neural correlates of consciousness. The two major goals of this project in non-human primates are:

Goal #1. Investigate the behavioral effects of chemogenetically deactivating the central thalamus.
Goal #2. Investigate how central thalamic deactivation influences cortico-cortical interactions.

To achieve Goals #1 and #2, first, **(A)** we simultaneously record neural activity from interconnected central thalamic, frontal cortical and parietal cortical sites from anesthetized or awake macaques, to characterize

thalamo-cortical dynamics in conscious and unconscious states. Next, **(B)** we electrically stimulate the central thalamus to demonstrate its influence on the level of consciousness and cortical activity. Finally, **(C)** we chemogenetically deactivate central thalamus to influence the level of consciousness and cortical activity. We report progress below.

A) Simultaneously neural recordings from central thalamus, frontal cortex and parietal cortex.

We used linear multi-electrode arrays to simultaneously record (spikes and local field potentials, LFPs) from interconnected sites in the central lateral thalamus (CL), frontal eye field (FEF) and lateral intraparietal area (LIP) of two macaques under general anesthesia (propofol or isoflurane) or during wakefulness. Current source density analyses identified superficial, middle and deep layers in FEF and LIP, thereby allowing us to measure feedforward (between superficial layers in LIP and superficial/middle layers in FEF) and feedback (between deep layers in FEF and superficial/deep layers in LIP) interactions across fronto-parietal cortex. There was greater feedforward coherence at gamma frequencies (>30Hz) and feedback coherence at theta-alpha frequencies (4-15Hz) for awake versus anesthetized animals. Further, in both FEF and LIP, there was increased spike rate and a shift from periodic to tonic spiking activity at higher levels of arousal. Finally, the spike rate of CL neurons increased during wakefulness (relative to anesthesia).

B) Stimulation of central thalamus to influence level of consciousness and cortical activity.

To establish causal influences, we electrically stimulated electrode contacts in CL (at 10Hz, 50Hz or 200Hz) of the same two macaques during general anesthesia or wakefulness. Our data suggest that stimulation of CL at 50Hz, mimicking the spike rate of CL neurons during wakefulness, overrode effects of isoflurane and propofol anesthesia, including permitting eye opening and purposeful movements. At the same time, 50Hz CL stimulation induced cortical dynamics resembling the wake state, including increased gamma coherence in fronto-parietal feedforward pathways, and increased theta-alpha coherence in fronto-parietal feedback pathways. Further, stimulation-induced arousal altered cortical spiking dynamics, with a shift from periodic spiking to tonic spiking. These effects were maintained during CL stimulation, not other nearby thalamic nuclei, and ended shortly after terminating CL stimulation. In contrast, stimulating at 10Hz, mimicking the spike rate of CL neurons during unconsciousness, or 200Hz, akin to clinical deep brain stimulation (DBS), did not produce the same effects. Taken together, CL thalamic stimulation at 50Hz reconfigured cortical dynamics for arousal.

C) Chemogenetic deactivation of central thalamus.

We have developed the targeted injection procedure at the MRI scanner to verify viral vector delivery. Having completed neural recordings to characterize thalamo-cortical dynamics in conscious and unconscious states, we are now able to proceed with chemogenetic manipulations in the next phase of experiments.

This work has been presented at the Society for Neuroscience Annual Meeting:
Redinbaugh MJ, Phillips JM, Kambi NA, Mohanta S, Raz A, Saalmann YB (2018) “Central lateral thalamus causally influences states of consciousness by regulating fronto-parietal cortical dynamics” 445.04 (talk at nanosymposium 445).

Full bibliographic materials on each paper published, in press, or submitted: The first paper based on this work is currently in preparation and will be submitted later this year.

Grant applications and funded grants resulting from this project:

United States-Israel Binational Science Foundation Research Grant 201732
PIs Redacted by agreement
Title: “Anesthetic modulation of thalamo-cortical interactions”
1 October 2018 – 30 September 2022

Project Title: Vaccine to Induce Ab Production in Cervicovaginal Mucosa

Name, Title, Institutional Affiliation: Redacted by agreement Research Associate, Department of Microbiology and Immunology, University of Minnesota; Redacted by agreement Associate Scientist, Wisconsin National Primate Research Center, University of Wisconsin-Madison

Years Funded: 09/01/17 – 04/30/19

Project Abstract:

Vaccination of rhesus macaques (RMs) with live attenuated SIV virus (LAV) consistently induces robust protection against pathogenic SIV challenge by all routes, and thus provides an excellent animal model for elucidating protective mechanisms to facilitate HIV vaccine design. To that end, we have been investigating SIVmac239deltanef (SIVdeltanef) vaccination in the SIV-RM model of HIV-1 sexual transmission to women to identify protective correlates. In studies to date, we discovered one strong correlate of protection – SIVdeltanef vaccine effectively blocks establishment of early infection at the portal of entry by eliciting an organized system to locally produce IgG antibodies (Ab), predominantly to trimeric gp41 (gp41t) in cervicovaginal mucosa, and concentrate these Ab by neonatal Fc receptor (FcRn) in cervicovaginal epithelium on the path of virus entry. This discovery provides a vaccine design principle: Develop immunogens/adjuvants and immunization strategies that reproduce local production and concentration of Ab in the mucosa, and consequently the protection conferred by SIVdeltanef, but circumvent safety issues of LAV replication.

Based on this principle, we designed a liposomal nanoparticle gp41t immunogen and administrated it to RMs intramuscularly and intranasally with MPLA and CpG adjuvants. The immunization elicited high-level Ab to gp41t in the circulation and FcRn+ cervical epithelium, but not in vaginal epithelium. Most importantly, this strategy did not reproduce the local system of Ab production and concentration to a level equivalent to SIVdeltanef vaccination, and thus failed to protect vaccinated RMs from vaginal challenge with pathogenic SIVmac251.

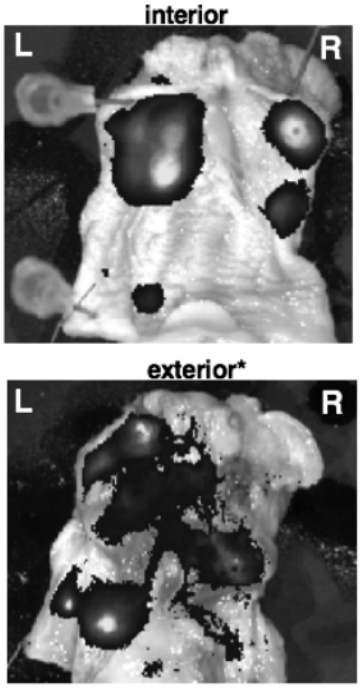
These results, although disappointing, suggest that systemic immunization alone cannot reproduce the local production of IgG, which, however, correlates with persistent low levels of SIVdeltanef replication in cervicovaginal mucosa. In parallel experiments in mice, we found that both systemic and mucosal immunizations are required to induce B resident cells and local Ab production in cervicovaginal mucosa. We now propose experiments in RMs to optimize vaccine strategies and test the central hypothesis that **combining systemic immunization with persistent mucosal antigen exposure will establish a local system of IgG Ab production in cervicovaginal mucosa.**

Specific Aim 1: **Evaluate persistent systemic and mucosal antigen exposure as a strategy to induce a local system of Ab production using the RM model and a novel method for mucosal immunization**. We will repetitively immunize RMs with gp41t in both systemic and mucosal routes to better mimic SIVdeltanef infection, using newly formulated microneedle patches with optimized kinetics for sustained immunogen/adjuvant release.

Progress to Date:

Specific Aim 1: **Evaluate persistent systemic and mucosal antigen exposure as a strategy to induce a local system of Ab production using the RM model and a novel method for mucosal immunization**. We will repetitively immunize RMs with gp41t in both systemic and mucosal routes to better mimic SIVΔnef infection, using newly formulated microneedle patches with optimized kinetics for sustained immunogen/adjuvant release.

Microneedle (MN) patches with gp41t immunogen and adjuvants were prepared, but, prior to embarking on repetitive mucosal immunizations, we first tested the approach in test animals. We discovered that the MN patches that work so well for intra-dermal immunization would not adhere to vaginal mucosa. We then tested direct inoculation in a test animal but this too did not reliably introduce immunogen into the vaginal submucosa. Currently we are exploring methods for vaginal introduction via needles of phosphoserine modified gp41t bound to Alum. We have promising preliminary results in excised cervical vaginal tissue from a practice animal injected with a fluorescent antigen, as shown in the figure below:



We plan to further optimize vaginal inoculations in additional test animals and then initiate the combined systemic and mucosal immunization scheme to see if we can reproduce the correlate of SIVΔnef protection of a local system of gp41t antibody production and concentration by the neonatal Fc receptor in cervical vaginal epithelium

Full bibliographic materials on each paper published, in press, or submitted: Nothing to report.

Grant applications and funded grants resulting from this project: Nothing to report.

NEW WNPRC PILOT PROJECTS FUNDED IN 2018

PERIOD OF SUPPORT: SEPTEMBER 1, 2018 – AUGUST 31, 2020

Project Title	Principal Investigator(s)	Dates of funding	Amount of funding (Direct costs)	Co-funded?
Neisseria colonization of the female reproductive tract	Redacted by agreement	9/1/2018 – 8/31/2020	$49,454	WNPRC only
Novel model assessment for neural effects of differential infant care		9/1/2018 – 8/31/2020	$36,416	WNPRC only
Advancing CRISPR-mediated Genome Editing Technology at UW-Madison to Model Human Disease		9/1/2018 – 8/31/2020	$48,870	WNPRC / UW-Madison UW2020 Program
Nanoplatforms for targeted in vivo LRRK2 genomic editing in nonhuman primates		9/1/2018 – 8/31/2020	$50,000	WNPRC only

NEW PILOT PROJECT ABSTRACTS

Project Title: Neisseria colonization of the female reproductive tract.

Name, Title, Institutional Affiliation: Redacted by agreement Assistant Professor, Department of Biological Sciences, Ohio University; Redacted by agreement, Professor, Wisconsin National Primate Research Center, University of Wisconsin-Madison

Years Funded: 09/01/18 – 08/31/20

Project Abstract:

Defining the mechanisms of infection for human-restricted pathogens like Neisseria gonorrhoeae (Ng) faces many roadblocks because of the strict tropism of this pathogen for the human host. Ng, the second leading cause of bacterial STDs, frequently colonizes the human genitourinary tract, rectum and pharynx asymptomatically. Ng does not persistently colonize monkeys when inoculated into the pharynx, rectum, urethra or conjuctiva. We recently reported a monkey model that circumvents Neisseria host restrictions by utilizing Neisseria species indigenous to macaques. This system was used successfully to study pharyngeal colonization for greater than 70 days. We believe this approach holds great promise for modeling asymptomatic carriage of Ng in human reproductive tract.

We will test the following three hypotheses: 1) Macaque-adapted Neisseria will colonize the lower reproductive tract (LRT) following intravaginal inoculation; 2) LRT colonization will stimulate local and systemic immune responses; 3) Neisseria will disseminate from the LRT into the upper reproductive tract (URT). Based on previous experience with the macaque pharyngeal colonization model we anticipate that intravaginal inoculation of Neisseria will result in persistent asymptomatic colonization of the ectocervix within two weeks post-inoculation. Based on carriage studies in humans we expect Neisseria inoculation to activate innate and adaptive cellular and humoral responses. We will also survery for cytokine stimulation. Our previous studies in macaques detected dissemination of Nessiera to sites high in the nasal cavity. For this reason, we predict Nesseria will disseminate from the LRT to the URT.

We propose the following aims to extend this approach to the modeling of Ng interactions with the female reproductive tract.

Specific Aim 1: Establish if intravaginal inoculation of Neisseria results in reproductive tract colonization. Following intravaginal inoculation of antibiotic-resistant Neisseria weekly ectocervix swabs will be monitored for bacterial load. The time of bacterial persistence post-inoculation will be determined. We will use necropsy tissues to monitor viable bacteria that persist until the end of the study. Tissue-associated bacterial counts and immunohistochemistry will be used to monitor Neisseria association with reproductive tract tissues and determine if Neisseria disseminate from the lower reproductive tract to the upper reproductive tract. Select Neisseria isolates' genomes will be sequenced to monitor for within-host genome variation at two points post-inoculation.

Specific Aim 2: Characterize the systemic and mucosal innate and adaptive immune responses to Neisseria strain AP678. Work associated with this aim will immunotype the frequency and activation of immune cells and measure surface and intracellular molecules including cytokines and transcription factors. Cytokines will be measured in serum. Immunoglobulins levels will be measured in serum, plasma and vaginal lavages. Serum will be evaluated for the development bactericidal of antibodies. Blood will be collected for transcriptional profiling.

Should this colonization model prove successful future studies will allow the in vivo functions of orthologs for Ng virulence factors to be investigated in the female reproductive tract. The model could also open the doors to studying URT infections and the ability of Ng to promote HIV infections. Understanding the mechanisms of asymptomatic carriage by Neisseria species in the LRT and URT is crucial to the development of therapies efficacious against mucosal colonization.

Project Title: Novel model assessment for neural effects of differential infant care.

Name, Title, Institutional Affiliation Redacted by agreement, Professor of Neuroscience, Neuroscience Institute, Georgia State University Redacted by agreement Associate Scientist, Wisconsin National Primate Research Center, University of Wisconsin-Madison; Redacted by agreement Associate Professor, Psychology Department, University of Wisconsin-Madison

Years Funded: 09/01/18 – 08/31/20

Project Abstract:

In primates, early development is characterized by a relatively immature brain, coupled with a prolonged period of infancy. The combined immature brain and prolonged period of infancy provides a context for an extended period of learning and cognitive development that is highly malleable in response to a variety of socio-cultural and experiential factors, including negative or adverse events such as infectious disease, prenatal perturbations, physical and psychological abuse, and neglect, just to name a few. Early childhood sociological and psychological adversity can have profound long-term impacts on a variety of neuroanatomical, affective and cognitive systems. Indeed, early adversity and stress contributes to many forms of psychopathology and mental illness. Therefore, identifying the specific role that early adversity has on long-term changes in brain, cognition and health are critically important. Further, evaluating the influence of different interventions on outcomes associated with early adversity are needed to evaluate their efficacy. Previous NIH funded studies by the PI and his colleagues have demonstrated that early social rearing experiences influence a variety of aspects of social behavior, social cognition and the brain in chimpanzees. However, changes in NIH policy on the use of chimpanzees in research prevents further inquiry into this important topic. Thus, we are proposing to develop rhesus monkeys as model species for studies of the effect of early adversity on brain and behavioral development. Building on our previous work with chimpanzees, we are proposing to obtain magnetic resonance images of rhesus monkeys that have been raised by their conspecific mothers (MR), cross-fostered and raised by an unrelated rhesus monkey mother (NR-CF) and (3) raised and experiencing standard nursery care by humans (NR-SC). T1-weighted structural and diffusion tensor images (DTI) will be obtained in all subjects and compared for (1) whole brain gray matter variation and (2) whole brain fractional anisotropy and radial diffusion values. Specifically, we will use support vector machine language learning to determine whether reliably predict individual subjects rearing history based on weighted co-varying voxel intensity values throughout the cortex. Additionally, we will use region of interest analyses to test whether early intervention in the form of cross-fostering infants to unrelated females blunts the long term changes in gray matter volume and white matter integrity found in monkeys raised in standard nursery conditions. Collectively, the results of the proposed pilot studies will provide the foundation for data to be used in future grant submissions that will allow us to expand the scope of (1) brain and behavioral phenotypes and (2) to further how variation in early social rearing interacts with the genome to influence a variety of behavioral and neurological outcomes.

Project Title: Advancing CRISPR-mediated Genome Editing Technology at UW-Madison to Model Human Disease

Name, Title, Institutional Affiliation: Redacted by agreement Professor, Comparative Biosciences Wisconsin, National Primate Research Center, University of Wisconsin-Madison; Redacted by agreement Associate Professor, Biomolecular Chemistry, University of Wisconsin-Madison

Years Funded: 09/01/18 – 08/31/20

Project Abstract:

This project will establish advanced CRISPR technologies to enable genome editing in multiple mammalian species. Advancing the use of CRISPR-mediated genome editing technology at UW-Madison will accelerate the ability to generate genetically modified animal models of human disease.

Accurately modeling human disease states is critical for the development of new therapeutics. These efforts will promote groundbreaking research across the UW-Madison campus and fundamentally transform our ability to address critical biomedical issues across a wide spectrum of fields.

Project Title: Nanoplatforms for targeted in vivo LRRK2 genomic editing in nonhuman primates.

Name, Title, Institutional Affiliation: Redacted by agreement, Professor, Wisconsin National Primate Research Center, University of Wisconsin-Madison; Redacted by agreement, Vilas Distinguished Achievement Professor, Biomedical Engineering, Wisconsin Institute for Discovery, University of Wisconsin-Madison

Years Funded: 09/01/18 – 04/30/19

Project Abstract:

Genomic editing with CRISPR/Cas9 presents unique opportunities for development of novel therapies, yet until now it has depended on viral vectors, which require laborious customization and have troublesome safety profiles. Our team has developed an efficient non-viral CRISPR/Cas9 delivery system for in vivo genome editing. Our strategy requires the delivery of preassembled Cas9-gRNA ribonucleoproteins (RNPs) using nanocapsules (NCs) specifically engineered for delivering an RNP payload through the blood-brain barrier (BBB). RNPs are short lived in the cytoplasm, limiting exposure to the host genome and hence decreasing the odds of off-target editing. The NCs in our system are small (dH~13 nm), stable in blood, and conjugated to facilitate crossing of the BBB and neuronal uptake.

The leucine-rich repeat kinase 2 (LRRK2) G2019S (glycine to serine) is the most common mutation associated with sporadic and familial Parkinson's disease (PD). The G2019S mutation affects the kinase domain of LRRK2, increasing the catalytic rate of the enzyme. LRRK2 G2019S-related neurodegeneration is proposed to be induced by way of hyperphosphorylation of dual specificity mitogen-activated protein kinase kinase 4 (MAP2K4), an activator of MAPK, which deregulates mechanisms of cell proliferation, differentiation, and survival, increase overall levels of autophagy by overactivation of the MAPK1/3 pathway; abnormal mitochondrial morphology, fragmentation, and damaged mitochondrial DNA resulting in elevated reactive oxygen species. In vitro and in vivo studies demonstrated that inhibitors of LRRK2 kinase activity attenuate LRRK2 G2019S-induced neuronal cell death and related mechanisms of dysfunction. Although current evidence supports the concept that inhibition of the LRRK2 kinase domain may delay or prevent PD pathology, chronic dosing with kinase inhibitors induced pathologies in lung and kidney. Genomic editing, targeting neuronal populations may be an ideal method to selectively affect kinase neuronal activity. Our preliminary work in marmoset-derived neural stem cells demonstrates that CRISPR/Cas 9 can be used for editing the LRRK2 gene in this nonhuman primate species. Therefore, here we propose:

Hypothesis: RNP/NC can be used for in vivo genomic editing to truncate the kinase domain of neuronal LRRK2.

Specific Aim: To assess the feasibility of using a novel RNP/NC delivery system for in vivo CRISPR/Cas9 truncation of the LRRK2 gene in a common marmoset model.

We will evaluate the overall response to the RNP/NC formulation by assessing two animals with a battery of behavioral measures before and a period of 2 weeks after intravenous administration. We will assess the efficacy of neuron targeting and systemic genome editing efficiency in the brain, liver, kidneys, spleen, heart, colon, pancreas, lung, and femoral muscle. We will evaluate kinase activity of the edited enzyme and employ deep genome sequencing to determine on-target and off-target editing efficacy. We will further assess the biocompatibility of the NCs using a serum component panel and pathological post-mortem evaluation. Immune response will be assessed by immunohistochemistry in all collected organs. Because PD is a complex multisystem disease that affects the central and peripheral nervous system, the data gathered in both central and peripheral tissues will provide invaluable information for developing a comprehensive treatment approach using RNP/NC for PD.

2018 WNPRC Pilot Program Review Committee Members

Last, First Name	Title	Institution
Redacted by agreement	Professor of Comparative Developmental Psychology	University of Portsmouth
	Associate Professor of Neurobiology	Stanford University
	Professor of Immunology and Microbial Sciences	The Scripps Research Institute, La Jolla
	Associate Professor of Pediatrics	University of Wisconsin-Madison
	Professor of Obstetrics and Gynecology	University of Auckland
	Professor of Psychology	University of Wisconsin-Madison
	Professor of Pathology and Laboratory Medicine	University of Wisconsin-Madison
	Professor of Medicine	Emory University School of Medicine
	Professor of Microbiology and Immunology	University of Minnesota
	Associate Professor Psychological Brain Sciences	University of Massachusetts
	Senior Lecturer Psychology	University of Sussex
	Professor of Biomedical Engineering/Neurobiology/Ophthalmology	Northwestern University
	Professor of Neurosurgery	University of Minnesota Medical School
	Professor of Microbiology and Immunology	University of California, Davis
	Endowed Professor of Obstetrics and Gynecology	Oregon Health & Sciences University
	Associate Professor of Psychiatry	Stanford University School of Medicine
	Assistant Professor Physiology/Pharmacology/Psychology	Schulich School of Medicine & Dentistry
	Research Assistant Professor, Yerkes National Primate Research Center	Emory University
	Assistant Professor of Bacteriology	University of Wisconsin-Madison
	Executive Director Obstetrics and Gynecology	University of Pittsburgh, Magee-Womens Research Institute
	Professor of Pathology and Laboratory Medicine	University of Wisconsin-Madison
	Associate Professor of Bioengineering	University of Pittsburgh

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5904

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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. Costs to support new and ongoing and WNPRC Pilot Research Awards	211,785.00
Total Other Direct Costs	**211,785.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**211,785.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	211,785.00	78,360.00
		Total Indirect Costs	**78,360.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**290,145.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Non-Human Primate Precision Medicine Core (Resource-Rel-Res-Pro-001)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The major goals of Precision Medicine Embryonic Genome Editing Subunit are: 1) to provide pluripotent cell, gamete and embryo platforms for CRISPR/Cas9 genomic editing for Precision Medicine NHP models, 2) to develop innovative precision NHP models and tools for assessing novel stem cell-based therapies, and 3) to integrate the Core into a functional pipeline for pre-clinical scientific discovery and development of novel therapeutic intervention, establishing collaboration between research and clinical studies.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2. Accomplishments_Precision Med Core.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?

- Evaluated collected data to quantitatively develop a database of normal embryo development timelines with the MIRI self-contained embryo culture/videomicroscopy unit. Assess whether data support a seasonal effect on embryo quality.
- Evaluate collected data to establish normal sperm motility parameters with the CASA platform to identify the best male marmosets and macaques for semen collection on a rigorously quantitative basis. Preliminary analysis suggests a seasonal effect on sperm quality, but between-animal variability may override seasonal within-animal variability. Rigorous statistical analysis will be implemented.
- Rhesus macaques have been integrated into the PMC animal cohort and LRRK2 editing will be initiated with rhesus embryos. This work will be in conjunction with the new UW2020 in which Drs. Golos and Schmidt are co-investigators.
- Compare oviductal and transcervical embryo transfer efficiency for establishment of cynomolgus macaque pregnancies with CCR5 edited embryos.
- Continue to reprogram additional marmoset fibroblasts to obtain more cell lines.
- Perform preliminary evaluation of rejuvenated SIV TCR-specific CTLs in setting of SIV infection in vivo.
- Continue improving gene editing in NHP stem cells using CRISPR/Cas9 technologies.
- Produce CAR-iPSCs and used them to generate CAR-T cells.
- Complete studies on derivation of myeloid-derived suppressor cells from NHP iPSCs.
- Continue assisting other UW and outside investigators in employing the BMT model.
- Continue to advance precision MHC-defined NHP models for assessment of iPSC-based immunotherapies.

NONHUMAN-PRIMATE PRECISION MEDICINE CORE (PMC)

Unit Heads: Redacted by agreement Ph.D.
Redacted by agreement M.D., Ph.D.

Accomplishments – Embryonic Genomic Editing Subunit

Major activities and Significant Results

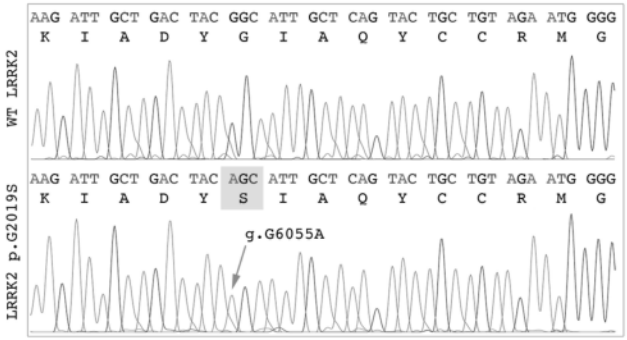


***Fig. 1**. Biallelic single nucleotide mutation by homology-directed repair in marmoset LRRK2 by CRISPR/Cas9.*

The PMC Embryo Genome Editing Core worked with marmoset iPSC and ESC to test CRISPR/Cas9 genomic editing effects on differentiation, piloting this work in parallel with genome editing initiation in marmoset embryos. We introduces a g.G6055A mutation into marmoset LRRK2 (encoding G2019S) which is predominant in human sporadic as well as familial cases of Parkinson's Disease. These cells will be used for *in vitro* differentiation studies to predict the impact of this mutation in the marmoset experimental platform.

With success in editing marmoset fibroblasts and ESC (Fig. 1) we have initiated editing experiments in cynomolgus macaque embryos (Fig. 2) and marmoset embryos (Fig. 3).

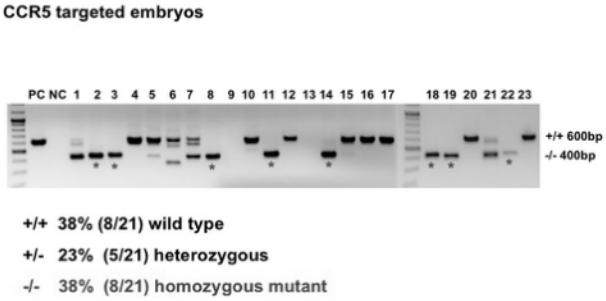


***Fig. 2**. Cynomolgus monkey embryo targeting of CCR5 by non-homologous end joining in fertilized zygotes. 38% homozygous mutants were obtained in this trial.*

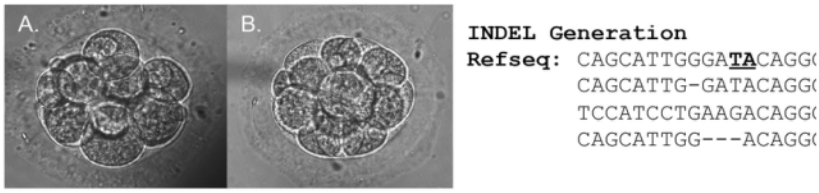


***Fig. 3**. A: control embryo. B. Embryo injected at the Zygote stage with CRISPR/Cas9 editing reagents. Indels generated from this pilot experiment identified by NGS analysis are shown at the right.*

In a project targeting the HIV co-receptor in cynomolgus macaque embryos, PMC Embryo Genome Editing supported the production of cynomolgus macaque embryos there was promising success with paired constructs targeting CCR5 (e.g., Fig. 2). Work thusfar with marmosets also has shown that there is no deleterious impact of the introduction of CRISPR/ Cas9 ribonucleoprotein complex into zygotes (Fig. 3), and pilot editing has provided evidence of the targeting of LRRK2.

Key outcomes

New grant awarded:
UW2020 Redacted by agreement PI Redacted by agreement co-Is) 6/1/18-5/31/20
Total Direct Cost $474,250 ($48,870 to PMC Embryo Genome Editing Subunit)
Advancing CRISPR-mediated Genome Editing Technology at UW-Madison to Model Human Disease
The PMC will be responsible for incorporating newly developed and optimized genome editing tools into a nonhuman primate embryonic genome editing component.

Accomplishments – Precision Therapies Subunit

Major activities

- Continued to develop precision MHC-defined NHP models for gene and stem cell-based therapies.
- Continued to create precision MHC-defined NHP models for assessment of iPSC-based immunotherapies.
- Working on an HSC platform for genomic editing with CRISPR/Cas9 technologies to facilitate development of precision NHP models for novel gene therapies.
- In effort to integrate NHP stem cell transplantation model into a functional pipeline for translational studies, Precision Medicine Precision Therapeutics subunit:
  - Assisted UW and outside investigators in employing the BMT model, including 1) Redacted by agreement group (Department of Surgery, Division of Transplantation; UW-Madison) who, in collaboration with Dr. Samuel Strober (Stanford University School of Medicine), explores the role of hematopoietic chimerism in establishing immune tolerance toward solid organ transplant; 2) Redacted by agreement (The Scripps Research Institute), who is developing novel approaches for highly efficient methods of genetic modification of HSCs; and 3 Redacted by agreement (Morgridge Institute for Research, Madison, WI) who is developing an NHP model for MHC homozygous iPSC banking.
  - Provided a platform for executing two projects by WNPRC investigators: R24OD021322-01A1 "CCR5-mutant monkey model to facilitate the development of novel stem cell-based therapies for AIDS" Redacted by agreement Redacted by agreement PIs, Redacted by Co-I), and R01 HL132891-01 entitled "Nonhuman Primate Model for Preclinical Evaluation of Haplotype-Based iPSC Banking for HLA-matched Blood Products" Redacted by agreement Redacted by PI and Redacted by agreement Co-I).
  - Initiated new collaboration between Redacted by agreement to study potential utility of rejuvenated through reprogramming SIV-specific TCLs for AIDS therapies.

Significant results

- Several innovative NHP MHC-defined bone marrow transplantation models were established. These models include i) transplantation of autologous genetically modified CD34+ cells and ii) allogeneic transplantation of TCRα/β-depleted bone marrow cells. Allogeneic transplantation of TCRα/β-depleted bone marrow cells has been performed in five animals. Following optimization conditioning and post-transplant immunosuppression we were able to achieve successful HSC engraftment without a significant GVHD in MHC-matched and blood group identical Mauritian cynomolgus macaques (MCMs).
- The effect of allogeneic TCRα/β-depleted bone marrow transplantation on SHIV infected animals on retroviral therapy was evaluated in two animals. Results of these studies demonstrated that latent reservoir can persist in ART-treated macaques after profound lymphocyte depletion and allogeneic HSCT.
- CRISPR/Cas9 protocols for gene editing in NHP stem cells were established.
- Novel protocol for generation of myeloid-derived suppressor cells from nonhuman primate iPSCs was established.
- Protocols for reprogramming T cells into iPSCs and differentiating them back to "rejuvenated" T cells were established.
- SIV-resistant iPSC lines with homozygous CCR5 knockout were established.

Key outcomes

- ICTR grant "Generation myeloid-derived suppressor cells from nonhuman primate iPSCs" was awarded to support a joint project between Redacted by agreement
- New collaboration between Redacted by agreement to assess the use the utility of using rejuvenated T cells for treating SIV infection was initiated.
- Studies aimed to evaluate immune responses in setting MHC homozygous arterial transplants were completed.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5905

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Project Lead	Institutional Base Salary	EFFORT			18,960.00	6,314.00	25,274.00
2.					MD	Project Lead					12,027.00	4,005.00	16,032.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **41,306.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
1	Undergraduate Students	EFFORT			3,367.00	104.00	3,471.00
	Secretarial/Clerical						
7	Co-Investigators / Assistant Researchers				132,430.00	44,099.00	176,529.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**180,000.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**221,306.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	2,943.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,943.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	46,083.00
2. Publication Costs	1,000.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal research-related costs	164,697.00
Total Other Direct Costs	**211,780.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**436,029.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	436,029.00	161,331.00
		Total Indirect Costs	**161,331.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**597,360.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Stem Cell Resources (Resource-Rel-Res-Pro-002)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Non-human primates provide a long-lived animal model that closely reflects human physiology and immunology that will allow for the testing of the safety and efficacy of iPS cell-based transplantation therapies. Human embryonic stem (ES) cells are pluripotent cells with the ability to self-renew and differentiate into advanced derivatives of all three germ layers, but immunological barriers may prevent their widespread application in transplantation medicine. Induced pluripotent stem (iPS) cells have a developmental potential similar to that of ES cells but also allow for greater control over genetic background. Both patient-specific iPS cells and HLA homozygous iPS cells have been proposed as ways to eliminate or greatly reduce immune rejection in transplantation therapies, but the benefits of these strateg have yet to be tested in an appropriate animal model. In the short time since the initial derivation of human iPS cells by the Thomson Yamanaka labs in 2007, we have developed methods for deriving human iPS cells free of vector sequences in fully defined conditions and have demonstrated their differentiation to heart, blood, and neural tissues. These protocols are currently being adapted to the generation and differentiation of primate cells. This rapid progress was only possible because of the existing depth of human ES cell expertise at UW, which emerged directly from primate ES cell work by the [redacted] lab at the WNPRC in the mid-1990s and the derivation of human ES cells at UW in 1998. Combined with world-class expertise in MHC typing and the diseases of aging, the WNPRC is in a leadership position to develop and test stem cell-based therapies in primate models. To facilitate the translation of basic pluripotent stem cell research to human therapies, the Stem Cell Resources Unit will develop expertise and reagents broadly needed by investigators developing primate iPS cell-based transplantation models, with a new focus on a unique population of MHC homozygous cynomolgus macaques.

Redacted by agreement

To support this mission, the Stem Cell Resources Unit will accomplish the following SPECIFIC AIMS:

Specific Aim 1: Improve the defined culture of primate iPS cells and distribute unique culture reagents to other investigators.

Specific Aim 2: Improve reprogramming efficiency of primate hematopoietic cells.

Specific Aim 3: Provide primate iPS cell gene targeting services for other investigators.

Specific Aim 4: Produce clinically relevant cell types for testing iPS cell-based transplantation therapies.

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: B.2. Accomplishments_Stem Cell.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: Improve the defined culture of primate iPS cells and distribute unique culture reagents to other investigators.

We will continue to screen for molecules in the Enamine 2011 diversity library that improve cloning efficiency and/or primate culture media. We will continue to modify the media as we better understand the culture requirements for primate iPS cells. We will also continue to tease apart our existing media for primate culture. As a stem cell resource, we will derive primate iPS cells upon request and review and distribute technical support, reagents, and iPSC lines.

Specific Aim 2: Improve reprogramming efficiency of primate hematopoietic cells.

We are able to adapt our existing episomal reprogramming protocol to human EBV transformed LCL's to generate iPSC colonies at low efficiency. However, we have been unsuccessful in generating iPSC colonies with our current episomal reprogramming protocol in transformed cynomolgus LCL's. To begin screening combinations of transcription factors we need to optimize electroporation conditions in 96 well format. Once electroporation in plate format is optimized we will complete our combinatorial screen on human EBV transformed LCL cells and cynomolgus transformed LCL's. We will then use the best combination of transcription factors to test on cynomolgus macaque EBV transformed LCL cells. When we feel confident in a combination of transcription factors we will attempt reprogramming primary blood cells from cynomolgus macaques.

Specific Aim 3: Provide primate iPS cell gene targeting services for other investigators.

We have successfully created transgenic (SOX2) and knock out (B2M) lines in both Cynomolgus and Rhesus pluripotent cells. In addition, we have received a request form Ted Golo's lab (WNPRC) to provide technical support to create B2M knock out lines in marmoset pluripotent cells.

Any future requests for targeting services will be reviewed and projects pursued if merited.

Specific Aim 4: Produce clinically relevant cell types for testing iPS cell-based transplantation therapies.
We currently optimizing conditions for maintenance of NHP arterial specified endothelial cells. We will make the AEC differentiation more consistent between species, lines and differentiations. Small molecule screens and RNA seq will be explored to look for growth factors and small molecules that improve differentiation efficiency and long-term maintenance of NHP AECs. We will then characterize the cells by LDL uptake, vascular formation, pericyte recruitment, leukocyte adhesion, and shear stress behavior. Finally, we will begin to test our AEC's in translational models. In addition to AEC's differentiation, we want to begin generating NHP derived smooth muscle cells. Over the next year we will begin adapting human protocols for smooth muscle cell differentiation.
We will also provide support to other labs working on alternative cell types. Any requests for differentiation services will be reviewed and projects pursued if merited.

Continuing services supported by stem cell resources:
- Derivation and banking of NHP iPSCs including MHC homozygous NHPs
- Develop protocols for efficient gene editing and providing NHP iPSC gene editing services for other investigators
- Develop protocols for defined maintenance and growth of NHP iPSCs
- Develop protocols to differentiate and purify specific NHP PSC derivatives
- Proved large-scale production of NHP PSCs and their derivatives for transplantation and in vitro studies
- Coordinate and assist in animal procedures for PSC transplantation studies

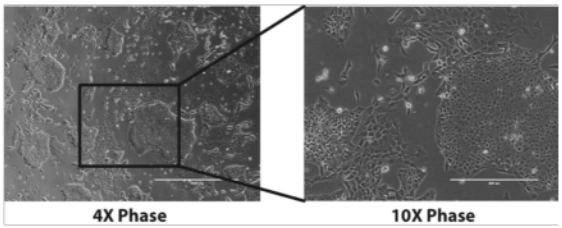
STEM CELL RESOURCES

Unit Head: Redacted by agreement Ph.D.

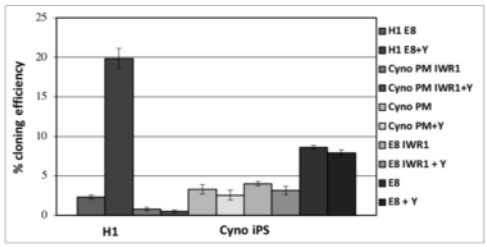
Accomplishments

Specific Aim 1: Improve the defined culture of primate iPS cells and distribute unique culture reagents to other investigators.

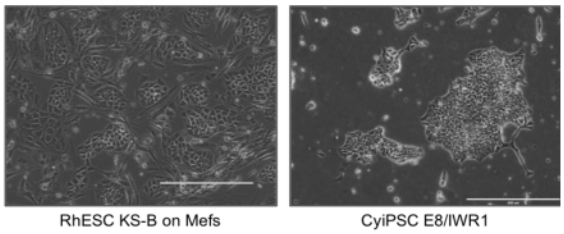
A.



B.



C.



In 2011, we replaced our lab's original serum-free, feeder-free system (TeSR/Matrigel) for human ES/iPS cell culture with the improved, fully defined culture medium E8. With the absence of serum or albumin, this medium supports long-term culture of human ES and iPS cells showing essentially no background differentiation and reduced batch variation. E8 medium has significantly increased the consistency and quality of human ES/iPS cell culture; however, E8 is not optimal for primate ES/iPS cell culture. To date, we have not been able to culture most primate species pluripotent cells in human conditions.

Supplementing E8 with Nodal and other factors (glutathione, lipids, glutamax) improved the culture of primate pluripotent cells. Additionally, this primate media enabled us to move some NHP iPS cells from MEF feeder layers to vitronectin-coated plates. By supplementing this primate media with WNT inhibitors (IWP2 or IWR1), we were able to decrease background differentiation and maintain cynomolgus iPS colonies with normal morphology in culture long-term. While we have improved NHP culture conditions, we still see increased background differentiation (A) and lower cloning efficiency compared to Human pluripotent cells. Additionally, not all NHP iPS cell lines behave similarly. For example, our current best culture conditions for Rhesus ES cells is KS-B on MEFs (C) while Cyno iPS cells grow well with E8 + IWR1 on vitronectin coated plates (C). Primate pluripotent cell culture remains and evolving process and no one condition works for all primate ES/iPS cells. Culture conditions currently used in lab include KS-B, KS-B + IWR1, and E8 + IWR1 grown on either MEFs or VTN depending on cell line. We continue to perform small molecule screens for cloning efficiency with cynomolgus macaque iPS cells on our automated screening equipment. We are optimistic that discovery of molecules that increase cloning efficiency, will also help or provide clues to improving our growth and maintenance conditions.

The screens consist of plating individualized primate iPS cells at a density of 100 cells/well in 96 well format and adding small molecules selected from our libraries. Over 1500 small molecules were screened for increased colony formation over 7 days. Plates were stained with alkaline phosphatase and read on the fluorescent plate reader. Previous screens included our stem cell modulator small molecule library (163 compounds) and the Prestwick Chemical Library (1,200 compounds). We were able to find a few modest hits that we followed up with. We were not able to confirm any increase in cloning efficiency. We continue to perform cloning efficiency screens with the Enamine 2011 Representative Diversity Set (20,160 compounds). Since this is a much larger set, it will require multiple screens to get through the complete set.

We continue to reprogram multiple NHP iPS cell lines and distribute unique resources for labs. Historically stem cell resources has provided many pluripotent cells lines, genetic material, and technical assistance to researchers within the WNPRC and University of Wisconsin Madison as well as outside the University. In 2018 alone, we have sent Rhesus, Cynomolgus, and marmoset pluripotent cells to the University of Macau, University of Massachusetts, Amherst, University of Minnesota, and University of Texas Southwestern in addition to researchers at the University of Wisconsin Madison.

Specific Aim 2: Improve reprogramming efficiency of primate hematopoietic cells.

Non-integrating episomal reprogramming of human blood samples has become routine and has been used to produce GMP HLA-homozygous human iPS cell lines at the Waisman Clinical Biomanufacturing Facility on the UW campus. Because of the ease of access to peripheral blood and compatibility of episomal vectors with GMP procedures, this approach to obtaining human iPS cells is quickly becoming standard. However, to date, we have been unable to use similar approaches to reprogram NHP blood samples. This failure is likely due to the poor cloning efficiencies supported by NHP ES/iPS cell culture media and poor reprogramming efficiencies of the blood itself. Here, we will optimize reprogramming of NHP primary peripheral blood samples.

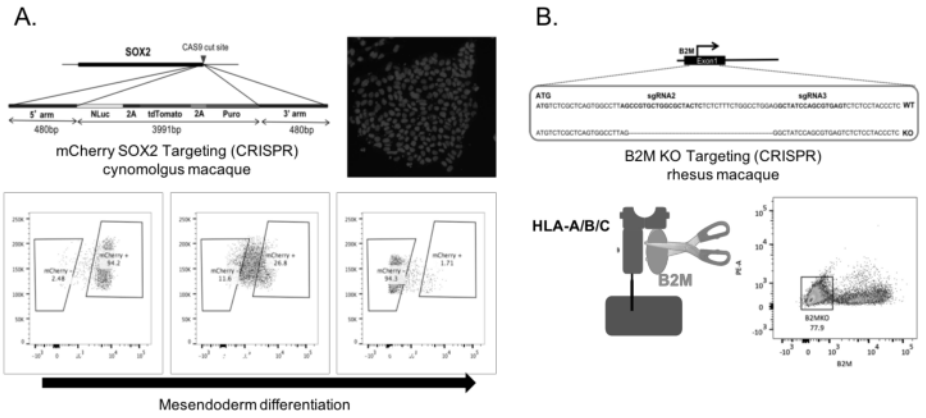
We are currently developing a reprogramming screen on our robotics platform. 15 candidate transcriptions factors have been cloned into episomal reprogramming plasmids. We are currently optimizing episomal reprogramming with human EBV transformed LCL cell lines which have been successfully reprogrammed previously with our normal episomal reprogramming methods, however the efficiency is very low. Furthermore, optimizing electroporation conditions of these cells in 96 well format required for screening has remained challenging.

While working on reprogramming of primate hematopoietic cells, we continue to reprogram fibroblasts for investigators.

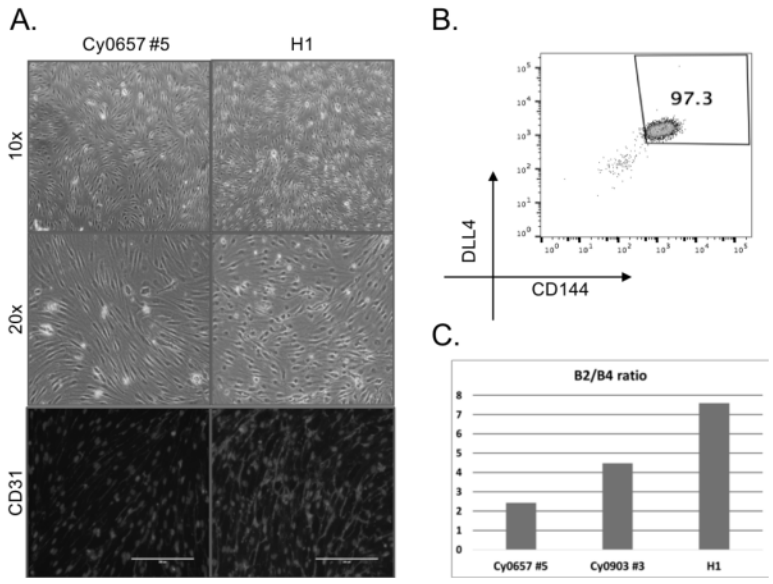
Specific Aim 3: Provide primate iPS cell gene targeting services for other investigators.

With the discovery of CRISPR, gene targeting has become much more efficient. CRISPR uses a RNA-guided nuclease, such as Cas9, to make modifications of the genome. We have been successful using CRISPR to target both Cynomolgus macaque iPS cells as well as Rhesus ES cells. Shown below (A), we generated a SOX2 reporter cell line in Cynomolgus iPS cells to be used in media optimization screens. The transgene insertion contains both luciferase and tdTomato for endpoint readouts. A Representative picture showing tdTomato fluorescence in targeted cynomolgus macaque iPS clone (A) while mCherry expression is lost 48hrs after mesendoderm differentiation (A).

To prevent immune rejection of iPS derived cell types we are not only exploring MHC homozygous cell lines for therapeutics but also genetically engineering cell lines that do not express MHC class I and II. In addition to creating transgenic lines we also created beta 2 microglobulin knock out cell lines in Rhesus ES cells (B). This gene is part of the MHC class I presentation complex. Over 70% of the Rhesus ES cells were negative for B2M expression (B).



Specific Aim 4: Produce clinically relevant cell types for testing iPS cell-based transplantation therapies.



Although NHP and human ES/iPS cells are very similar, human ES/iPS cell differentiation procedures generally require modification for NHP use. In this AIM, the Stem Cell Resources Unit will derive NHP primate iPS cells from specific genetic backgrounds for investigators and will help in adapting their human ES/iPS cells differentiation procedures to NHP iPS cells to aid in the testing of transplantation therapies.

Redacted by agreement lab is interested in making tissue engineered blood vessels for therapeutic use. To accomplish this goal, we will need to produce both arterial endothelial and smooth muscle cells from NHP iPS cells.

Over the course of the past year, we have developed a more robust protocol for making arterial defined endothelial cells (AECs) from both Cynomolgus and Rhesus pluripotent cell lines. The NHP derived AECs look morphologically similar to Human derived AECs (A), can be made at high purity (B) when analyzed for the endothelial marker CD144 and the arterial specific marker DLL4, and express a higher EFNB2 (Arterial) to EPHB4 (venous) ratio similar to human derived AEC's. These cells will be used to engineer blood vessels that will be tested in future primate models.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5906

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Project Lead	Institutional Base	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	Assistant Scientist / Research Specialist	EFFORT			85,193.00	28,369.00	113,562.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**113,562.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**113,562.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	1,892.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**1,892.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	83,644.00
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. Karyotyping costs	4,500.00
Total Other Direct Costs	**88,144.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**203,598.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	203,598.00	75,331.00
		Total Indirect Costs	**75,331.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**278,929.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Research Services Division (Scientific-Units-001)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The Research Services Division of the WNPRC consist of the following five units:

Assay Services unit
Electronic Health Records Services unit
Genetic Services unit
Immunology Services unit
Virology Services unit

While each of the units has their own individual specific aims, they work in unison and communicate on a monthly basis as a centralized full service entity to fulfill the following over-arching specific aims of the Division:

Specific Aim 1: To support NHP studies on a fee-for-service basis with state-of-the-art assays such as comprehensive MHC genotyping, NHP and viral genomic sequencing, profiling cellular immune responses, and quantitative assessments of a wide variety of biomarkers including viral loads steroids, proteins, peptides, vitamins, neurotransmitters and drugs.

Specific Aim 2: To adapt existing fee-for-service assays as new analytical technologies become available in order to improve sensitivity, accuracy and efficiency as well as decreasing costs to NHP investigators.

Specific Aim 3: To develop new assays to address the constantly changing questions that are presented in basic and translational NHP research, e.g. development of a NHP model of Zika virus pathogenicity during pregnancy.

Specific Aim 4: To meet the Specific Aims of the individual units within the Research Services Division.

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: Research Services Division_02202019.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?

Please see related Unit Reports, which includes future goals for the next reporting period.

RESEARCH SERVICES DIVISION

UNIT REPORTS

DIVISION OVERVIEW AND SUMMARY OF ACTIVITIES

Division Head: Redacted by agreement **Ph.D.**

The Research Services Division of the WNPRC consists of five units: Assay Services, Genetics Services, Immunology Services, Informatics and Data Services, and Virology Services. These service units support investigators engaged in infectious disease, regenerative and reproductive medicine, neuroscience, and aging research who study nonhuman primates (NHPs). Research Services provides technical expertise, database management, and generates quality data from complex assays using sophisticated instrumentation. In this way, investigators have the support needed to maximize findings from each NHP experiment. In 2018, Research Services faculty and staff contributed to more than 30 peer-reviewed publications. Furthermore, each unit actively expanded their skill set to offer additional state-of-the-art services to enhance NHP research. Research Service units provided training to 33 young scientists including postdoctoral fellows, graduate students, undergraduates and high school students.

Notable activities of the WNPRC Research Service units in 2018 include:

- Assay Services implemented many process and assay improvements to reduce the use of radiation, optimize assays, and improve unit operations.
- Genetic Services began to develop Macaque Exome Sequencing as a service (host genotyping) and sequenced 120 full viral genomes for SIV and ZIKV researchers (pathogen sequencing).
- Immunology Services developed a new flow cytometry-based method to identify cell surface markers that delineate the phenotypes of neutrophil progenitors in rhesus macaque bone marrow.
- Informatics and Data Services deployed a food deprive system to facilitate scheduling the start and completion of food deprives.
- Virology Services developed sensitive methods for recovering viral RNA (SIV or Zika) from tissues.

ASSAY SERVICES

Unit Head: Redacted by agreement Ph.D.

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1: Maintain an up-to-date, efficient, cost-effective Assay Service for the WNPRC, the UW-Madison, and investigators from universities nationally and internationally. The unit will continue to offer our current assays and support innovative research for nonhuman primates (NHPs), translational and human research. Our current lab members focus on specialized areas that can address the research needs of our clients. We continue to improve upon the methods available within the service and maintain our quality assurances.

Specific Aim 2: Develop new methods for analyses of steroids, proteins, peptides and other biomarkers for endocrine, neural, and metabolic analysis. The unit will continue to develop new methods, provide consultation when needed, and maintain our high throughput for our current long-term and anticipated new clients. New planned developments include C-peptide for marmosets, a metabolic panel for insulin, leptin, ghrelin and adiponectin specific for marmosets and one specific for rhesus macaques using methodologies for triple quadrupole mass spectrometer.

Specific Aim 3: Develop the use of hair as a long-term assessment of steroids and Vitamin D. The use of hair steroids to assess long-term glucocorticoid function noninvasively is in high demand both nationally and internationally for both human and nonhuman primate studies of stress effects on health. However, no standard methodology has been established and validations assessing what steroid metabolites are found in hair are needed. We plan to fully validate steroid metabolites in hair using the rhesus monkey as the model. We have adapted our multisteroid LC/MS/MS method for the measurement of multiple steroids in hair (Kapoor et al., 2014, 2016) and plan to establish these methods for a variety of research purposes.

Accomplishments

Specific Aim 1:

1. Under this aim we ran 39,600 samples in 2018. The samples were run by radioimmunoassay (RIA)-based assays, enzyme immunoassay (EIA)-based assays and liquid chromatography (LC)-based methods.

   Numbers of samples:
   EIA = 15,331
   RIA = 17,392
   LC-MS = 6873 samples (this number includes multiple analytes measured in each sample as LC-based assays can be run in panels with multiple analytes measured simultaneously)

We developed a vitamin D metabolic panel that was used to examine wild, native baboons in Africa to captive baboons to determine appropriate levels and to determine the metabolic process. This paper has now been published: **Ziegler TE**, Kapoor A, Binkley N, Rice KS, Rogers J, Jolly CJ, Phillips-Conroy J (2018). Comparison of Vitamin D metabolites in Wild and Captive Baboons. American Journal of Primatology, 2018 Dec;80(12):e22935. doi: 10.1002/ajp.22935. A project using the Vitamin D panel for measuring serum vitamin D in common marmosets is in progress.

2. We served 30 different clients. Most were charged for several months during this time.

3. We made progress on improving sample preparation, modernization and efficiency for existing methods.
   3.1. During the past year, we completed transitioning all data, methods, validations and quality-control documents to cloud-based storage. All Assay Services staff have access to these documents to review

as needed. These developments were made in consultation with Research Data Services at UW-Madison.
3.2. We initiated cross-training of staff to ensure that more than one person is able to perform each type of assay.
3.3. We established a database for antibodies and tagged hormones used in EIAs and RIAs, respectively, to ensure all reagents are available for the assays.
3.4. We established a new extraction method for our multisteroid analyses by LC/MS/MS to limit staff exposure to volatile chemicals while enhancing efficiency.
3.5. We modernized analyses of EIA data.
3.6. We identified an antibody for the estradiol EIA that improves specificity.
3.7. We obtained a new high-performance liquid chromatography electrochemical detector (HPLC-ECD) to measure catecholamines. We optimized our previous method and greatly enhanced the measurability for the method.

4. The Oregon National Primate Research Center Endocrine Technology Lab and our Assay Services Lab are working together on LC/MS/MS-based measurements to ensure that steroid hormone values will be consistent between the two labs for rhesus macaque studies. In conjunction with external quality control programs, this inter-lab round robin will ensure the accuracy of our steroid hormone measurements.

5. The Assay Services website has been updated and further improvements are in progress.

Specific Aim 2:

1. Currently, there is no EIA or RIA assay sensitive enough to measure marmoset insulin. A LC/MS/MS method for marmoset insulin is in development with expected completion in early 2019. Marmoset insulin has been isolated and purified following extraction from marmoset pancreas.

2. We ran many new commercial kits for clients, such as assays on human samples to measure the following:
   Anti-Mullerian Hormone (AMH)
   Luteinizing hormone (LH)
   Follicle-stimulating hormone (FSH)

3. We continue to develop methods for specific projects such as transferring a method for multisteroids excreted during pregnancy in the common marmoset from our single quad mass spec to our triple quad mass spec. This will also allow us to measure the androgens simultaneously with the glucocorticoids and the estrogens that are in much higher amounts in pregnant urine than androgens.

4. We continue development of a new method for free steroids that will allow us to separate free from bound steroids and analyze both in the same sample. Further advances are expected in early 2019.

Specific Aim 3:

The sample preparation step for the hair steroid LC/MS/MS method was improved by extracting intact hair without grinding. The improved protocol saves time and generates a cleaner sample for LC/MS/MS, thereby increasing the efficiency of the analysis.

The radiolabeled study for hair cortisol has been completed, analyzed and published: Kapoor A, Schultz-Darken N, **Ziegler TE**. (2018). Radiolabel validation of cortisol in the hair of rhesus monkeys. Psychoneuroendocrinology, 97:190-195; doi:10.1016/j.psyneuen.2018.07.022. This was the first direct physiological validation of hair cortisol which is becoming a more popular and important biological matrix.

In addition, funding to further validate hair glucocorticoids was obtained (R03, NICHD, Kapoor A & **Ziegler TE**, Validating the use of hair glucocorticoids as a marker of central hypothalamic-pituitary-adrenal axis activity).

FUTURE GOALS

Specific Aim 1: Maintain an up-to-date, efficient, cost-effective Assay Service for the WNPRC, the UW-Madison, and investigators from universities nationally and internationally. As both older (RIA and EIA) and newer (EIA and LC/MS/MS) methods are in demand, we will continue to use them per client requests. Our LC/MS/MS methods are as much in demand as our more classical methods.

Specific Aim 2: Develop new methods for analyses of steroids, proteins, peptides and other biomarkers for endocrine, neural, and metabolic analysis. We plan to do more method refinement to improve our existing assay methodologies throughout the next year. For example, we will be working on adapting some of our RIA methods to EIA methods to reduce the amount of radioactivity used in the labs. We anticipate new methods being developed and new assay kits being validated for future projects. We will be working on measuring marmoset insulin using LC/MS/MS which will be Assay Services' first peptide method by LC/MS/MS. We expect to use LC/MS/MS for peptide measurements more frequently in the future.

Specific Aim 3: Develop the use of hair as a long-term assessment of steroids and Vitamin D. We will continue to conduct validation studies in hair for other reproductive and adrenal steroids and vitamin D incorporation into hair. These studies are necessary to ensure that the correct steroids are being measured, to determine the time period of circulating hormone in the body that is reflected by the hair hormone level, and to understand the variability in hair growth and its influences on steroid levels in hair. Publication of the validation studies from the other steroid hormones is anticipated. More specific validations of hair cortisol are planned, including identification of unknown cortisol metabolites in hair.

GENETICS SERVICES

Unit Head: Redacted by agreement Ph.D.

GOALS AND ACCOMPLISHMENTS

Goals

Specific Aim 1: Provide fee-for-service major histocompatibility complex (MHC) class I and class II genotyping. Providing fee-for-service major histocompatibility complex (MHC) class I and class II genotyping. We expect to genotype at least 1,500 animals per year for the nonhuman primate community with Illumina MiSeq sequencing-based assays.

Specific Aim 2: Develop MHC, KIR and FcγR full-length transcript genotyping. We will sequence full-length transcripts in Mauritian cynomolgus macaques and Indian rhesus macaques. We will then establish fee-for-service genotyping assays to detect allelic variants of genes.

Specific Aim 3: Perform deep sequencing of viral inocula, replicating viruses from infected animals, and unknown pathogens from sick animals. We will continue sequencing virus stocks used for in vivo macaque challenges as well as viruses from infected animals. We will also develop a specific assay to detect antiretroviral drug resistance in SIV. Moreover, we will implement unbiased pathogen detection to rapidly identify infectious diseases that threaten NHP colonies and their caretakers.

Specific Aim 4: Establish genomic profiling for rhesus macaques, cynomolgus macaques, and common marmosets. We anticipate genomic profiling will be available on a fee-for-service basis at a cost of less than $1,000 per animal.

Accomplishments

Specific Aim 1:
For the period of January 1, 2018 through December 31, 2018, we completed Illumina MiSeq genotyping on a **total of 4,116 samples** for investigators across the nonhuman primate community. Over half of these samples (2528 samples) were from rhesus macaques (essentially all Indian-origin with only 11 Chinese-origin individuals). Mauritian-origin cynomolgus macaques were the second most common population with a total of 1014 samples evaluated. Another 542 samples were MHC genotyped for cynomolgus macaques from other geographic origins (Vietnam, Cambodia, China, Indonesia). Finally, MHC genotypes were also determined for 47 pig-tailed macaques. Fee-for-service Illumina MiSeq sequencing-based genotyping assays **generated $282,160.65 of fee-for-service income from 18 different academic and corporate clients**.

During the previous reporting period for this project, we also employed an **Illumina MiSeq sequence-based genotyping assay for TRIM5α** that has been incorporated into our standard panel for MHC genotyping. This assay was performed on **137 total samples from five different clients during the 2018 reporting period, generating $26,939.04 of additional fee-for-service income** from MiSeq sequencing-based host immune gene assays.

Specific Aim 2:
We have developed primer sets to amplify full open reading frames from cDNA templates for MHC class I (A, B, and I genes), MHC class II (DRA, DRB, DQA, DQB, DPA, and DPB genes), KIR (KIR1D, KIR2DL, KIR2DS, and KIR3DL genes), and FcγR (FcγR1A, FcγR2A, FcγR2B, and FcγR3A genes). These long amplicons are then sequenced on a Pacific Biosciences Sequel instrument. The MHC and FcγR full-length transcript genotyping assays are now offered in our fee-for-service portfolio for both Mauritian cynomolgus and Indian rhesus macaques. During the 2018, we performed fee-for-service **MHC class I and class II genotyping** on **52 Vietnamese-origin cynomolgus macaques** and **MHC class II genotyping on 60 Chinese-origin cynomolgus macaques.** These studies generated a total of **$65,669.92 in fee-for-service revenue.**
Since our published panel of full-length FcγR amplicons (Haj AK *et al*. J. Immunology **202**: 151-159, 2019) is

less robust than we would like, we evaluated a new panel of FcγR primers in a head-to-head comparison with our existing assays. Given the results of this comparison, it appears that the revised FcγR amplicons perform somewhat better than our existing assays so we intend to use this new primer panel for fee-for-service genotyping assays going forward.

Specific Aim 3:
We generated viral sequences for both full-length viral genomes and individual amplicons. We made this switch because there were several cases were we, and others, were interested in sequencing short viral segments from samples with low viral loads, which was more feasible to do via short amplicons.

In 2018, we sequenced 69 full-length SIV individual fee-for-service samples from 4 different academic clients during the period. We also sequenced 52 full-length Zika sequences for basic research purposes. We also sequenced 80 individual SIV amplicons for clients. These data have contributed to five manuscripts published in 2018. We have also been sequencing plasmids for different groups, including SIV plasmids and plasmids containing other immune genes. Sequencing of plasmids is easily performed through our library preparation pipeline, so we have led these efforts. We sequenced 427 plasmids during this past period as fee-for-service. These pathogen sequencing efforts have thus far generated about $45,000 in fee-for service revenue in 2018. In addition, we deposited 11 viral inocula sequences in the Sequencing Reads Archive (SRA). No progress was made on the antiretroviral drug resistance testing during this reporting period, but will be a focus in future years. For unbiased pathogen detection, we have published protocols established, but no clients requested this service during the reporting period.

Specific Aim 4:
Our Macaque Exome Sequencing (MES) program expanded during 2018 to become a standard component of our efforts to genetically characterize Indian rhesus macaques in the WNPRC SPF breeding colony. MES analyses have been performed on a total of **116 Indian rhesus progeny** born at WNPRC in 2017 and early 2018. MES analyses were also performed on at least one parent for 55 of these offspring (**29 sire and dams** in total). In addition, **31 rhesus macaques from SIV studies** performed at WNPRC and NIAID were subjected to MES analyses as part of our efforts to introduce genome profiling assays to the NHP research community.

Per sample costs for our MES assays continued to drop for the target capture and sequencing steps that are performed by Jeff Roger's group at the Baylor Human Genome Sequencing Center. Advances in Illumina sequencing enabled in large part by the release of the Illumina NovaSeq platform and the use of S4 flow cells **dropped these basic costs to $291 per sample by the end of 2018**, provided batches of ~70 samples are processed in parallel. During 2018, we established a workflow for MHC analysis of MES datasets that provides essentially comparable results to our standard Fluidigm/MiSeq assays. In addition, we completed proof-of-principle studies to demonstrate that Trim5 and FcγR genometypes can be extracted from MES datasets. Although additional analysis pipelines and the costs for these analyses still need to be finalized before making genomic profiling widely available on a fee-for-service basis, we did submit our inaugural fee-for-service cohort to the Baylor Human Genome Sequencing Center for MES analysis in early October. Baylor staff made the sequence data for this cohort of 70 Cambodian-origin cynos available for downloading on December 28th.

FUTURE GOALS

Specific Aim 1: Provide fee-for-service major histocompatibility complex (MHC) class I and class II genotyping. We expect to genotype at least 1,500 animals per year for the nonhuman primate community with Illumina MiSeq sequencing-based assays. We plan to continue performing our well-established MHC class I and class II genotyping assay (now inclusive of TRIM5α) because demand for this service from the NHP research community remains strong. As of the beginning of 2019, we already processing ~375 samples in our queue and ~200 additional samples are due to be delivered by the end of January 2019. Given that we have genotyped more than 1,500 animals per year with Illumina MiSeq sequencing-based assays since 2014, so we do not anticipate any difficulty in accomplishing this goal again in the next reporting period.

Specific Aim 2: Develop MHC, KIR and FcγR full-length transcript genotyping. We will sequence full-length transcripts in Mauritian cynomolgus macaques and Indian rhesus macaques. We will then establish fee-

for-service genotyping assays to detect allelic variants of genes. We plan to continue offering fee-for-service MHC and FcγR full-length transcript genotyping assays in the next reporting period. Future requests for FcγR genotyping assays will be processed with a revised primer panel to generate full-length cDNA amplicons for this gene family. Our KIR full-length transcript genotyping assay is still less robust than desired and we still need to work to develop improved primer panels and PCR conditions during the coming year. Our goal is to establish a fee-for-service assay for these genes that will be available by the end of 2019.

Specific Aim 3: Perform deep sequencing of viral inocula, replicating viruses from infected animals, and unknown pathogens from sick animals. We will continue sequencing virus stocks used for in vivo macaque challenges as well as viruses from infected animals. We will also develop a specific assay to detect antiretroviral drug resistance in SIV. Moreover, we will implement unbiased pathogen detection to rapidly identify infectious diseases that threaten NHP colonies and their caretakers. We plan to continue offering fee-for-service pathogen sequencing services in the coming year. The sequencing method will vary, depending on the goals of the client. We have also been adapting the short amplicon sequencing method to SIV, so we hope to incorporate that assay in our pipeline this year, as well. We cannot predict the number and types of samples we will sequence, but we anticipate continued steady business and research progress, as we have made in the past year.

Specific Aim 4: Establish genomic profiling for rhesus macaques, cynomolgus macaques, and common marmosets. We anticipate genomic profiling will be available on a fee-for-service basis at a cost of less than $1,000 per animal. With continued decreases in the sequencing costs associated with MES analysis, we plan to expand our genetic characterization the WNPRC breeding colony with this assay. We will complete genometyping assays for the remaining 57 WNPRC rhesus progeny born during the final three quarters of 2018 as well as new rhesus offspring who are born during the first quarter of 2019. We also plan to expand genometyping to include the majority of active Indian rhesus sires and dams (MES datasets have already been collected for ~48 WNPRC sires and dams). These MES studies will also be extended to all 59 Mauritian cynomolgus macaque breeders and progeny in our MHC-directed breeding groups that were transferred to WNPRC in the fall of 2018 from the Bioculture breeding facility in Florida.

We anticipate offering fee-for-service genomic profiling in the next year as well. Initially we anticipate that this profiling will consist of generation of MHC and TRIM5 genometyping reporting analogous to the current Illumina MiSeq genotyping reports, as well as full exome sequence data from each sample. Additional analysis of specific immune gene targets beyond the MHC would be available to be performed by our group on a sample-by-sample basis, charged at bioinformatician processing hourly rates. Requests for additional processing would also inform high-value targets for analysis pipeline development and eventual addition to the standard reporting.

There are several additional concerns with our MES assays in their current format. One set of issues revolves around the increased turnaround-times when gDNA samples must be shipped and processed off-site at the Baylor Human Genome Sequencing Center or another sequencing facility. Likewise, investigators with tight budgets are still reluctant to pay higher costs associated with collecting data from the entire exome when they believe that they only need MHC genotypes to get their studies published. Another concern it that our current Nimblegen SeqCap probe design does not recover a sufficient number of sequences reads to perform KIR genotyping for rhesus macaque MES datasets.

As a more targeted alternative to our existing MES workflow, we have designed a new custom panel of capture probes that are restricted to MHC class I and KIR genes initially rather than the entire exome. For these pilot studies we have decided to utilize reagents from Integrated DNA Technologies (IDT) that are marketed under the trade name xGEN Lockdown probes. Overall this initial MHC/KIR probe design spans a **total target size of 13,663 bp.** Since this target size is >3000-fold less that our current MES probe design of ~48 Mb, the hope is that we can generate enough sequence coverage for bar-coded sample pools in-house with our MiSeq instrument. This option will provide flexibility in scheduling that isn't possible for our current MES protocol where we must send samples out to a core facility like Baylor for analysis on an Illumina NovaSeq instrument. During the year we anticipate performing feasibility studies with this pool of xGEN target capture probes and multiplexed library pools from Mauritian cynos and Indian-origin rhesus samples from WNPRC that have been already genotyped by independent methods.

IMMUNOLOGY SERVICES

Unit Head: Redacted by agreement Ph.D.

GOALS AND ACCOMPLISHMENTS

Goals

Immunology Services (IS) at WNPRC has two primary functions: (1) providing support to NHP studies that address immunological questions, or use certain immunological methods and (2) developing novel immune-based assays that improve the use of nonhuman primate models. The unit specializes in ELISPOT-, and flow-cytometry-based analytical techniques. IS performs assays using freshly processed samples to avoid artifacts introduced by cryostorage or shipping. IS thus enables the WNPRC to function as a national and international resource for *in vivo* experiments. Principal investigators can conduct their NHP studies with the assistance of IS regardless of their geographical location.

Specific Aim 1: To operate a state-of-the-art flow cytometry facility and to develop novel flow cytometry-based analytical methods. We will upgrade our BL-3 level cell sorter and purchase a new generation, extra-sensitive desktop analyzer. We will develop multicolor flow cytometry staining panels as collaborating investigators request. We anticipate developing 4-6 novel staining panels per year.

Specific Aim 2: To define and measure antigen-specific cellular immune responses using ELISpot-based assays. IS routinely performs IFN-γ ELISPOT assays to quantify pathogen-specific immune responses. The majority of these tests are supporting SIV vaccination projects. As a resource development we will define minimal optimal epitopes of rhesus cytomegalovirus (rhCMV) IE1 and pp65-2 proteins restricted by the most frequent rhesus macaque MHC-I alleles. These epitopes will provide a set of critical tools for studies that investigate the effect of various health conditions (e.g. stress, metabolic diseases, transplantation etc.) on cellular immune responses.

Specific Aim 3: To measure antiviral antibody responses in NHP models of viral diseases. We will quantify and isolate antibody-producing plasmablast cells from blood, or bone marrow. We will also measure antibodies in plasma, or serum capable of binding viral antigens, neutralizing viral infectivity, and directing the elimination of virus-infected cells by antibody-dependent cell-mediated cytotoxicity (ADCC).

Specific Aim 4: To support vaccination and pathogenesis studies using NHP models. We will assemble appropriate animal cohorts selecting animals with desired genetic markers in close collaboration with Genetics Services (MHC and FcγR haplotype). We will screen for pre-existing antigen-specific immune responses, coordinate vaccination and sample collection schedules with the Scientific Protocol Implementation Unit at WNPRC, and viral load measurements with Virology Services. We will perform various immune assays (cellular phenotyping, T cell, and NK function, antigen-specific antibody level quantification) as requested by the individual investigators. Based on current and anticipated funding, we will support 8-9 studies per year.

The specific aims proposed above include expanding our existing facility, defining new reagents, and introducing innovative assays. Our team, together with other service units of the primate center, is uniquely qualified to provide comprehensive support for a broad range of investigators that are interested in performing NHP studies.

Accomplishments

Specific Aim 1:
We perform high-resolution phenotype and functional analysis of T cells, NK cell subsets, dendritic cells, monocyte/macrophage cells, and neutrophil leukocytes. Our clientele includes a broad range of investigators using nonhuman primates to study infectious diseases, or solid organ transplantation. In the reporting period, we developed four new multicolor flow cytometry staining panels and performed 3955 flow cytometry assays. We published an original peer-reviewed paper outlining a method to identify cell surface markers that delineate

the phenotypes of neutrophil progenitors in rhesus macaque bone marrow. We have offered this flow cytometry-based method as a routine service, and it is now being used by our collaborators in a kidney transplantation study.

Specific Aim 2:
IS performed 240 IFN-γ ELISPOT assays to quantify pathogen-specific immune responses using 15-mers covering the entire length of the phosphoprotein 65-2 (pp65-2) and immediate early protein 1 (IE1) of rhesus cytomegalovirus (rhCMV). We identified two putative epitopes in the IE1 protein. One of the epitopes is restricted by the Mamu-A*02 MHC-I allele. The Mamu-A*02 allele is present in approximately 20-25% frequency in our animal colony.

Specific Aim 3:
Measurement of antibody-dependent cell-mediated cytotoxicity (ADCC): we developed a novel assay for measuring the ability of antibodies to kill SIV-infected cells by ADCC. A significant advantage of this approach is that ADCC responses are measured against virus-infected cells expressing native conformations of the viral envelope. IS performed 65 ADCC assays for two NIH-funded studies during the reporting period.

IS performed ADCC assays for extramural investigators, including testing several dozen plasma samples from Redacted by agreement University of Manitoba, and Redacted by agreement University of Miami, for ADCC responses to SIV-infected cells.

Measurement of antigen-specific neutralization: we improved a novel, flow cytometry-based method to quantify Zika neutralizing antibodies in serum samples of rhesus macaques in collaboration with the laboratory of Dr. Theodore Pierson of NIAID.

Although these activities are newly established in the repertoire of Immunology Services, we have implemented them successfully to support several laboratories.

Specific Aim 4:
NHP models represent invaluable intermediate steps in translating vaccination concepts that were successfully tested in small animal models. We have accumulated ample experience with different vaccination platforms and challenge models. Our expertise puts us in a central role to guide vaccination experiments, in addition to performing study-related immune assays. We participated in 22 vaccination or pathogenesis NHP studies during the reporting period. We coordinated vaccination and sample collection with the Scientific Protocol Implementation Unit at WNPRC, and viral load measurements with Virology Services or with Dr. Jeffrey Lifson (Frederick National Laboratory for Cancer Research) according to the demand of the collaborating investigator. We processed >5,300 blood samples, and performed > 1,600 flow cytometry assays as part of these studies. As examples, we highlight the following studies:

We performed a series of passive antibody transfer studies for Redacted by agreement (The Scripps Institute) to assess the extraordinary neutralizing capability of antibody PGT121 and its Fc domain mutated variant against mucosal SHIV162P3 challenges.

Redacted by agreement investigated the efficacy of various novel vaccination platforms with our support using a repeated low-dose SIVmac239 challenge-model in MHC-defined rhesus macaques. In addition to recombinant Ad5, Vaccinia, and VSV-based vaccine vectors, Redacted by also tested whether persistent infection with SIVmac239 gene-expressing recombinant γ herpes viruses (rhesus rhadinovirus) would prevent SIVmac239 infection.

Redacted by agreement (University of Miami) tested the protective and therapeutic efficacy of several rAAV constructs expressing HIV-1-specific broadly neutralizing antibodies using a low dose SHIV-AD8 challenge model. Furthermore, he studied the protection provided by various SIVmac239 gene-expressing RRV vaccines against repeated low-dose SIVmac239 challenges. We quantified SIVmac239-specific T cells by performing tetramer staining in these studies.

For Redacted by agreement (The Scripps Institute-Florida), we tested the therapeutic and protective efficacy of a

recombinant AAV vaccine expressing eCD4-Ig, a fusion of CD4-Ig with a small CCR5-mimetic sulfopeptide.

Redacted by agreement (University of Arizona) and Redacted by agreement (University of Minnesota) were the first to show that follicular regulatory T cells expand and impair the function of follicular T helper cells in SIV Infection. As part of an ongoing collaboration, we quantified the cell-associated viral burden in sorted cell populations.

For Redacted by agreement (University of Miami), we performed a vaccination experiment to determine if CTLA-4 blockade during vaccine priming can increase the breadth of vaccine-induced T-cell responses against SIV.

FUTURE GOALS

Specific Aim 1: To operate a state-of-the-art flow cytometry facility and to develop novel flow cytometry-based analytical methods. We will continue developing new multicolor flow cytometry methods to support our collaborating scientists. Based on previous demand, we anticipate developing 4-6 new staining panels. The majority of these assays will be used in infectious disease studies, but there is demand for our expertise in transplantation studies, also. We will continue our efforts to secure funding for a new, cutting-edge flow cytometer. We will introduce a new flow cytometry assay that is based on measuring mRNA intracellularly. Our first targets are the NKG2A and NKG2C RNAs. NKG2A is an inhibitory receptor while NKG2C is an activating receptor on NK cells and CD8 T cells. There is no available antibody that recognizes these molecules separately. Therefore, an assay that measures their respective mRNAs will facilitate both infectious and transplantation studies. This novel RNA-based flow cytometry assay has been established in Dr. Keith Reeves' laboratory at Harvard University. He is supporting our efforts to introduce the assay at our location.

Specific Aim 2: To define and measure antigen-specific cellular immune responses using ELISpot-based assays. We will continue screening for new rhCMV-specific epitopes defined by the Mamu-B*08, B*17 and A*01 MHC-I alleles.

Specific Aim 3: To measure antiviral antibody responses in NHP models of viral diseases. Our goal for the next year is to attract more collaborators that will use the ADCC assay. We will continue advertising this new activity on different forums, including scientific meetings, core managers' meetings, a new white paper linked to our website, and personal communications.

Specific Aim 4: To support vaccination and pathogenesis studies using NHP models. We will continue working with Genetics Services, the Scientific Protocol Implementation Unit, and Virology Services to support various NHP studies. We will give higher priority to NIH-funded research projects.

INFORMATICS AND DATA SERVICES (IDS)

Unit Head: Redacted by agreement Ph.D.

GOALS AND ACCOMPLISHMENTS

Goals

The main goal of the Informatics and Data Services (IDS) unit is to support the operation of the Wisconsin National Primate Research Center (WNPRC) by providing nonhuman primate (NHP) health information, managing procedures and protocols of research done on these animals. The unit also supports tracking compliance and training records for all staff and associated researchers who work with NHPs housed at the center. This includes working closely with the other units at WNPRC to gather needs and deliver improvements to how users search, request, and interact with animal health and research information.

The IDS unit has an additional long-term goal of providing and improving methods for PIs and research staff associated with the center to store and link lifelong health and clinical information with their research data and aid in the analysis and dissemination of their results.

The unit accomplishes these goals by maintaining and improving the Electronic Health Record (EHR) system that stores animal health and research information, which is accessed by an average of more than 183 users per day excluding weekends. The EHR system is an extension of LabKey Server, an open-source platform designed for securely sharing and storing biomedical research data. The IDS unit evaluates updates to the LabKey Server installation and the underlying database management system and updates the system whenever new features are needed. The IDS unit also works closely with the Information Technology and System Services (ITSS) unit to maintain system reliability and availability, secure daily backups, and test new technologies to help in the development and deployment of the system. Additionally, the unit advances these goals via the following specific aims:

Specific Aim 1: Develop and extend the EHR platform. The IDS unit is actively engaged in in-house development of the EHR system. The unit maintains a support contract with LabKey software company, which provides the training and skills needed to develop additional features to this open source system. Additionally, the unit is overseeing a development contract to modify a finance and billing module originally developed at the Oregon National Primate Research Center (ONPRC).

Specific Aim 2: Improve and enhance the user experience. The IDS unit meets with end-users on a regular basis to identify need and requirements from the different units at the WNPRC.

Specific Aim 3: Increase data quality by reducing manual data entry.

Specific Aim 4: Provide EHR-powered data management and sharing capabilities to WNPRC investigators. The IDS unit, in collaboration with the ITSS unit, develops tools to support investigator needs.

Accomplishments

Specific Aim 1:
The requirements and needs for the EHR system continue to increase. The IDS unit hired a new FTE so that the unit has two developers and the unit's manager, all of whom contribute to the source code. The EHR production system was updated to LabKey version 17.2 in 2018 and testing has begun for LabKey version 18.3, the version against which the financial module is being developed. The new version uses modules from both SVN and GitHub that provide all the capabilities needed by the center staff.

The unit completely migrated to use GitHub as the version control system to keep track of custom modules developed in-house. The unit maintains public (https://github.com/WNPRC-EHR-Services) and private repositories. During the last reporting period, the unit had more than 500 changes made to the source code.

Because we encourage other primate centers to review, comment, and use the code developed by the IDS unit, the source code for all the custom modules is publicly available.

The IDS unit continues to oversee the development of the financial module by the LabKey Software company. At the beginning of 2018, the initial campus contract with LabKey ran out of funds, and due to UW-Madison's policies, a new RFP needed to be submitted and an open bid process conducted before the work on the financial module could be completed. This delayed the project.

Specific Aim 2:
During the last reporting cycle, the EHR system was down for a total of three times, two of which were unscheduled problems with the network or server. For these two outages, the ITSS unit and UW-Madison's IT department were able to bring the server backup promptly after identifying the problems. The IDS unit maintains a log of all scheduled and unscheduled downtimes that are longer than five minutes. Because the system is used at all hours of the day, a reliable system is essential to ensuring a positive user experience.

The necropsy request and scheduling system developed and deployed during the last reporting cycle had some performance problems. The IDS unit worked with LabKey to improve the performance of the necropsy system. Now, staff can save and update necropsies in real time without needing to wait for the web page to reload because the system does all the required validations on the server side before the data is saved into the database.

The IDS unit deployed a food deprive system to facilitate scheduling the start and completion of food deprives. Since the system went live at the end of June 2018, there were more than 1200 successfully completed food deprives and only one error.

Specific Aim 3:
The IDS unit continues working on the network connected scale project. It was determined that the original prototype would not work correctly behind the barrier when used on a regular basis with animals. It was also decided that the system should be developed using an Arduino microcontroller connected to an iPad, rather than using a RasberryPi device, which was the original prototype. The ITSS unit at the center already maintains several iOS devices. The ITSS unit has plans to install server-side software to manage all iOS devices used by center's staff, so it is logical and cost-effective to use iOS-enabled iPads for the scale project. Adding ten more devices to this management software will not add overhead to the ITSS unit's overall plans to centrally manage these devices.

The iPad for this project will have a rugged enclosure to protect it from damage when used behind the barrier. Additionally, all the other components for this project will be housed on a metal enclosure added to the digital scales. The IDS unit has purchased the components for this project and started developing the code needed to enable them to communicate with each other.

Specific Aim 4:
The IDS unit worked with the ITSS unit to migrate the all the EHR servers to the virtual platform hosted by the University's IT department. During this reporting period, senior management at WNPRC approved addition of another virtual server to facilitate research data sharing with researchers outside the center. The configuration of this new server will be modified as needed based on data sharing needs of center PIs. Data stored on our production server will be copied over to the new virtual server to accomplish the proposed data sharing plans for two research projects.

FUTURE GOALS

The IDS unit plans to accomplish the following goals during the next reporting cycle:

1. Update the EHR system to LabKey version 18.3, which will include the development of the financial and billing module done by LabKey. This will be done before July 1, 2019.
2. Deploy a working prototype of the network scale project and collect feedback from end-users. The code will be written using the Swift programming language and will be maintained in-house.

3. Finish developing the pregnancy and breeding project. This will allow veterinary, colony management and research staff to better track pregnancies in the colony.
4. Extend the use of the PrimateID module to allow users to add the PrimateID column to data exported from the EHR system.
5. Currently, data entry updates into the system use ExtJS version 4, and the IDS unit plans to migrate to a more modern UI library. The unit will investigate alternatives that will work well with the LabKey system. One of the more modern alternatives the unit plans to use is React JS, alongside other responsive frameworks, which will allow for data entry on mobile devices.
6. Connecting other devices to enter data directly into the EHR system will be a major focus on the next reporting cycle. The IDS unit is looking into connecting glucometers to keep track of sugar levels on aging animals.
7. Setup a second instance of the LabKey server to store and share research data. The unit plans to provide this as a service for any PI or research group associated with the center. This new instance will be available to investigators to view and download research data collected from NHPs housed at the center. To enhance data tracking, PrimateIDs will identify NHPs in these data.

VIROLOGY SERVICES

Unit Head: Redacted by agreement Ph.D.

GOALS AND ACCOMPLISHMENTS

Goals

The primary role of Virology Services is to facilitate and provide support for virological research in non-human primates. To fulfill this role, Virology Services offers an array of highly sensitive diagnostic assays to detect and quantify viruses; supplies critical reagents and services to the virology research community; and develops novel assays and techniques to enhance virological research. Virology Services offers assays for quantifying RNA and DNA from many viruses; historically the most requested assay has been the SIV gag RNA assay for monitoring plasma viral loads. Virology Services also produces and characterizes virus stocks (including SIVs, SHIVs, influenza) for use in both in vivo and in vitro experiments. Finally, Virology Services is continually developing novel assays to meet different and evolving needs of the field. Anticipating increased need to support HIV "cure" studies in NHP, a main focus for this activity currently is developing assays for measuring the SIV/ SHIV latent reservoir. We are also working to develop assays to support research into the ongoing Zika virus outbreak.

Specific Aim 1: To provide validated molecular diagnostic assays for viruses as fee-for-service. We will continue to provide validated molecular diagnostic assays for viruses in support of studies of vaccines, treatments, and viral pathogenesis. We anticipate that quantitative (Q)RT-PCR for SIV and Zika virus RNA in plasma will continue to be our most-requested service. But we also anticipate growing demand for other assays and modalities we have recently developed, including QRT-PCR for other emerging and re-emerging viruses, such as influenza, dengue, arboviruses and hepaciviruses.

Specific Aim 2: To provide characterized stocks of viruses for in vitro and in vivo use as fee-for-service. We will continue to produce well-characterized virus stocks for use in challenge studies, but we will move to a "pay-as-you-go" model for investigators requesting in-vivo-titrated viruses. That is, we will continue to produce high-titer stocks of SIV, influenza, and other viruses in tissue culture, and will offer vials of these viruses to users on a fee-for-service basis, but we will not undertake an in-vivo titration of any virus "on spec;" rather, we will partner with users to perform titrations of specific virus stock according to their needs on a fee-for-service basis.

Specific Aim 3: To develop new culture methods and molecular diagnostics to facilitate virological research in nonhuman primates, to be deployed as future services. We are continually asked by users to develop, or support the development of, novel assays. We will therefore continue to develop and validate Q(RT)-PCR and ddPCR assays against novel targets in the new P51 cycle. We will partner with users to define these targets, but anticipated new targets include the vaccine vectors AAV, RRV, and CMV as well as the emerging Zika virus (ZIKV) and re-emerging chikungunya virus (CHIKV) and dengue virus (DENV).

Specific Aim 4: To develop new methods for quantifying the latent SIV/SHIV reservoir. As HIV/SIV research shifts to focus on "cure" strategies, there will be increasing needs for assays to quantify the latent reservoir. Currently available assays are difficult, expensive in terms of both personnel time and supplies, and are poorly reproducible. We will therefore develop novel approaches to measuring the latent reservoir that increase reproducibility and decrease cost. As first steps, we are developing novel "readouts" for the quantitative viral outgrowth assay (QVOA) that could reduce costs by over 25%. With support from a new UW-Madison pilot, we will also partner with UW-Madison colleagues in biomedical engineering to use microfluidics approaches to reduce requirements for reservoir sample sizes and user manipulations.

Accomplishments

Specific Aim 1:

During the reporting period from January 1, 2018 to December 31, 2018 Virology Services performed over 4600 viral quantification assays. This number includes assays to quantify viral RNA from SIVs, Zika virus, influenza and dengue. During this reporting period demand for the Zika virus assay surpassed that for SIV, accounting for about 60% of the samples tested. The Zika virus viral load assays supported 4 publications during the reporting period:

Aliota MT, Dudley DM, Newman CM, Weger-Lucarelli J, Stewart LM, Koenig MR, Breitbach ME, Weiler AM, Semler MR, Barry GL, Zarbock KR, Haj AK, Moriarty RV, Mohns MS, Mohr EL, Venturi V, Schultz-Darken N, Peterson E, Newton W, Schotzko ML, Simmons HA, Mejia A, Hayes JM, Capuano S, Davenport MP, Friedrich TC, Ebel GD, O'Connor SL and O'Connor DH. 2018. Molecularly barcoded Zika virus libraries to probe in vivo evolutionary dynamics. *PLoS Pathog* 14: e1006964. PMC5891079

Dudley DM, Van Rompay KK, Coffey LL, Ardeshir A, Keesler RI, Bliss-Moreau E, Grigsby PL, Steinbach RJ, Hirsch AJ, MacAllister RP, Pecoraro HL, Colgin LM, Hodge T, Streblow DN, Tardif S, Patterson JL, Tamhankar M, Seferovic M, Aagaard KM, Martín CS, Chiu CY, Panganiban AT, Veazey RS, Wang X, Maness NJ, Gilbert MH, Bohm RP, Adams Waldorf KM, Gale M, Rajagopal L, Hotchkiss CE, Mohr EL, Capuano SV, Simmons HA, Mejia A, Friedrich TC, Golos TG and O'Connor DH. 2018. Miscarriage and stillbirth following maternal Zika virus infection in nonhuman primates. *Nat Med* 24: 1104-1107. PMC6082723

Mohr EL, Block LN, Newman CM, Stewart LM, Koenig M, Semler M, Breitbach ME, Teixeira LBC, Zeng X, Weiler AM, Barry GL, Thoong TH, Wiepz GJ, Dudley DM, Simmons HA, Mejia A, Morgan TK, Salamat MS, Kohn S, Antony KM, Aliota MT, Mohns MS, Hayes JM, Schultz-Darken N, Schotzko ML, Peterson E, Capuano S, Osorio JE, O'Connor SL, Friedrich TC, O'Connor DH and Golos TG. 2018. Ocular and uteroplacental pathology in a macaque pregnancy with congenital Zika virus infection. *PLoS One* 13: e0190617. PMC5790226

Weger-Lucarelli J, Garcia SM, Rückert C, Byas A, O'Connor SL, Aliota MT, Friedrich TC, O'Connor DH and Ebel GD. 2018. Using barcoded Zika virus to assess virus population structure in vitro and in Aedes aegypti mosquitoes. *Virology* 521: 138-148. PMC6309320

While SIV demand continues to be strong, it only accounted for close to 40% of total samples tested. The SIV virus viral load assays supported three publications during the reporting period:

Rodgers MA, Ameel C, Ellis-Connell AL, Balgeman AJ, Maiello P, Barry GL, Friedrich TC, Klein E, O'Connor SL and Scanga CA. 2018. Preexisting Simian Immunodeficiency Virus Infection Increases Susceptibility to Tuberculosis in Mauritian Cynomolgus Macaques. *Infect Immun* 86: PMC6246917

Schouest B, Weiler AM, Janaka SK, Myers TA, Das A, Wilder SC, Furlott J, Baddoo M, Flemington EK, Rakasz EG, Evans DT, Friedrich TC and Maness NJ. 2018. Maintenance of AP-2-Dependent Functional Activities of Nef Restricts Pathways of Immune Escape from CD8 T Lymphocyte Responses. *J Virol* 92: PMC5809740

Sutton MS, Ellis-Connell A, Moriarty RV, Balgeman AJ, Gellerup D, Barry G, Weiler AM, Friedrich TC and O'Connor SL. 2018. Acute-Phase CD4^{+}T Cell Responses Targeting Invariant Viral Regions Are Associated with Control of Live Attenuated Simian Immunodeficiency Virus. *J Virol* 92: PMC6189504

Previously, the vast majority of samples submitted for viral quantification were plasma, serum, urine, or other types of fluids. Over the past 2 years we experienced increasing demand for viral quantification from tissue samples for both the Zika and SIV assays. In response to this demand we developed a method for isolating RNA from tissue samples, partnering with Redacted by agreement at Leidos, who developed sensitive methods for recovering SIV RNA from tissues. Over the past year we have focused efforts on optimizing this protocol to increase the mass of tissue we can test and more importantly to increase the yield of RNA and lower the limit of detection of the assay. We now have a more sensitive method that has successfully been used to test hundreds of samples for either Zika virus or SIV.

In order to ensure the accuracy of our data we routinely perform sample exchanges with outside labs. During the past year we performed an exchange of SIV samples with the Molecular Virology core at OHSU. We found good correlation between results measured by the two labs. We also participated in a multicenter comparison of Zika RNA assays coordinated by Redacted by agreement at the Blood Systems Research Institute and UC-Davis.

Virology Services is continually looking to improve our assays. We are currently working to lower the limit of detection for our plasma viral load assay. To accomplish this goal, we have developed new reaction conditions for our QRT-PCR assay that will allow for testing a greater amount of template RNA per reaction. An increased workload over the past year has prevented us from fully testing these new conditions, but we continue to optimize these conditions so we can implement them in the next year.

Specific Aim 2:
Between January 1, 2018 and December 31, 2018, Virology Services provided 237 vials of virus to users on a per-vial basis. The bulk of this was a single stock of SIVmac239 provided to a client for in vivo studies. Use of this stock in vivo has led to several publications during this reporting period (Ellis-Connell et al., 2018) including one about the role of pre-existing SIV infection in tuberculosis (Rogers et al., 2018). Additionally, we provided SIVmac239 stocks to clients for in vitro studies, as well as a few vials of SHIVsf162p3 and SIVmac316E.

Virology Services also offers a service to provide virus stocks as requested by users. In this case, users contract Virology Services to produce a stock of a specific virus. In June of 2018 Virology Services provided such a stock of a mutant SIVmac239 virus for Redacted by agreement lab at the University of Wisconsin. This virus stock is currently being used for an in vivo study at the WNPRC.

Specific Aim 3:
Over the previous year, Virology Services developed QRT-PCR assays to quantify dengue viruses from plasma of infected macaques. We introduced assays for DENV-1 and DENV-2 as fee-for-service in the end of 2017. During the current reporting period Virology Services performed about 70 of these DENV-2 viral quantification assays for a study investigating the interaction of dengue virus and Zika virus in pregnant macaques; Unpublished

Virology Services was recently approached by Redacted by agreement, who wants to measure cytomegalovirus (CMV) in plasma from rhesus macaques involved in kidney transplantation studies as part of a U01-funded national consortium aimed at developing novel methods to induce immune tolerance of transplanted tissues. Not only does Redacted by agreement have an ongoing need for CMV testing, but there may be additional interest in CMV testing offered by Virology Services. Indeed, Virology Services has provided consultation on developing CMV molecular diagnostic assays to the entire NIH-funded transplant consortium, which involves investigators at multiple sites nationwide. The consortium's goal is to standardize CMV viral load testing in macaques across the consortium; Virology Services will lead this effort along with investigators at Columbia University. We plan to establish a single optimized assay protocol by March, at which point we will move forward with establishing the assay as fee-for service, to be deployed by the summer of 2019.

Specific Aim 4:
A major goal for Virology Services over the past few years has been to offer the quantitative viral outgrowth assay (QVOA) as fee-for-service. This assay is considered the "gold standard" for HIV/SIV cure studies, and it is therefore imperative that we offer this service to the SIV field. This assay is both difficult to perform and costly in time and resources. Though we continue to work to optimize the assay and bring the cost down, we are now offering QVOA as a fee-for-service assay. At the end of 2018 we received our first set of samples for fee-for-service QVOA testing from an investigator outside of WNPRC This was a large set of samples; testing is currently ongoing.

In addition to offering QVOA to measure the latent reservoir of virus, Virology Services has been offering assays to measure cell-associated SIV RNA and DNA. While these assays do not specifically measure replication-competent virus as does the QVOA, they offer insights into the number of infected cells in a population. Because these assays are more cost effective and can be used to answer different questions than the QVOA, they appeal to many clients. We have been experiencing an increase in interest in both of these

assays. In 2018, we performed 27 cell-associated SIV RNA quantifications and 66 SIV DNA tests. We already have 16 samples to be tested for both cell-associated SIV RNA and DNA in 2019.

FUTURE GOALS

Specific Aim 1: To provide validated molecular diagnostic assays for viruses as fee-for-service.
During the next reporting period Virology Services will continue to perform fee-for-service molecular diagnostic viral load assays for SIV, Zika virus, dengue virus, influenza and possibly pegiviruses. Because of a P01 grant recently awarded to a team of investigators at UW, we anticipate the majority of demand to be for Zika virus assays, though we expect SIV demand to remain high. In order to ensure that our assays are reliable and accurate to the highest standard and to validate our results, we routinely perform sample exchanges with other laboratories performing the same assays. We are currently in the midst of organizing a sample exchange with the Virology Core of ONPRC.

Virology Services is always seeking to improve on our assays. For this reason, we have been working to lower the limit of detection of our standard viral load assay. We have already developed a protocol and begun testing. Using this protocol, we can test a larger amount of sample RNA, thus increasing the sensitivity of the assays. Additionally, this new protocol will lower the cost of the assay. In 2019 we will finish this testing and rigorously define the limit of detection of the assay begin using it for our molecular diagnostic tests.

Specific Aim 2: To provide characterized stocks of viruses for in vitro and in vivo use as fee-for-service.
Virology Services will continue to provide high-titer, characterized stocks of SIV, SHIVs and Zika virus for both in vitro and in vivo use to investigators requesting virus. Because we recently sold a large portion of our 'for-in-vivo-use' SIV stock, we will consider producing a new stock of SIVmac239 suitable for in vivo use. Before undertaking this endeavor, we will consult with users to gauge how much interest exists in such a virus stock.

Virology Services is currently under contract to produce a custom, small-scale SHIV stock for Redacted by agreement Redacted by agreement lab. This stock will be produced in the end of January and will be used for in vivo studies being conducted at the WNPRC.

Specific Aim 3: To develop new culture methods and molecular diagnostics to facilitate virological research in nonhuman primates, to be deployed as future services.
In response to a user request, Virology Services is in the midst of developing and validating an assay to measure CMV from plasma/serum from rhesus macaques. We are currently working with a consortium to choose a universal CMV QPCR assay, which we will optimize and deploy as fee-for-service by the end of the first half of this year.

In addition to offering an assay for rhesus CMV, Virology Services will entertain other user requests for new molecular diagnostic assays. For example, an investigator studying primate pegiviruses has expressed interest in developing assays to measure viral loads of several different pegiviruses in plasma from non-human primates.

Specific Aim 4: To develop new methods for quantifying the latent SIV/SHIV reservoir.
Virology Services is now offering several assays as fee-for-service for measuring the latent reservoir of SIV, including QVOA and measuring cell-associated SIV RNA and DNA. We will continue to work to improve these assays (in terms of increasing sensitivity and bringing down cost). Additionally, we will also advertise our services to bring in new clients to take advantage of these assays.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Associate Director	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	EFFORT			8,840.00	3,757.00	12,597.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**12,597.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**12,597.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	10,372.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**10,372.00**

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**22,969.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	22,969.00	8,499.00
		Total Indirect Costs	**8,499.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**31,468.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Assay Services Unit (Scientific-Units-002)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1: Maintain an up-to-date, efficient, cost-effective Assay Service for the WNPRC, the UW-Madison, and investigators from universities nationally and internationally. The unit will continue to offer our current assays and support innovative research for nonhuman primates (NHPs), translational and human research. Our current lab members focus on specialized areas that can address the research needs of our clients. We continue to improve upon the methods available within the service and maintain our quality assurances.

Specific Aim 2: Develop new methods for analyses of steroids, proteins, peptides and other biomarkers for endocrine, neural, and metabolic analysis. The unit will continue to develop new methods, provide consultation when needed, and maintain our high throughput for our current long-term and anticipated new clients. New planned developments include C-peptide for marmosets, a metabolic panel for insulin, leptin, ghrelin and adiponectin specific for marmosets and one specific for rhesus macaques using methodologies for triple quadrupole mass spectrometer.

Specific Aim 3: Develop the use of hair as a long-term assessment of steroids and Vitamin D. The use of hair steroids to assess long-term glucocorticoid function noninvasively is in high demand both nationally and internationally for both human and nonhuman primate studies of stress effects on health. However, no standard methodology has been established and validations assessing what steroid metabolites are found in hair are needed. We plan to fully validate steroid metabolites in hair using the rhesus monkey as the model. We have adapted our multisteroid LC/MS/MS method for the measurement of multiple steroids in hair (Kapoor et al., 2014, 2016) and plan to establish these methods for a variety of research purposes.

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: B.2 Accomplishments_Assay.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: Maintain an up-to-date, efficient, cost-effective Assay Service for the WNPRC, the UW-Madison, and investigators from universities nationally and internationally.

As both older (RIA and EIA) and newer (EIA and LC/MS/MS) methods are in demand, we will continue to use them per client requests. Our LC/MS/MS methods are as much in demand as our more classical methods.

Specific Aim 2: Develop new methods for analyses of steroids, proteins, peptides and other biomarkers for endocrine, neural, and metabolic analysis.

We plan to do more method refinement to improve our existing assay methodologies throughout the next year. For example, we will be working on adapting some of our RIA methods to EIA methods to reduce the amount of radioactivity used in the labs. We anticipate new methods being developed and new assay kits being validated for future projects. We will be working on measuring marmoset insulin using LC/MS/MS which will be Assay Services' first peptide method by LC/MS/MS. We expect to use LC/MS/MS for peptide measurements more frequently in the future.

Specific Aim 3: Develop the use of hair as a long-term assessment of steroids and Vitamin D.

We will continue to conduct validation studies in hair for other reproductive and adrenal steroids and vitamin D incorporation into hair. These studies are necessary to ensure that the correct steroids are being measured, to determine the time period of circulating hormone in the body that is reflected by the hair hormone level, and to understand the variability in hair growth and its influences on steroid levels in hair. Publication of the validation studies from the other steroid hormones is anticipated. More specific validations of hair cortisol are planned, including identification of unknown cortisol metabolites in hair.

ASSAY SERVICES UNIT

Unit Head: Redacted by agreement Ph.D.

Accomplishments

Specific Aim 1:

1. Under this aim we ran 39,600 samples in 2018.
   The samples were run by radioimmunoassay (RIA)-based assays, enzyme immunoassay (EIA)-based assays and liquid chromatography (LC)-based methods.
   Number of samples:
   EIA = 15,331
   RIA = 17,392
   LC = 6873 samples (this number includes multiple analytes measured in each sample as LC-based assays can be run in panels with multiple analytes measured simultaneously)

   We developed a vitamin D metabolic panel that was used to examine wild, native baboons in Africa to captive baboons to determine appropriate levels and to determine the metabolic process. This paper has now been published: **Ziegler TE**, Kapoor A, Binkley N, Rice KS, Rogers J, Jolly CJ, Phillips-Conroy J (2018). Comparison of Vitamin D metabolites in Wild and Captive Baboons. American Journal of Primatology, 2018 Dec;80(12):e22935. doi: 10.1002/ajp.22935. A project using the Vitamin D panel for measuring serum vitamin D in common marmosets is in progress.

2. We served 30 different clients. Most were charged for several months during this time.
3. We made progress on improving sample preparation, modernization and efficiency for existing methods.
   3.1. During the past year, we completed transitioning all data, methods, validations and quality-control documents to cloud-based storage. All Assay Services staff have access to these documents to review as needed. These developments were made in consultation with Research Data Services at UW-Madison.
   3.2. We initiated cross-training of staff to ensure that more than one person is able to perform each type of assay.
   3.3. We established a database for antibodies and tagged hormones used in EIAs and RIAs, respectively, to ensure all reagents are available for the assays.
   3.4. We established a new extraction method for our multisteroid analyses by LC/MS/MS to limit staff exposure to volatile chemicals while enhancing efficiency.
   3.5. We modernized analyses of EIA data.
   3.6. We identified an antibody for the estradiol EIA that improves specificity.
   3.7. We obtained a new high-performance liquid chromatography electrochemical detector (HPLC-ECD) to measure catecholamines. We optimized our previous method and greatly enhanced the measurability for the method.
4. The Oregon National Primate Research Center Endocrine Technology Lab and our Assay Services Lab are working together on LC/MS/MS-based measurements to ensure that steroid hormone values will be consistent between the two labs for rhesus macaque studies. In conjunction with external quality control programs, this inter-lab round robin will ensure the accuracy of our steroid hormone measurements.
5. The Assay Services website has been updated and further improvements are in progress.

Specific Aim 2:

1. Currently, there is no EIA or RIA assay sensitive enough to measure marmoset insulin. A LC/MS/MS method for marmoset insulin is in development with expected completion in early 2019. Marmoset insulin has been isolated and purified following extraction from marmoset pancreas.
2. We ran many new commercial kits for clients, such as assays on human samples to measure the following:
   Anti-Mullerian Hormone (AMH)
   Luteinizing hormone (LH)
   Follicle-stimulating hormone (FSH)

3. We continue to develop methods for specific projects such as transferring a method for multisteroids excreted during pregnancy in the common marmoset from our single quad mass spec to our triple quad mass spec. This will also allow us to measure the androgens simultaneously with the glucocorticoids and the estrogens that are in much higher amounts in pregnant urine than androgens.
4. We continue development of a new method for free steroids that will allow us to separate free from bound steroids and analyze both in the same sample. Further advances are expected in early 2019.

Specific Aim 3:
The sample preparation step for the hair steroid LC/MS/MS method was improved by extracting intact hair without grinding. The improved protocol saves time and generates a cleaner sample for LC/MS/MS, thereby increasing the efficiency of the analysis.

The radiolabeled study for hair cortisol has been completed, analyzed and published: Kapoor A, Schultz-Darken N, **Ziegler TE**. (2018). Radiolabel validation of cortisol in the hair of rhesus monkeys. Psychoneuroendocrinology, 97:190-195; doi:10.1016/j.psyneuen.2018.07.022. This was the first direct physiological validation of hair cortisol which is becoming a more popular and important biological matrix.

In addition, funding to further validate hair glucocorticoids was obtained (R03, NICHD, Kapoor A & **Ziegler TE**, Validating the use of hair glucocorticoids as a marker of central hypothalamic-pituitary-adrenal axis activity).

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5908

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Unit Head	Institutional Base Salary	EFFORT			53,653.00	17,866.00	71,519.00
2.					PhD	Core Investigator					15,280.00	5,088.00	20,368.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **91,887.00**

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						
1	Undergraduate Students	EFFORT			10,100.00	313.00	10,413.00
	Secretarial/Clerical						
7	Assistant Scientist / Research Specialist				94,306.00	31,404.00	125,710.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**136,123.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**228,010.00**

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

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

ORGANIZATIONAL DUNS*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	37,642.00
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	**37,642.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**265,652.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	265,652.00	98,291.00
		Total Indirect Costs	**98,291.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**363,943.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Informatics and Data Services (Scientific-Units-003)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

The main goal of the Informatics and Data Services (IDS) unit is to support the operation of the Wisconsin National Primate Research Center (WNPRC) by providing nonhuman primate (NHP) health information, managing procedures and protocols of research done on these animals. The unit also supports tracking compliance and training records for all staff and associated researchers who work with NHPs housed at the center. This includes working closely with the other units at WNPRC to gather needs and deliver improvements to how users search, request, and interact with animal health and research information.

The IDS unit has an additional long-term goal of providing and improving methods for PIs and research staff associated with the center to store and link lifelong health and clinical information with their research data and aid in the analysis and dissemination of their results.

The unit accomplishes these goals by maintaining and improving the Electronic Health Record (EHR) system that stores animal health and research information, which is accessed by an average of more than 183 users per day excluding weekends. The EHR system is an extension of LabKey Server, an open-source platform designed for securely sharing and storing biomedical research data. The IDS unit evaluates updates to the LabKey Server installation and the underlying database management system and updates the system whenever new features are needed. The IDS unit also works closely with the Information Technology and System Services (ITSS) unit to maintain system reliability and availability, secure daily backups, and test new technologies to help in the development and deployment of the system. Additionally, the unit advances these goals via the following specific aims:

Specific Aim 1: Develop and extend the EHR platform. The ES unit is actively engaged in in-house development of the EHR system. The unit maintains a support contract with LabKey software company, which provides the training and skills needed to develop additional features to this open source system. Additionally, the unit is overseeing a development contract to modify a finance and billing module originally developed at the Oregon National Primate Research Center (ONPRC).

Specific Aim 2: Improve and enhance the user experience. The ES unit meets with end-users on a regular basis to identify need and requirements from the different units at the WNPRC.

Specific Aim 3: Increase data quality by reducing manual data entry.

Specific Aim 4: Provide EHR-powered data management and sharing capabilities to WNPRC investigators. The ES unit, in collaboration with the ITSS unit, develops tools to support investigator needs.

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: B.2 Accomplishments_IDS.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 IDS unit plans to accomplish the following goals during the next reporting cycle:

1. Update the EHR system to LabKey version 18.3, which will include the development of the financial and billing module done by LabKey. This will be done before July 1, 2019.
2. Deploy a working prototype of the network scale project and collect feedback from end-users. The code will be written using the Swift programming language and will be maintained in-house.
3. Finish developing the pregnancy and breeding project. This will allow veterinary, colony management and research staff to better track pregnancies in the colony.
4. Extend the use of the PrimateID module to allow users to add the PrimateID column to data exported from the EHR system.
5. Currently, data entry updates into the system use ExtJS version 4, and the IDS unit plans to migrate to a more modern UI library. The unit will investigate alternatives that will work well with the LabKey system. One of the more modern alternatives the unit plans to use is React JS, alongside other responsive frameworks, which will allow for data entry on mobile devices.
6. Connecting other devices to enter data directly into the EHR system will be a major focus on the next reporting cycle. The IDS unit is

looking into connecting glucometers to keep track of sugar levels on aging animals.
7. Setup a second instance of the LabKey server to store and share research data. The unit plans to provide this as a service for any PI or research group associated with the center. This new instance will be available to investigators to view and download research data collected from NHPs housed at the center. To enhance data tracking, PrimateIDs will identify NHPs in these data.

INFORMATICS AND DATA SERVICES

Unit Head: Redacted by agreement Ph.D.

Accomplishments

Specific Aim 1: Develop and extend the EHR platform.
The requirements and needs for the EHR system continue to increase. The IDS unit hired a new FTE so that the unit has two developers and the unit's manager, all of whom contribute to the source code. The EHR production system was updated to LabKey version 17.2 in 2018 and testing has begun for LabKey version 18.3, the version against which the financial module is being developed. The new version uses modules from both SVN and GitHub that provide all the capabilities needed by the center staff.

The unit completely migrated to use GitHub as the version control system to keep track of custom modules developed in-house. The unit maintains public (https://github.com/WNPRC-EHR-Services) and private repositories. During the last reporting period, the unit had more than 500 changes made to the source code. Because we encourage other primate centers to review, comment, and use the code developed by the IDS unit, the source code for all the custom modules is publicly available.

The IDS unit continues to oversee the development of the financial module by the LabKey Software company. At the beginning of 2018, the initial campus contract with LabKey ran out of funds, and due to UW-Madison's policies, a new RFP needed to be submitted and an open bid process conducted before the work on the financial module could be completed. This delayed the project.

Specific Aim 2: Improve and enhance the user experience.
During the last reporting cycle, the EHR system was down for a total of three times, two of which were unscheduled problems with the network or server. For these two outages, the ITSS unit and UW-Madison's IT department were able to bring the server back up promptly after identifying the problems. The IDS unit maintains a log of all scheduled and unscheduled downtimes that are longer than five minutes. Because the system is used at all hours of the day, a reliable system is essential to ensuring a positive user experience.

The necropsy request and scheduling system developed and deployed during the last reporting cycle had some performance problems. The IDS unit worked with LabKey to improve the performance of the necropsy system. Now, staff can save and update necropsies in real time without needing to wait for the web page to reload because the system does all the required validations on the server side before the data is saved into the database.

The IDS unit deployed a food deprive system to facilitate scheduling the start and completion of food deprives. Since the system went live at the end of June 2018, there were more than 1200 successfully completed food deprives and only one error.

Specific Aim 3: Increase data quality by reducing manual data entry.
The IDS unit continues working on the network connected scale project. It was determined that the original prototype would not work correctly behind the barrier when used on a regular basis with animals. It was also decided that the system should be developed using an Arduino microcontroller connected to an iPad, rather than using a RasberryPi device, which was the original prototype. The ITSS unit at the center already maintains several iOS devices. The ITSS unit has plans to install server-side software to manage all iOS devices used by center's staff, so it is logical and cost-effective to use iOS-enabled iPads for the scale project. Adding ten more devices to this management software will not add overhead to the ITSS unit's overall plans to centrally manage these devices.

The iPad for this project will have a rugged enclosure to protect it from damage when used behind the barrier. Additionally, all the other components for this project will be housed on a metal enclosure added to the digital scales. The IDS unit has purchased the components for this project and started developing the code needed to enable them to communicate with each other.

Specific Aim 4: Provide EHR-powered data management and sharing capabilities to WNPRC investigators.
The IDS unit worked with the ITSS unit to migrate the all the EHR servers to the virtual platform hosted by the University's IT department. During this reporting period, senior management at WNPRC approved addition of another virtual server to facilitate research data sharing with researchers outside the center. The configuration of this new server will be modified as needed based on data sharing needs of center PIs. Data stored on our production server will be copied over to the new virtual server to accomplish the proposed data sharing plans for two research projects.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5909

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Unit Head	Institutional Base Salary	EFFORT			37,064.00	12,342.00	49,406.00
2.					PhD	Core Investigator					9,480.00	3,157.00	12,637.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **62,043.00**

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	Inform Proc Consultant	EFFORT			55,694.00	18,546.00	74,240.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**74,240.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**136,283.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	1,892.00
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	83,510.00
Total Other Direct Costs	**85,402.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**221,685.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	221,685.00	82,024.00
		Total Indirect Costs	**82,024.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**303,709.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Genetics Services Unit (Scientific-Units-004)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Specific Aim 1: Providing fee-for-service major histocompatibility complex (MHC) class I and class II genotyping. We expect to genotype at least 1,500 animals per year for the nonhuman primate community with Illumina MiSeq sequencing-based assays.

Specific Aim 2: Developing MHC, KIR and FcγR full-length transcript genotyping. We will sequence full-length transcripts in Mauritian cynomolgus macaques and Indian rhesus macaques. We will then establish fee-for-service genotyping assays to detect allelic variants of genes.

Specific Aim 3: Deep sequencing viral inocula, replicating viruses from infected animals, and unknown pathogens from sick animals. We will continue sequencing virus stocks used for in vivo macaque challenges as well as viruses from infected animals. We will also develop a specific assay to detect antiretroviral drug resistance in SIV. Moreover, we will implement unbiased pathogen detection to rapidly identify infectious diseases that threaten NHP colonies and their caretakers.

Specific Aim 4: Establishing genomic profiling for rhesus macaques, cynomolgus macaques, and common marmosets. We anticipate genomic profiling will be available on a fee-for-service basis at a cost of less than $1,000 per animal.

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: B.2 Accomplishments_Genetics.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: Providing fee-for-service major histocompatibility complex (MHC) class I and class II genotyping. We expect to genotype at least 1,500 animals per year for the nonhuman primate community with Illumina MiSeq sequencing-based assays.

We plan to continue performing our well-established MHC class I and class II genotyping assay (now inclusive of TRIM5) because demand for this service from the NHP research community remains strong. As of the beginning of 2019, we already processing ~375 samples in our queue and ~200 additional samples are due to be delivered by the end of January 2019. Given that we have genotyped more than 1,500 animals per year with Illumina MiSeq sequencing-based assays since 2014, so we do not anticipate any difficulty in accomplishing this goal again in the next reporting period.

Specific Aim 2: Developing MHC, KIR and FcγR full-length transcript genotyping. We will sequence full-length transcripts in Mauritian cynomolgus macaques and Indian rhesus macaques.

We will then establish fee-for-service genotyping assays to detect allelic variants of genes.
We plan to continue offering fee-for-service MHC and FcγR full-length transcript genotyping assays in the next reporting period. Future requests for FcγR genotyping assays will be processed with a revised primer panel to generate full-length cDNA amplicons for this gene family. Our KIR full-length transcript genotyping assay is still less robust than desired and we still need to work to develop improved primer panels and PCR conditions during the coming year. Our goal is to establish a fee-for-service assay for these genes that will be available by the end of 2019.

Specific Aim 3: Deep sequencing viral inocula, replicating viruses from infected animals, and unknown pathogens from sick animals. We will continue sequencing virus stocks used for in vivo macaque challenges as well as viruses from infected animals. We will also develop a specific assay to detect antiretroviral drug resistance in SIV. Moreover, we will implement unbiased pathogen detection to rapidly identify infectious diseases that threaten NHP colonies and their caretakers.

We plan to continue offering fee-for-service pathogen sequencing services in the coming year. The sequencing method will vary, depending on the goals of the client. We have also been adapting the short amplicon sequencing method to SIV, so we hope to incorporate that assay in our pipeline this year, as well. We cannot predict the number and types of samples we will sequence, but we

anticipate continued steady business and research progress, as we have made in the past year.

Specific Aim 4: Establishing genomic profiling for rhesus macaques, cynomolgus macaques, and common marmosets. We anticipate genomic profiling will be available on a fee-for-service basis at a cost of less than $1,000 per animal.

With continued decreases in the sequencing costs associated with MES analysis, we plan to expand our genetic characterization the WNPRC breeding colony with this assay. We will complete genometyping assays for the remaining 57 WNPRC rhesus progeny born during the final three quarters of 2018 as well as new rhesus offspring who are born during the first quarter of 2019. We also plan to expand genometyping to include the majority of active Indian rhesus sires and dams (MES datasets have already been collected for ~48 WNPRC sires and dams). These MES studies will also be extended to all 59 Mauritian cynomolgus macaque breeders and progeny in our MHC-directed breeding groups that were transferred to WNPRC in the fall of 2018 from the Bioculture breeding facility in Florida.

We anticipate offering fee-for-service genomic profiling in the next year as well. Initially we anticipate that this profiling will consist of generation of MHC and TRIM5 genometyping reporting analogous to the current Illumina MiSeq genotyping reports, as well as full exome sequence data from each sample. Additional analysis of specific immune gene targets beyond the MHC would be available to be performed by our group on a sample-by-sample basis, charged at bioinformatician processing hourly rates. Requests for additional processing would also inform high-value targets for analysis pipeline development and eventual addition to the standard reporting.

There are several additional concerns with our MES assays in their current format. One set of issues revolves around the increased turnaround-times when gDNA samples must be shipped and processed off-site at the Baylor Human Genome Sequencing Center or another sequencing facility. Likewise, investigators with tight budgets are still reluctant to pay higher costs associated with collecting data from the entire exome when they believe that they only need MHC genotypes to get their studies published. Another concern it that our current Nimblegen SeqCap probe design does not recover a sufficient number of sequence reads to perform KIR genotyping for rhesus macaque MES datasets.

As a more targeted alternative to our existing MES workflow, we have designed a new custom panel of capture probes that are restricted to MHC class I and KIR genes initially rather than the entire exome. For these pilot studies we have decided to utilize reagents from Integrated DNA Technologies (IDT) that are marketed under the trade name xGEN Lockdown probes. Overall this initial MHC/KIR probe design spans a total target size of 13,663 bp. Since this target size is >3000-fold less that our current MES probe design of ~48 Mb, the hope is that we can generate enough sequence coverage for bar-coded sample pools in-house with our MiSeq instrument. This option will provide flexibility in scheduling that isn't possible for our current MES protocol where we must send samples out to a core facility like Baylor for analysis on an Illumina NovaSeq instrument. During the year we anticipate performing feasibility studies with this pool of xGEN target capture probes and multiplexed library pools from Mauritian cynos and Indian-origin rhesus samples from WNPRC that have been already genotyped by independent methods.

GENETIC SERVICES UNIT

Unit Head Redacted by agreement Ph.D.

Accomplishments

Specific Aim 1: Providing fee-for-service major histocompatibility complex (MHC) class I and class II genotyping. We expect to genotype at least 1,500 animals per year for the nonhuman primate community with Illumina MiSeq sequencing-based assays.

For the period of January 1, 2018 through December 31, 2018, we completed Illumina MiSeq genotyping on a **total of 4,116 samples** for investigators across the nonhuman primate community. Over half of these samples (2528 samples) were from rhesus macaques (essentially all Indian-origin with only 11 Chinese-origin individuals). Mauritian-origin cynomolgus macaques were the second most common population with a total of 1014 samples evaluated. Another 542 samples were MHC genotyped for cynomolgus macaques from other geographic origins (Vietnam, Cambodia, China, Indonesia). Finally, MHC genotypes were also determined for 47 pig-tailed macaques. Fee-for-service Illumina MiSeq sequencing-based genotyping assays **generated $282,160.65 of fee-for-service income from 18 different academic and corporate clients**.

During the previous reporting period for this project, we also employed an **Illumina MiSeq sequence-based genotyping assay for TRIM5α** that has been incorporated into our standard panel for MHC genotyping. This assay was performed on **137 total samples from five different clients during the 2018 reporting period, generating $26,939.04 of additional fee-for-service income** from MiSeq sequencing-based host immune gene assays.

Specific Aim 2: Developing MHC, KIR and FcγR full-length transcript genotyping. We will sequence full-length transcripts in Mauritian cynomolgus macaques and Indian rhesus macaques. We will then establish fee-for-service genotyping assays to detect allelic variants of genes.

We have developed primer sets to amplify full open reading frames from cDNA templates for MHC class I (A, B, and I genes), MHC class II (DRA, DRB, DQA, DQB, DPA, and DPB genes), KIR (KIR1D, KIR2DL, KIR2DS, and KIR3DL genes), and FcγR (FcγR1A, FcγR2A, FcγR2B, and FcγR3A genes). These long amplicons are then sequenced on a Pacific Biosciences Sequel instrument. The MHC and FcγR full-length transcript genotyping assays are now offered in our fee-for-service portfolio for both Mauritian cynomolgus and Indian rhesus macaques. During the 2018, we performed fee-for-service **MHC class I and class II genotyping** on **52 Vietnamese-origin cynomolgus macaques** and **MHC class II genotyping on 60 Chinese-origin cynomolgus macaques.** These studies generated a total of **$65,669.92 in fee-for-service revenue.**

Since our published panel of full-length FcγR amplicons (Haj AK *et al*. J. Immunology **202**: 151-159, 2019) is less robust than we would like, we evaluated a new panel of FcγR primers in a head-to-head comparison with our existing assays. Given the results of this comparison, it appears that the revised FcγR amplicons perform somewhat better than our existing assays so we intend to use this new primer panel for fee-for-service genotyping assays going forward.

Specific Aim 3: Deep sequencing viral inocula, replicating viruses from infected animals, and unknown pathogens from sick animals. We will continue sequencing virus stocks used for in vivo macaque challenges as well as viruses from infected animals. We will also develop a specific assay to detect antiretroviral drug resistance in SIV. Moreover, we will implement unbiased pathogen detection to rapidly identify infectious diseases that threaten NHP colonies and their caretakers.

We generated viral sequences for both full-length viral genomes and individual amplicons. We made this switch because there were several cases were we, and others, were interested in sequencing short viral segments from samples with low viral loads, which was more feasible to do via short amplicons.

In 2018, we sequenced 69 full-length SIV individual fee-for-service samples from 4 different academic clients during the period. We also sequenced 52 full-length Zika sequences for basic research purposes. We also sequenced 80 individual SIV amplicons for clients. These data have contributed to five manuscripts published in 2018. We have also been sequencing plasmids for different groups, including SIV plasmids and plasmids containing other immune genes. Sequencing of plasmids is easily performed through our library preparation pipeline, so we have led these efforts. We sequenced 427 plasmids during this past period as fee-for-service. These pathogen sequencing efforts have thus far generated about $45,000 in fee-for service revenue in 2018. In addition, we deposited 11 viral inocula sequences in the Sequencing Reads Archive (SRA). No progress was made on the antiretroviral drug resistance testing during this reporting period, but will be a focus in future years. For unbiased pathogen detection, we have published protocols established, but no clients requested this service during the reporting period.

Specific Aim 4: Establishing genomic profiling for rhesus macaques, cynomolgus macaques, and common marmosets. We anticipate genomic profiling will be available on a fee-for-service basis at a cost of less than $1,000 per animal.

Our Macaque Exome Sequencing (MES) program expanded during 2018 to become a standard component of our efforts to genetically characterize Indian rhesus macaques in the WNPRC SPF breeding colony. MES analyses have been performed on a total of **116 Indian rhesus progeny** born at WNPRC in 2017 and early 2018. MES analyses were also performed on at least one parent for 55 of these offspring (**29 sire and dams** in total). In addition, **31 rhesus macaques from SIV studies** performed at WNPRC and NIAID were subjected to MES analyses as part of our efforts to introduce genome profiling assays to the NHP research community.

Per sample costs for our MES assays continued to drop for the target capture and sequencing steps that are performed by Redacted by agreement group at the Baylor Human Genome Sequencing Center. Advances in Illumina sequencing enabled in large part by the release of the Illumina NovaSeq platform and the use of S4 flow cells **dropped these basic costs to $291 per sample by the end of 2018**, provided batches of ~70 samples are processed in parallel. During 2018, we established a workflow for MHC analysis of MES datasets that provides essentially comparable results to our standard Fluidigm/MiSeq assays. In addition, we completed proof-of-principle studies to demonstrate that Trim5 and FcγR genometypes can be extracted from MES datasets. Although additional analysis pipelines and the costs for these analyses still need to be finalized before making genomic profiling widely available on a fee-for-service basis, we did submit our inaugural fee-for-service cohort to the Baylor Human Genome Sequencing Center for MES analysis in early October. Baylor staff made the sequence data for this cohort of 70 Cambodian-origin cynos available for downloading on December 28th.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5910

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Unit Head	Institutional Base Salary	EFFORT			18,960.00	6,314.00	25,274.00
2.					PhD	Core Investigator					7,435.00	2,476.00	9,911.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **35,185.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
6	Scientist / Research Specialist	EFFORT			67,243.00	22,393.00	89,636.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**89,636.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**124,821.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	49,994.00
2. Publication Costs	1,892.00
3. Consultant Services	0.00
4. ADP/Computer Services	5,128.00
5. Subawards/Consortium/Contractual Costs	49,595.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**106,609.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**231,430.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	181,835.00	67,279.00
		Total Indirect Costs	**67,279.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**298,709.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

RPPR - Other-5910

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 051113330

Budget Type*: ❍ Project ● Subaward/Consortium

Enter name of Organization: BAYLOR COLLEGE OF MEDICINE

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Redacted by agreement			PhD	Subcontract PI	Redacted by agreement	EFFORT			25,513.00	5,777.00	31,290.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **31,290.00**

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)	**31,290.00**

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

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

ORGANIZATIONAL DUNS*: 051113330
Budget Type*: ❍ Project ● Subaward/Consortium
Enter name of Organization: BAYLOR COLLEGE OF MEDICINE

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 051113330
Budget Type*: ❍ Project ● Subaward/Consortium
Enter name of Organization: BAYLOR COLLEGE OF MEDICINE

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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)	**31,290.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Salary and wages Base	58.5	31,290.00	18,305.00
		Total Indirect Costs	**18,305.00**

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)	**49,595.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Immunology Services Unit (Scientific-Units-005)

Component Project Lead Information:

Redacted by agreement

B. COMPONENT ACCOMPLISHMENTS

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

Immunology Services (IS) at WNPRC has two primary functions: (1) providing support to NHP studies that address immunological questions, or use certain immunological methods and (2) developing novel immune-based assays that improve the use of nonhuman primate models. The unit specializes in ELISPOT-, and flow-cytometry-based analytical techniques. IS performs assays using freshly processed samples to avoid artifacts introduced by cryostorage or shipping. IS thus enables the WNPRC to function as a national and international resource for in vivo experiments. Principal investigators can conduct their NHP studies with the assistance of IS regardless of their geographical location.

List the major goals below (NIH recommended length is up to 1 page. Limit is 8000 characters or approximately 3 pages.)

Specific Aim 1: To operate a state-of-the-art flow cytometry facility and to develop novel flow cytometry-based analytical methods. We will upgrade our BL-3 level cell sorter and purchase a new generation, extra-sensitive desktop analyzer. We will develop multicolor flow cytometry staining panels as collaborating investigators request. We anticipate developing 4-6 novel staining panels per year.

Specific Aim 2: To define and measure antigen-specific cellular immune responses using ELISPOT-based assays. IS routinely performs IFN- ELISPOT assays to quantify pathogen-specific immune responses. The majority of these tests are supporting SIV vaccination projects. As a resource development we will define minimal optimal epitopes of rhesus cytomegalovirus (rhCMV) IE1 and pp65-2 proteins restricted by the most frequent rhesus macaque MHC-I alleles. These epitopes will provide a set of critical tools for studies that investigate the effect of various health conditions (e.g. stress, metabolic diseases, transplantation etc.) on cellular immune responses.

Specific Aim 3: To measure antiviral antibody responses in NHP models of viral diseases. We will quantify and isolate antibody-producing plasmablast cells from blood, or bone marrow. We will also measure antibodies in plasma, or serum capable of binding viral antigens, neutralizing viral infectivity, and directing the elimination of virus-infected cells by antibody-dependent cell-mediated cytotoxicity (ADCC).

Specific Aim 4: To support vaccination and pathogenesis studies using NHP models. We will assemble appropriate animal cohorts selecting animals with desired genetic markers in close collaboration with Genetics Services (MHC and FcR haplotype). We will screen for pre-existing antigen-specific immune responses, coordinate vaccination and sample collection schedules with the Scientific Protocol Implementation Unit at WNPRC, and viral load measurements with Virology Services. We will perform various immune assays (cellular phenotyping, T cell, and NK function, antigen-specific antibody level quantification) as requested by the individual investigators. Based on current and anticipated funding, we will support 8-9 studies per year.

The specific aims proposed above include expanding our existing facility, defining new reagents, and introducing innovative assays. Our team, together with other service units of the primate center, is uniquely qualified to provide comprehensive support for a broad range of investigators that are interested in performing NHP studies.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Accomplishments_Immunology.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: To operate a state-of-the-art flow cytometry facility and to develop novel flow cytometry-based analytical methods. We will continue developing new multicolor flow cytometry methods to support our collaborating scientists. Based on previous demand we anticipate developing 4-6 new staining panels. The majority of these assays will be used in infectious disease studies, but there is demand for our expertise in transplantation studies also.

Specific Aim 2: To define and measure antigen-specific cellular immune responses using ELISpot-based assays. We will define the restricting MHC-I alleles of the two minimal optimal epitopes that we identified in the IE1 protein of rhesus cytomegalovirus. Furthermore, we will continue screening for new epitopes defined by the Mamu-B*08, B*17 and A*01 MHC-I alleles.

Specific Aim 3: To measure antiviral antibody responses in NHP models of viral diseases. Our goal for the next year is to establish the quantification and isolation of antibody-producing plasmablast cells and memory B cells from bone marrow. Redacted by agreement Immunology Services technician, will visit the Immunology Core Laboratory of the Vaccine Research Center of the NIAID in January of 2018 to acquire new skills to meet this goal.

Specific Aim 4: To support vaccination and pathogenesis studies using NHP models. We will continue working with Genetics Services, the Scientific Protocol Implementation Unit, and Virology Services to support various NHP studies. We will give priority to NIH-funded research projects.

IMMUNOLOGY SERVICES UNIT

Unit Head: Redacted by agreement, Ph.D.

Accomplishments

FLOW CYTOMETRY SERVICES

We perform high-resolution phenotype and functional analysis of T cells, NK cell subsets, dendritic cells, monocyte/macrophage cells, and neutrophil leukocytes. Our clientele includes a broad range of investigators studying either infectious diseases, or other model systems such solid organ transplantation. In the reporting period we developed four new multicolor flow cytometry staining panels, and performed 3955 flow cytometry assays. We have published an original peer reviewed paper that details the phenotype of neutrophil progenitors in rhesus macaque bone marrow. We have offered our method as a routine service, and it is now being used by our collaborators in a kidney transplantation study.

DEFINE AND MEASURE ANTIGEN-SPECIFIC CELLULAR IMMUNE RESPONSES

IS performed 240 IFN-γ ELISPOT assays to quantify pathogen-specific immune responses using 15-mers covering the entire length of the phosphoprotein 65-2 (pp65-2) and immediate early protein 1 (IE1) of rhesus cytomegalovirus (rhCMV). We identified two putative epitopes in the IE1 protein. One of the epitopes is restricted by the Mamu-A*02 MHC-I allele. The Mamu-A*02 allele is present in approximately 20-25% frequency in our animal colony.

MEASUREMENT OF ANTIVIRAL ANTIBODY RESPONSES

Measurement of antibody-dependent cell-mediated cytotoxicity (ADCC): we developed a novel assay for measuring the ability of antibodies to kill SIV-infected cells by ADCC. A significant advantage of this approach is that ADCC responses are measured against virus-infected cells expressing native conformations of the viral envelope. IS performed 65 ADCC assays for two NIH funded studies during the reporting period.

Measurement of antigen-specific neutralization: we improved a novel, flow cytometry-based method to quantify Zika neutralizing antibodies in serum samples of rhesus macaques in collaboration with the laboratory of Dr. Theodore Pierson of NIAID.

The above listed activities are newly established in the repertoire of Immunology Services. Therefore, we are very encouraged that we were able to support several laboratories already with these new assays.

SUPPORT OF VACCINATION/PATHOGENESIS STUDIES

NHP models represent invaluable intermediate steps in translating vaccination concepts that were successfully tested in small animal models. We have accumulated ample experience with different vaccination platforms and challenge models. Our expertise puts us in a central role to guide vaccination experiments, in addition to performing study-related immune assays. We participated in 22 vaccination or pathogenesis NHP studies during the reporting period. We coordinated vaccination and sample collection with the Scientific Protocol Implementation Unit at WNPRC, and viral load measurements with Virology Services or with Redacted by agreement Redacted by agreement according to the demand of the collaborating investigator. We processed >5,300 blood samples, and performed > 1,600 flow cytometry assays as part of these studies. As examples, we highlight the following studies:

We performed a series of passive antibody transfer studies for Redacted by agreement (The Scripps Institute) to assess the extraordinary neutralizing capability of antibody PGT121 and its Fc domain mutated variant against mucosal SHIV162P3 challenges.

Redacted by agreement investigated the efficacy of various novel vaccination platforms with our support using a repeated low-dose SIVmac239 challenge-model in MHC-defined rhesus macaques. In addition to recombinant Ad5, Vaccinia, and VSV-based vaccine vectors, Redacted by agreement also tested whether persistent infection with SIVmac239 gene-expressing recombinant γ herpes viruses (rhesus rhadinovirus) would prevent SIVmac239 infection.

Redacted by agreement (University of Miami) tested the protective and therapeutic efficacy of several rAAV constructs expressing HIV-1-specific broadly neutralizing antibodies using a low dose SHIV-AD8 challenge model. Furthermore, he studied the protection provided by various SIVmac239 gene-expressing RRV vaccines against repeated low-dose SIVmac239 challenges. We quantified SIVmac239-specific T cells by performing tetramer staining in these studies.

For Redacted by agreement (The Scripps Institute-Florida) we tested the therapeutic and protective efficacy of a recombinant AAV vaccine expressing eCD4-Ig, a fusion of CD4-Ig with a small CCR5-mimetic sulfopeptide.

Redacted by agreement (University of Arizona) and Redacted by agreement (University of Minnesota) were the first to show that follicular regulatory T cells expand and impair the function of follicular T helper cells in SIV Infection. As part of an ongoing collaboration we quantified cell-associated viral burden in sorted cell populations.

For Redacted by agreement (University of Miami) we performed a vaccination experiment to determine if CTLA-4 blockade during vaccine priming can increase the breadth of vaccine-induced T-cell responses against SIV.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5911

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.		Eva		Rakasz	PhD	Co-Unit Head	111,618.00	4.0			37,206.00	12,390.00	49,596.00
2.		David	T.	Evans	PhD	Co-Unit Head	189,600.00	1.2			18,960.00	6,314.00	25,274.00
3.		Matthew		Reynolds	PhD	Core Investigator	100,400.00	0.6			5,020.00	1,672.00	6,692.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **81,562.00**

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	Assoc Scientist / Research Specialist	18.0			75,617.00	25,180.00	100,797.00
8	**Total Number Other Personnel**					**Total Other Personnel**	**100,797.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**182,359.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	62,767.00
2. Publication Costs	2,326.00
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	**65,093.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**247,452.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	247,452.00	91,557.00
		Total Indirect Costs	**91,557.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**339,009.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

A. COMPONENT COVER PAGE

Project Title: WNPRC Virology Services Unit (Scientific-Units-006)

Component Project Lead Information:

Friedrich, Thomas C.

B. COMPONENT ACCOMPLISHMENTS

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

The primary role of Virology Services is to facilitate and provide support for virological research in nonhuman primates. To fulfill this role, Virology Services offers an array of highly sensitive diagnostic assays to detect and quantify viruses; supplies critical reagents and services to the virology research community; and develops novel assays and techniques to enhance virological research. Virology Services offers assays for quantifying RNA and DNA from many viruses; historically the most requested assay has been the SIV gag RNA assay for monitoring plasma viral loads. Virology Services also produces and characterizes virus stocks (including SIVs, SHIVs, influenza) for use in both in vivo and in vitro experiments. Finally, Virology Services is continually developing novel assays to meet different and evolving needs of the field. Anticipating increased need to support HIV “cure” studies in NHP, a main focus for this activity currently is developing assays for measuring the SIV/ SHIV latent reservoir. We are also working to develop assays to support research into the ongoing Zika virus outbreak.

Specific Aim 1: Provide validated molecular diagnostic assays for viruses as fee-for-service. We will continue to provide validated molecular diagnostic assays for viruses in support of studies of vaccines, treatments, and viral pathogenesis. We anticipate that quantitative (Q)RT-PCR for SIV and Zika virus RNA in plasma will continue to be our most-requested service. But we also anticipate growing demand for other assays and modalities we have recently developed, including QRT-PCR for other emerging and re-emerging viruses, such as influenza, dengue, arboviruses and hepaciviruses.

Specific Aim 2: Provide characterized virus stocks for in vitro and in vivo use as fee-for-service. We will continue to produce well-characterized virus stocks for use in challenge studies, but we will move to a “pay-as-you-go” model for investigators requesting in-vivo-titrated viruses. That is, we will continue to produce high-titer stocks of SIV, influenza, and other viruses in tissue culture, and will offer vials of these viruses to users on a fee-for-service basis, but we will not undertake an in-vivo titration of any virus “on spec;” rather, we will partner with users to perform titrations of specific virus stock according to their needs on a fee-for-service basis.

Specific Aim 3: Develop new culture methods and molecular diagnostics to facilitate virological research in nonhuman primates, to be deployed as future services. We are continually asked by users to develop, or support the development of, novel assays. We will therefore continue to develop and validate Q(RT)-PCR and ddPCR assays against novel targets in the new P51 cycle. We will partner with users to define these targets, but anticipated new targets include the vaccine vectors AAV, RRV, and CMV as well as the emerging Zika virus (ZIKV) and re-emerging chikungunya virus (CHIKV) and dengue virus (DENV).

Specific Aim 4: Develop methods for quantifying the latent SIV/SHIV reservoir. As HIV/SIV research shifts to focus on “cure” strategies, there will be increasing needs for assays to quantify the latent reservoir. Currently available assays are difficult, expensive in terms of both personnel time and supplies, and are poorly reproducible. We will therefore develop novel approaches to measuring the latent reservoir that increase reproducibility and decrease cost. As first steps, we are developing novel “readouts” for the quantitative viral outgrowth assay (QVOA) that could reduce costs by over 25%. With support from a new UW-Madison pilot, we will also partner with UW-Madison colleagues in biomedical engineering to use microfluidics approaches to reduce requirements for reservoir sample sizes and user manipulations.

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: B.2 Accomplishments_Virology.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: Provide validated molecular diagnostic assays for viruses as fee-for-service.

During the next reporting period Virology Services will continue to perform fee-for-service molecular diagnostic viral load assays for SIV, Zika virus, dengue virus, influenza and possibly pegiviruses. Because of a P01 grant recently awarded to a team of investigators at UW, we anticipate the majority of demand to be for Zika virus assays, though we expect SIV demand to remain high. In order to ensure that our assays are reliable and accurate to the highest standard and to validate our results, we routinely perform sample exchanges with other laboratories performing the same assays. We are currently in the midst of organizing a sample exchange with the Virology Core of

ONPRC.

Virology Services is always seeking to improve on our assays. For this reason, we have been working to lower the limit of detection of our standard viral load assay. We have already developed a protocol and begun testing. Using this protocol, we can test a larger amount of sample RNA, thus increasing the sensitivity of the assays. Additionally, this new protocol will lower the cost of the assay. In 2019 we will finish this testing and rigorously define the limit of detection of the assay begin using it for our molecular diagnostic tests.

Specific Aim 2: Provide characterized virus stocks for in vitro and in vivo use as fee-for-service.

Virology Services will continue to provide high-titer, characterized stocks of SIV, SHIVs and Zika virus for both in vitro and in vivo use to investigators requesting virus. Because we recently sold a large portion of our for-in-vivo-use SIV stock, we will consider producing a new stock of SIVmac239 suitable for in vivo use. Before undertaking this endeavor we will consult with users to gauge how much interest exists in such a virus stock.

Virology Services is currently under contract to produce a custom, small-scale SHIV stock for Dr. Matt Reynolds lab. This stock will be produced in the end of January and will be used for in vivo studies being conducted at the WNPRC.

Specific Aim 3: Develop new culture methods and molecular diagnostics to facilitate virological research in nonhuman primates, to be deployed as future services.

In response to a user request, Virology Services is in the midst of developing and validating an assay to measure CMV from plasma/serum from rhesus macaques. We are currently working with a consortium to choose a universal CMV QPCR assay, which we will optimize and deploy as fee-for-service by the end of the first half of this year.

In addition to offering an assay for rhesus CMV, Virology Services will entertain other user requests for new molecular diagnostic assays. For example, an investigator studying primate pegiviruses has expressed interest in developing assays to measure viral loads of several different pegiviruses in plasma from non-human primates.

Specific Aim 4: Develop methods for quantifying the latent SIV/SHIV reservoir

Virology Services is now offering several assays as fee-for-service for measuring the latent reservoir of SIV, including QVOA and measuring cell-associated SIV RNA and DNA. We will continue to work to improve these assays (in terms of increasing sensitivity and bringing down cost). Additionally, we will also advertise our services to bring in new clients to take advantage of these assays.

VIROLOGY SERVICES UNIT

Unit Head: Thomas Friedrich, Ph.D.

Accomplishments

Specific Aim 1: **Provide validated molecular diagnostic assays for viruses as fee-for-service**.
During the reporting period from January 1, 2018 to December 31, 2018 Virology Services performed over 4600 viral quantification assays. This number includes assays to quantify viral RNA from SIVs, Zika virus, influenza and dengue. During this reporting period demand for the Zika virus assay surpassed that for SIV, accounting for about 60% of the samples tested. The Zika virus viral load assays supported 4 publications during the reporting period:

Aliota MT, Dudley DM, Newman CM, Weger-Lucarelli J, Stewart LM, Koenig MR, Breitbach ME, Weiler AM, Semler MR, Barry GL, Zarbock KR, Haj AK, Moriarty RV, Mohns MS, Mohr EL, Venturi V, Schultz-Darken N, Peterson E, Newton W, Schotzko ML, Simmons HA, Mejia A, Hayes JM, Capuano S, Davenport MP, Friedrich TC, Ebel GD, O'Connor SL and O'Connor DH. 2018. Molecularly barcoded Zika virus libraries to probe in vivo evolutionary dynamics. *PLoS Pathog* 14: e1006964. PMC5891079

Dudley DM, Van Rompay KK, Coffey LL, Ardeshir A, Keesler RI, Bliss-Moreau E, Grigsby PL, Steinbach RJ, Hirsch AJ, MacAllister RP, Pecoraro HL, Colgin LM, Hodge T, Streblow DN, Tardif S, Patterson JL, Tamhankar M, Seferovic M, Aagaard KM, Martín CS, Chiu CY, Panganiban AT, Veazey RS, Wang X, Maness NJ, Gilbert MH, Bohm RP, Adams Waldorf KM, Gale M, Rajagopal L, Hotchkiss CE, Mohr EL, Capuano SV, Simmons HA, Mejia A, Friedrich TC, Golos TG and O'Connor DH. 2018. Miscarriage and stillbirth following maternal Zika virus infection in nonhuman primates. *Nat Med* 24: 1104-1107. PMC6082723

Mohr EL, Block LN, Newman CM, Stewart LM, Koenig M, Semler M, Breitbach ME, Teixeira LBC, Zeng X, Weiler AM, Barry GL, Thoong TH, Wiepz GJ, Dudley DM, Simmons HA, Mejia A, Morgan TK, Salamat MS, Kohn S, Antony KM, Aliota MT, Mohns MS, Hayes JM, Schultz-Darken N, Schotzko ML, Peterson E, Capuano S, Osorio JE, O'Connor SL, Friedrich TC, O'Connor DH and Golos TG. 2018. Ocular and uteroplacental pathology in a macaque pregnancy with congenital Zika virus infection. *PLoS One* 13: e0190617. PMC5790226

Weger-Lucarelli J, Garcia SM, Rückert C, Byas A, O'Connor SL, Aliota MT, Friedrich TC, O'Connor DH and Ebel GD. 2018. Using barcoded Zika virus to assess virus population structure in vitro and in Aedes aegypti mosquitoes. *Virology* 521: 138-148. PMC6309320

While SIV demand continues to be strong, it only accounted for close to 40% of total samples tested. The SIV virus viral load assays supported three publications during the reporting period:

Rodgers MA, Ameel C, Ellis-Connell AL, Balgeman AJ, Maiello P, Barry GL, Friedrich TC, Klein E, O'Connor SL and Scanga CA. 2018. Preexisting Simian Immunodeficiency Virus Infection Increases Susceptibility to Tuberculosis in Mauritian Cynomolgus Macaques. *Infect Immun* 86: PMC6246917

Schouest B, Weiler AM, Janaka SK, Myers TA, Das A, Wilder SC, Furlott J, Baddoo M, Flemington EK, Rakasz EG, Evans DT, Friedrich TC and Maness NJ. 2018. Maintenance of AP-2-Dependent Functional Activities of Nef Restricts Pathways of Immune Escape from CD8 T Lymphocyte Responses. *J Virol* 92: PMC5809740

Sutton MS, Ellis-Connell A, Moriarty RV, Balgeman AJ, Gellerup D, Barry G, Weiler AM, Friedrich TC and O'Connor SL. 2018. Acute-Phase $CD4^{+}$T Cell Responses Targeting Invariant Viral Regions Are Associated with Control of Live Attenuated Simian Immunodeficiency Virus. *J Virol* 92: PMC6189504

Previously, the vast majority of samples submitted for viral quantification were plasma, serum, urine, or other types of fluids. Over the past 2 years we experienced increasing demand for viral quantification from tissue samples for both the Zika and SIV assays. In response to this demand we developed a method for isolating

RNA from tissue samples, partnering with Dr. Jeff Lifson at Leidos, who developed sensitive methods for recovering SIV RNA from tissues. Over the past year we have focused efforts on optimizing this protocol to increase the mass of tissue we can test and more importantly to increase the yield of RNA and lower the limit of detection of the assay. We now have a more sensitive method that has successfully been used to test hundreds of samples for either Zika virus or SIV.

In order to ensure the accuracy of our data we routinely perform sample exchanges with outside labs. During the past year we performed an exchange of SIV samples with the Molecular Virology core at OHSU. We found good correlation between results measured by the two labs. We also participated in a multicenter comparison of Zika RNA assays coordinated by Mike Busch and Lark Coffey at the Blood Systems Research Institute and UC-Davis.

Virology Services is continually looking to improve our assays. We are currently working to lower the limit of detection for our plasma viral load assay. To accomplish this goal, we have developed new reaction conditions for our QRT-PCR assay that will allow for testing a greater amount of template RNA per reaction. An increased workload over the past year has prevented us from fully testing these new conditions, but we continue to optimize these conditions so we can implement them in the next year.

Specific Aim 2: **Provide characterized virus stocks for in vitro and in vivo use as fee-for-service**.
Between January 1, 2018 and December 31, 2018 Virology Services provided 237 vials of virus to users on a per-vial basis. The bulk of this was a single stock of SIVmac239 provided to a client for in vivo studies. Use of this stock in vivo has led to several publications during this reporting period (Ellis-Connell et al., 2018) including one about the role of pre-existing SIV infection in tuberculosis (Rogers et al., 2018). Additionally, we provided SIVmac239 stocks to clients for in vitro studies, as well as a few vials of SHIVsf162p3 and SIVmac316E.

Virology Services also offers a service to provide virus stocks as requested by users. In this case, users contract Virology Services to produce a stock of a specific virus. In June of 2018 Virology Services provided such a stock of a mutant SIVmac239 virus for Dr. David Evans' lab at the University of Wisconsin. This virus stock is currently being used for an in vivo study at the WNPRC.

Specific Aim 3: **Develop new culture methods and molecular diagnostics to facilitate virological research in nonhuman primates, to be deployed as future services**.
Over the previous year Virology Services developed QRT-PCR assays to quantify dengue viruses from plasma of infected macaques. We introduced assays for DENV-1 and DENV-2 as fee-for-service in the end of 2017. During the current reporting period Virology Services performed about 70 of these DENV-2 viral quantification assays for a study investigating the interaction of dengue virus and Zika virus in pregnant macaques; a manuscript describing this study will be submitted in early 2019.

Virology Services was recently approached by Dr. Dixon Kaufman, who was looking to measure cytomegalovirus (CMV) in plasma from rhesus macaques involved in kidney transplantation studies as part of a U01-funded national consortium aimed at developing novel methods to induce immune tolerance of transplanted tissues. Not only does Dr. Kaufman have an ongoing need for CMV testing, but there may be additional interest in CMV testing offered by Virology Services. Indeed, Virology Services has provided consultation on developing CMV molecular diagnostic assays to the entire NIH-funded transplant consortium, which involves investigators at multiple sites nationwide. The consortium's goal is now to standardize CMV viral load testing in macaques across the consortium; Virology Services will lead this effort along with investigators at Columbia. We plan to establish a single optimized assay protocol by March, at which point we will move forward with establishing the assay as fee-for service, to be deployed by the summer of 2019.

Specific Aim 4: **Develop methods for quantifying the latent SIV/SHIV reservoir**
A major goal for Virology Services over the past few years has been to offer the quantitative viral outgrowth assay (QVOA) as fee-for-service. This assay is considered the "gold standard" for HIV/SIV cure studies, and it is therefore imperative that we offer this service to the SIV field. This assay is both difficult to perform and costly in time and resources. Though we continue to work to optimize the assay and bring the cost down, we are now offering QVOA as a fee-for-service assay. At the end of 2018 we received our first set of samples for

fee-for-service QVOA testing from an investigator outside of WNPRC This was a large set of samples; testing is currently ongoing.

In addition to offering QVOA to measure the latent reservoir of virus Virology Services has been offering assays to measure cell-associated SIV RNA and DNA. While these assays do not specifically measure replication competent virus like the QVOA, they do offer insights into the number of infected cells in a population. Because these assays are more cost effective and can be used to answer different questions than the QVOA, they are appealing to many clients. We have been experiencing an increase in interest in both of these assays. In 2018 we performed 27 cell-associated SIV RNA quantifications and 66 SIV DNA tests. We already have 16 samples to be tested for both cell-associated SIV RNA and DNA in 2019.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

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

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

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

Not Applicable

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

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

RPPR - Other-5912

RESEARCH & RELATED BUDGET - SECTION A & B **FINAL**

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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.	Thomas		Friedrich	PhD	Unit Head	144,644.00	1.2			14,464.00	4,817.00	19,281.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **19,281.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	3.0			14,358.00	4,781.00	19,139.00
1	Research Specialist	2.4			14,479.00	4,822.00	19,301.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**38,440.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**57,721.00**

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

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

ORGANIZATIONAL DUNS*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

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*: 161202122

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF WISCONSIN-MADISON

Start Date*: 05-01-2019 **End Date*:** 04-30-2020

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	78,158.00
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	**78,158.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**135,879.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost Base	37.0	135,879.00	50,275.00
		Total Indirect Costs	**50,275.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)	Department of Health & Human Services, Division of Cost Allocation Services, Contact: Arif Karim 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**186,154.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name:

(Only attach one file.)

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