QVR *Notice of Award*

Notice of Award for Project:5P51OD011132-57
Support of Yerkes National Primate Research Center

PRINT CI
PI: LEWIN, JONATHAN S I
Total Award: $10,

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Rev0

Notice of Award:

◆◆◆

Notice of Award

PRIMATE RESEARCH CENTER GRANT
Federal Award Date: 07/26/2017

Department of Health and Human Services
National
Institutes of Health

OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P51OD011132-57
FAIN: P51OD011132

Principal
Investigator(s):
JONATHAN S LEWIN, MD

Project Title: Support of Yerkes National Primate Research Center

Barry C. Pine
Director, Pre-award Grants Adm
1599 Clifton Road NE, 4th Floor
1599-001-1BA
Atlanta, GA 303224250

Award e-mailed to: osp@emory.edu

Period Of Performance:
Budget Period: 05/01/2017
◆◆◆ 04/30/2018
Project Period: 05/01/1997 ◆◆◆ 04/30/2021

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount
of $10,013,573 (see ◆◆◆Award Calculation◆◆◆ in Section I and ◆◆◆Terms and Conditions◆◆◆ in Section III) to EMORY UNIVERSITY in support of the above 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 Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number P51OD011132. The content is solely the responsibil the authors and does not necessarily represent the official views of the National Institutes of Health.◆◆◆ Prior to issuing a press release concerning 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 resulting from an Investigator◆◆◆s Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. ◆ 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 Innovat 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,

Dawn Walker
Grants Management Officer
OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Additional information follows
SECTION I ◆◆◆ AWARD DATA ◆◆◆ 5P51OD011132-57

Award Calculation (U.S. Dollars)

Salaries and Wages		$3,607,718
Fringe Benefits	$891,107	
Personnel Costs (Subtotal)		$4,498,825
Consultant Services		$7,600
Equipment	$570,000	
Materials & Supplies		$694,735
Travel		

$37,578
Other $1,274,071

Federal Direct Costs
$7,082,809
Federal F&A Costs
$2,930,764
Approved Budget
$10,013,573
Total Amount of
Federal Funds Obligated (Federal Share)
$10,013,573
TOTAL FEDERAL AWARD AMOUNT
$10,013,573

AMOUNT OF THIS ACTION (FEDERAL SHARE)
$10,013,573
SUMMARY TOTALS FOR ALL YEARS
YR
THIS AWARD
CUMULATIVE TOTALS

57
$10,013,573
$10,012,573

58
$10,540,602
$10,540,602

59
$10,540,602
$10,540,602
60
$10,540,602
$10,540,602

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:
1580566256A1
Document Number:
POD011132J
PMS Account Type:
P
(Subaccount)
Fiscal Year:
2017

IC
CAN
2017
2018
2019
2020
OD
8014499
$10,013,573
$10,540,602
$10,540,602
$10,540,602

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:
WALKERD0 07/25/2017
Award Processed: 07/26/2017 12:19:09 AM

SECTION II ◆◆◆ PAYMENT/HOTLINE INFORMATION ◆◆◆ 5P51OD011132-57

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 ◆◆◆ 5P51OD011132-57

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 NI
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
Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to repo
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 aud
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 Manag
(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) P51OD011132. Recipients must document the assigned FAIN on each consortium/subawar
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 Acces
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,
must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with th
or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclo
regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Fed
Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. Th
term does not apply to NIH fellowships.
Treatment of Program Income:
Additional Costs

SECTION IV ��� OD Special Terms and Conditions ��� 5P51OD011132-57
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 th
following link: https://grants.nih.gov/grants/guide/pa-files/PAR-14-226.html
��
ORIP FUNDING PLAN FOR FY2017
This non-competing award reflects the NIH Fiscal
Policy for Grant Awards for FY2017 (see NIH Guide Notice NOT-17-086) and the��implementation of the ORIP FY2017 grants funding policy (see "Grants Polic
Guidance"): 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):
��
Dr. Robert P. Johnson
��
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
project by 25 percent or more from the level that was approved at the time of award.
��
PRIOR APPROVAL REQUEST
Any prior approval request (e.g., changes to
key personnel as noted on the award, changes in human and animal subjects requiring prior approval, carryover requests) must be submitted to the assigned
Management Specialist and Programmatic Official.�� Please refer to Part II Chapter 8 the NIH Grants Policy Statement for the activities and/or expenditu
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 o
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.
??
ANNUAL FEDERAL FINANCIAL REPORT REQUIREMENT
An annual Federal
Financial Report (FFR, SF 425) is required on this award no later than 90 days after the end of the calendar quarter in which the budget period ends.
??
The
FFR must be submitted electronically through the NIH eRA Commons, available at https://commons.era.nih.gov/commons/. ??Additional information on electro
submission of FFRs is available at the Commons eRA Homepage or by contacting the eRA Helpdesk at: commons@od.nih.gov or (866) 504-9552.
??
COMMUNICATIONS/PRESS RELEASE
If the grantee plans to issue a press release concerning the outcome of ORIP grant-supported research, it should notify Ms.
Patricia Newman, ORIP Communications at 301-435-0744, in advance to allow for coordination.
??
The ORIP WWW home page is at http://dpcpsi.nih.gov/orip/??
??
STAFF CONTACTS

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

Grants Management Specialist: Jenelle D. Wiggins
Email:
jenelle.wiggins@nih.gov Phone: (301) 435-0843 Fax: (301) 480-3777

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

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011132-57

INSTITUTION: EMORY UNIVERSITY

Budget	Year 57	Year 58	Year 59	Year 60
Salaries and Wages	$3,607,718	$3,929,508	$3,929,508	$3,929,508
Fringe Benefits	$891,107	$966,666	$966,666	$966,666
Personnel Costs (Subtotal)	$4,498,825	$4,896,174	$4,896,174	$4,896,174
Consultant Services	$7,600	$7,791	$7,791	$7,791
Equipment	$570,000	$472,047	$199,672	$368,592
Materials & Supplies	$694,735	$992,146	$992,146	$992,146
Travel	$37,578	$30,189	$30,189	$30,189
Alterations and Renovations				
	$112,258	$384,633	$215,713	
Other	$1,274,071	$940,112	$940,112	$940,112
TOTAL FEDERAL DC	$7,082,809	$7,450,717	$7,450,717	$7,450,717
TOTAL FEDERAL F&A	$2,930,764	$3,089,885	$3,089,885	$3,089,885
TOTAL COST	$10,013,573	$10,540,602	$10,540,602	$10,540,602

Facilities and Administrative Costs	Year 57	Year 58	Year 59	Year 60
F&A Cost Rate 1	45%	45%	45%	45%
F&A Cost Base 1	$6,512,809	$6,866,412	$6,866,412	$6,866,412
F&A Costs 1	$2,930,764	$3,089,885	$3,089,885	$3,089,885

A. OVERALL COVER PAGE

Project Title: Support of Yerkes National Primate Research Center	
Grant Number: 5P51OD011132-57	**Project/Grant Period:** 05/01/1997 - 04/30/2021
Reporting Period: 06/01/2016 - 04/30/2017	**Requested Budget Period:** 05/01/2017 - 04/30/2018
Report Term Frequency: Annual	**Date Submitted:** 03/01/2017
Program Director/Principal Investigator Information: JONATHAN S LEWIN , MD **Phone number:** 404-778-4432 **Email:** jon.lewin@emory.edu	**Recipient Organization:** EMORY UNIVERSITY EMORY UNIVERSITY 1599 CLIFTON RD, 4TH FLOOR ATLANTA, GA 303224250 **DUNS:** 066469933 **EIN:** 1580566256A1 **RECIPIENT ID:**
Change of Contact PD/PI: No	
Administrative Official: MADISON GRAY 1599 Clifton Road NE, 4th Floor Atlanta, GA 30322 **Phone number:** 404-727-2819 **Email:** madison.gray@emory.edu	**Signing Official:** BARRY C PRINE 1599 Clifton Road, 4th Floor Atlanta, GA 30322 **Phone number:** 404-727-1405 **Email:** barry.c.prine@emory.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 Yerkes National Primate Research Center (YNPRC) of Emory University is one of seven National Primate Research Centers sponsored by the Office of Research Infrastructure Programs (ORIP) of the National Institutes of Health. The overarching goals of Yerkes are to conduct a research program focused on scientific problems relevant to human health and the NIH mission by providing resource infrastructure and expertise in appropriate scientific and veterinary specialties and to ensure the Center's ability to serve as a resource to Core Scientists, as well as to scientists regionally, nationally and internationally. With the support of the P51 Base Grant, the Yerkes Primate Center operates two principal facilities: a Main Station on the Emory University campus, which provides animal housing facilities, research laboratories and support services and a 117 acre Field Station located 30 miles north of Atlanta, which provides housing for nonhuman primate breeding colonies, research laboratories including a genetics laboratory, and facilities for studies of the social behavior and biology of semi-free ranging nonhuman primates.

During the current reporting period (5/1/2011 to present), the Yerkes Center has recorded remarkable progress, as evidenced by numerous (>790) publications, including multiple high-impact publications, construction of new animal facilities, including a state-of-the-art transplantation and ABSL3 facility, and expansion of its research funding base, even in the era of an extremely competitive NIH funding environment, with a 13% increase in research funding in FY 2014. Consequently, we have made significant contributions to behavioral, biomedical and translational research and research training at Emory University and via collaborations on a regional and national basis. In particular, the Yerkes Primate Center has maintained outstanding core research programs, extensive collaborative relationships with scientists based in other Emory University departments and provided resources and services to a broad multidisciplinary network of affiliate and collaborative investigators throughout the region and nation. These research programs, which involve the use of a variety of nonhuman primate species, are directed primarily toward four major research disciplines, representing the research divisions within the Yerkes Center: 1) Microbiology and Immunology; 2) Developmental and Cognitive Neuroscience, 3) Neuropharmacology and Neurologic Diseases and 4) Behavioral Neuroscience and Psychiatric Disorders. Also, through the Divisions of Animal Resources and Pathology, Yerkes provides support for outside investigators conducting research at the Yerkes Center, consistent with our ORIP mandated role as a regional and national resource.

Guided by ORIP NPRC program guidelines, NIH objectives and our own strategic planning process, we propose the following Specific Aims:

1. To carry out basic and translational research using nonhuman primates to expand knowledge, develop improved treatments, and advance cures that will benefit humanity;

2. To provide regional and national resources for data, consultative expertise, biologic materials, and specialized facilities useful in supporting nonhuman primate research;

3. To study basic nonhuman primate biology and improve nonhuman primate breeding, husbandry and genetic characterization to better serve the biomedical research community; and

4. To provide research and training opportunities involving nonhuman primates to graduate and undergraduate students, postdoctoral fellows, visiting scientists and faculty members.

The pursuit of these aims will enhance the Center's ability to serve as an enabling resource to Core and Affiliate Scientists for the conduct of nonhuman primate research, all for the ultimate goal of advancing human health.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B2 Accomplishment_overall.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

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

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
3P51OD011132-56S1	Support of Yerkes National Primate Research Center--Year 56 Supplement Request	The goal of this renovation project is to build on the interconnection of the three chilled water system at the Yerkes Main Station to provide an	Progress to date: 7/21/16NIH notice of award issued 12/1/16After preliminary design

	for AIDS-Related Renovation	efficient and reliable supply of cooling to the three largest research facilities. This optimization project will update the aging and vulnerable chilled water system that currently serves the Specific Animal Location where AIDS research studies are concentrated, provide a source of backup chilled water, and operate with much greater efficiency and reliability.	meetings with contractors and consultants it was determined that Excluded by Requester would be the most qualified mechanical engineer for this project due to previous experience replacing the Main Building Chiller in 2013. Excluded by Requester submits their consultant proposal. 1/17/17Emory University Ways and Means approval 1/30/17Emory consultant agreement sent to Excluded by Requester for approval and signing Estimated timeline: 3/1/2017Construction Document package submitted to NIH for approval and release of funds March 2017Start of construction April 2017 Completion of construction

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

File uploaded: B4 Training APR 2-8-17.pdf

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

The Yerkes National Primate Research Center shares its scientific advancements via researchers publishing in peer-reviewed scientific journals and presenting at local, national and international meetings. In addition, the Yerkes Public Affairs Department: 1) Coordinates the NPRC presence at the annual Society for Neuroscience meeting, including overseeing an exhibit booth and managing the NPRC support of the Animals in Research panel; 2) Organizes presentations to the public, such as lifelong-learning programs and educational outreach to elementary, junior and high school students; 3) Arranges tours of the Yerkes Research Center's two campuses, including our twice annual Field Station Open House; 4) Distributes informational materials to tour participants; 5) Works with Woodruff Health Sciences and central university staff to ensure Yerkes information is included in Emory publications (e.g., Emory Magazine); 6) Maintains the Yerkes website, including the News page that contains releases about the center's scientific advancements and other accomplishments; and 7) Hosts an internal Lunch and Learn program for Yerkes employees to learn directly from the center's researchers as well about healthy living initiatives the university sponsors. Non-Yerkes scientists also present lectures throughout the year.

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

In the upcoming funding period, the Yerkes National Primate Research Center will continue to advance our overarching goals:

1. To carry out basic and translational research using nonhuman primates to expand knowledge, develop improved treatments, and advance cures that will benefit humanity;

2. To provide regional and national resources for data, consultative expertise, biologic materials, and specialized facilities useful in supporting nonhuman primate research;

3. To study basic nonhuman primate biology and improve nonhuman primate breeding, husbandry and genetic characterization to better serve the biomedical research community; and

4. To provide research and training opportunities involving nonhuman primates to graduate and undergraduate students, postdoctoral fellows, visiting scientists and faculty members.

Detailed plans for each of our Divisions and Units are provided in the reports for the individual components that follow.

B.2. Accomplishments—Overall

The proposed major activities of the Yerkes National Primate Research Center, which are unchanged, are to:

1. To carry out basic and translational research using nonhuman primates to expand knowledge, develop improved treatments, and advance cures that will benefit humanity;

2. To provide regional and national resources for data, consultative expertise, biologic materials, and specialized facilities useful in supporting nonhuman primate research;

3. To study basic nonhuman primate biology and improve nonhuman primate breeding, husbandry and genetic characterization to better serve the biomedical research community; and

4. To provide research and training opportunities involving nonhuman primates to graduate and undergraduate students, postdoctoral fellows, visiting scientists and faculty members.

The Yerkes National Primate Research Center has demonstrated significant progress in meeting each of our key objectives during the reporting period (5/1/16 to 4/30/17) and consequently, has made significant contributions to behavioral, biomedical and translational research at Emory University and via collaborations on a regional and national basis. In particular, the Yerkes Primate Center has maintained outstanding core research programs, extensive collaborative relationships with scientists based in other Emory University departments and provided resources and services to a broad collective network of affiliate and collaborative investigators throughout the region and nation. These research programs, which involve the use of a variety of nonhuman primate species, are directed primarily toward four major research disciplines, representing the research divisions within the Primate Center: 1) Behavioral Neuroscience and Psychiatric Disorders, 2) Developmental and Cognitive Neuroscience, 3) Neuropharmacology and Neurologic Diseases and 4) Microbiology and Immunology. Also, through the Divisions of Animal Resources and Pathology, Yerkes provides support for outside investigators conducting research at the Yerkes Center, consistent with our ORIP-mandated role as a regional and national resource.

The project summaries that follow summarize the numerous contributions from our administrative units, animal resources and pathology units, pilot projects, service cores, and scientific programs.

We provide here a few vignettes to summarize representative achievements.

Research Funding

Sponsored research funding at Yerkes in FY16 (9/1/15 to 8/31/16) reached an all-time high of $79,097,405, representing an 18.7% increase from FY15. This funding is well-distributed among our four scientific divisions and the Emory Vaccine Center. Several notable new awards include:

- Emory Consortium for Innovative AIDS Research in NHP. PI's: Excluded by Requester $35.6M/5 years. This new research partnership brings together an interdisciplinary mix of highly collaborative investigators focused on a wide range of HIV vaccine and cure research, with the aim of developing a potent HIV vaccine that produces a broad and sustained immune response. The Consortium will develop advanced vaccines that provide sustained protection from retroviral infection. In addition, they aim to refine existing "shock and kill" approaches that seek to eliminate the virus from latent reservoirs in people who are infected with HIV, enhancing the possibility of a cure.
- DARPA Technologies for Host Resilience (THoR)—Host Acute Models of Malaria to study Experimental Resilience (HAMMER). PI: Excluded by Requester $6.4M. Researchers at Emory University, the University of Georgia, and the Georgia Institute of Technology, along with national and international collaborators, will investigate the mechanisms behind "resilience" following malaria infection. The investigators believe learning why malaria causes acute, potentially lethal disease in some humans and animals, while others are much more resilient or tolerant, could lead them to better intervention strategies for malaria and other diseases, including new and better drugs.

- 24/7 tracking of the movements of rhesus monkeys in 3D using RFIDs. PI: Excluded by Requester $2.6M. Dr. Excluded by Requester (Division of Cognitive Neuroscience) and collaborators have developed an automated tracking system for monkeys in social groups that will be worn by all tracked monkeys in their social group and will permit continuous monitoring of animal behavior and interactions with other animals.
- Udall Parkinson's Disease Center of Excellence. PI: Excluded by Requester $3.9M/5 years. This P50 continues a Center of Excellence in Parkinson's disease research at Emory University focused on translational studies of the basal ganglia-thalamocortical circuitry and the development of new medication therapies for Parkinson's disease.

Publications

Yerkes scientists published 169 articles and 5 book chapters in the past year, including a number of high profile publications in journals such as *Science, PNAS, and Nature Immunology*. Selected contributions include:

Excluded by Requester

Selected Honors and Awards

- Excluded by Requester
- R. Paul Johnson was appointed to the NIH Council of Councils. The Council is made up of approximately 30 members who advise the NIH Director on matters related to the policies and activities of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI).

Yerkes National Primate Research Center
2017 Annual Progress Report SPID Form

TITLE: OPERATION OF THE YERKES PRIMATE RESEARCH CENTER

SPID#: 0191

UNIT/DIVISION:

TYPE (indicate): MANAGEMENT (Management/Research/Pilot)

Percent P51 $: 6%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	LEWIN, JON	EXEC VP HEALTH SCIENCES	
Prin. NPRC Core Sci.	JOHNSON, RP	Yerkes NPRC Director	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

PROGRESS REPORT:
This component provides overall direction of the following components fo the Yerkes National Primate Research Center of Emory University to support the Center's scientific mission: administration, scientific leadership, management, comprehensive business services, information technology, human resources, and public information. In addition, the administrative core oversees facilities management, animal resources, veterinary medicine, animal care, animal records, environmental enrichment, research services, pathology, endocrinology, and several service cores, including a state-of-the-art imaging core. General direction also is provided for 4 scientific divisions: Microbiology and Immunology, Neuropharmacology and Neurologic Diseases, Developmental and Cognitive Neuroscience, and Behavioral Neuroscience and Psychiatric Disorders. The Center's goals are to conduct a research program focused on scientific problems relevant to human health problems – such as HIV, neurodegenerative disease, and the broad NIH mission, to provide the resource infrastructure and expertise in appropriate scientific and veterinary specialties to support such a program, and to enhance the Center's ability to serve as a resource to core investigators as well as to scientists regionally, nationally, and internationally.

PUBLICATIONS:
None

FUNDING SOURCES:
NIH/ORIP P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: EMORY VACCINE CENTER

SPID#: 0177

UNIT/DIVISION: EVC

TYPE (indicate): MANAGEMENT

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:

The mission of the Emory Vaccine Center (EVC) is to improve human health by conducting fundamental and clinical research that leads to the development of effective vaccines against diseases of global importance. The EVC is an epicenter of academic research and development of vaccines for both chronic and infectious diseases. With more than 250 faculty members and staff, it is the largest and most comprehensive academic vaccine research center in the world.

Our goal at the Emory Vaccine Center is to benefit people – to prevent and cure disease. That is why the Center's focus is on the continuum of vaccine research, from basic science to clinical trials to vaccine policy. We want to see what we do in the lab make a difference in – even save – people's lives. Working in our labs in Atlanta and New Delhi, with our partners across the United States and around the world, and with the assistance of thousands of supporters and volunteers in the community, we are improving human health.

PROGRESS REPORT:

The Emory Vaccine Center is making fundamental advances in immunology, virology and vaccine research to search for life saving cures against the world's most threatening diseases, plaguing millions of individuals around the globe. Comprehensive expertise in scientific, technological, and clinical research distinguishes the EVC as a world leader in the discovery, development and clinical analysis of safe, effective and affordable vaccines. Housed in one of the largest academic centers ever created to investigate new vaccine strategies, the 75,000-square-foot EVC fosters a deeper understanding of the complexities of infectious diseases, cancer biology and vaccine development. Excluded by Requester an internationally renowned scientist in viral pathogenesis and immunity and one of the world's leading experts on T-cell memory, leads the Center. Excluded by Requester has been instrumental in shaping EVC's research agenda that encompasses a continuum of basic, clinical and translational science.

The EVC encourages interdisciplinary collaborative research with investigators throughout Emory University's Woodruff Health Sciences Center, the Centers for Disease Control and Prevention (CDC), the Georgia Research Alliance and nearby academic institutions including Georgia Institute of Technology. Collectively,

scientists tackle prevention and treatment of diseases, including HIV/AIDS, malaria, tuberculosis, influenza and respiratory illnesses that pose a global threat.

The Center's affiliation with Emory's Yerkes National Primate Research Center also supports research at the forefront of immunology strategy and vaccine development. Long recognized as one of the leading centers for biomedical and biobehavioral research with non-human primates, Yerkes is home to a broad range of molecular and cellular research.

The Hope Clinic of the Emory Vaccine Center serves as the clinical arm, directing all current on-site clinical vaccine trials. As one of eight participating national sites in the NIAID's prestigious Vaccine Trials Evaluation Units (VTEUs), the Clinic plays a vital role in advancing the most promising pre-clinical vaccine research into human clinical trials.

PUBLICATIONS:
Included on list

FUNDING SOURCES:
Private Source; funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: CENTER for AIDS RESEARCH (CFAR)

SPID#: 0181

UNIT/DIVISION: M&I

TYPE (indicate): Management

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
The CFAR provides research facilities, institutional infrastructure and leadership, support for the recruitment and development of faculty, communication of scientific findings, and the promotion of interactions between CFAR members and with outside institutions and the community through an Administrative Core, a Developmental Core, and five Science Cores: Biostatistics & Bioinformatics, Clinical Research, Immunology, Prevention Science, and Virology & Molecular Biomarkers.

PROGRESS REPORT:
CFAR Investigators accomplished the following (details in separate SPIDs):
1)Eric Hunter and Rama Amara were awarded a UM1 (UM1AI124436), "The Emory Consortium for Innovative AIDS Research in Nonhuman Primates." The grant aims to understand the B and T Cell Biology of Protection from and Eradication of SIV/SHIV Infection. The Consortium will pursue Research Focus 1 aimed at optimizing and understanding the mechanism of protection for two partially protective vaccines that are currently in or entering clinical trials and Research Focus 2 aimed to determine whether combining these optimized vaccine concepts with latency reversing agents and immune modulators can result in sustained suppression of pathogenic SIV infection following interruption of high active antiretroviral treatment.
2)Rama Amara received an R01 (R01DE026333), "Optimizing Adjuvants and Needle Free Delivery Methods for Oral HIV Vaccination." The overall goal of this proposal is to develop a vaccination approach that induces strong HIV-specific humoral and cellular immunity in genital, intestinal and oral mucosae. We hypothesize that vaccines, which elicit strong anti-HIV immunity at these mucosal sites, will prevent infection and rapidly clear infected cells very early at the site of infection and enhance protection. .
3) Guido Silvestri and Ann Chahroudi received an R01 (R0AI125064), "Antiviral Role of CD8+ T Cells in ART-treated SIV-Infected Macaques." The study aims to determine the mechanisms by which CD8+ lymphocytes control viremia in the setting of ART. The knowledge we gain will be important for designing immune-based approaches to induce HIV remission.

PUBLICATIONS:
Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Private Source funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: The NIH Tetramer Facility

SPID#: 0243

UNIT/DIVISION: EVC

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: x Yes ☐No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology and Immunology (SOM), Vaccine Center	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:
The NIH Tetramer Facility provides custom synthesis and distribution of soluble major histocompatibility complex (MHC)-peptide tetramer reagents that can be used to detect antigen-specific T cells. These reagents include custom class I tetramers for mouse, non-human primate, and human alleles; class II reagents for mouse, non-human primate and human alleles; mouse and human CD1d tetramers; and human CD1a-c tetramers. The NIH Tetramer Facility also is developing novel technologies to improve production and expand the range of available MHC and CD1 tetramers. The tetramer reagents can be applied to studies ranging from basic immunology and protection against microbial pathogens to control of immune-mediated diseases and tumor metastases.

PROGRESS REPORT:
The NIH Tetramer Facility continues to provide conventional class I and class II MHC/peptide tetramers to investigators worldwide for the study of antigen-specific T cell responses. In past years, the spectrum of reagents was expanded to include non-classical CD1a-c reagents, as well as the popular CD1d reagents used to study NKT cells. Our most notable accomplishment in 2016 was the production and initiation of distribution of MR1 tetramers (mouse, human, rhesus macaque) for the study of mucosal associated invariant T cells (MAIT). In humans, MAIT cells are found in numerous anatomical compartments, and in fact constitute 2-10% of all CD3+ cells in the peripheral blood of healthy humans. We and others are studying the immunological functions of this large T cell subset.

PUBLICATIONS:
None.

In Preparation

FUNDING SOURCES:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

NIH Contract: 272201300006C.
Funding for this contract comes from 3 sources at NIH: TETRAMERS FOR BIODEFENSE RESEARCH, TETRAMERS FOR AIDS RESEARCH AND AIDS-RELATED RESEARCH, and TETRAMERS FOR IMMUNE-MEDIATED DISEASES RESEARCH
(https://projectreporter.nih.gov/Reporter_Viewsh.cfm?sl=12EAC8084C8DC4D07598B8961CAA4A01A2FFCEB861BF)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Maintenance of YNPRC Animal Colony

SPID#: 0292

UNIT/DIVISION: Animal Resources

TYPE (indicate): Management

Percent P51 $: 36%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Animal Resources	
Prin. NPRC Core Sci.		Animal Resources	
		Animal Resources	
		Animal Resources	

PROJECT DESCRIPTION:
The Yerkes nonhuman primate colony is maintained by the Division of Animal Resources, which is responsible for veterinary and animal care, environmental enrichment, animal records, and provision of research support. Maintenance of such a resource requires certain animal care and use procedures that are an integral part of the support of such a colony.

PROGRESS REPORT:
Divisin of Animal Resources manages holding the animals in captivity; maintaining breeding colonies (including SPF macaques and mangabey colonies for AIDS research); movement and handling of the animals as required for management purposes; periodic health surveillance, which may include physical examination, tuberculin testing, radiographs, blood collections, treatment of intercurrent diseases and injuries; and occasional euthanasia of animals unresponsive to treatment or animals with untreatable clinical problems or injuries. Additionally, the pedigree history and the genetics and genomics of individual animals is maintained by the Division of Animal Resources.

PUBLICATIONS:
None

FUNDING SOURCES:
ORIP/P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: SPF Breeding Colonies at the Yerkes NPRC

SPID#: 0309

UNIT/DIVISION: Animal Resources

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 29%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci.			
Other Core and Affil.	Excluded by Requester	Animal Resources MI Animal Resources MI	

PROJECT DESCRIPTION:
A central objective of this project is to breed Indian origin rhesus monkeys that are specific pathogen free (SPF) for Herpes B, STLV, and SRV. In addition, animals are fully pedigreed and genetically characterized for MHC alleles.

This project provides trained personnel and resources that are necessary to maintain and expand the SPF breeding groups and to manage them in order to optimize health and reproductive performance in support of national health related priorities. This objective is achieved at the center by utilizing an existing colony of SPF macaques. This colony is expanded via breeding of dedicated animals with known pedigrees. The colonies are virally maintained by routine blood collection for testing at specified intervals. These animals are made available as subjects to NIH supported investigators for AIDS related research and contribute to national health priorities. The YNPRC works closely with ORIP and the Coordinating Committee to implement recommendations regarding uniform husbandry procedures, standardization of screening tests and such other matters as the committee may deem necessary. To maximize the potential that national priorities for SPF production will be met, the YNPRC works in conjunction with other facilities, and investigators identified by ORIP, to maintain ORIP supported SPF colonies.

PROGRESS REPORT:
The Yerkes NPRC continues to expand the SPF Indian rhesus monkey breeding colony which consists of 1,884 Indian rhesus macaques managed for maximum production to support HIV/AIDS research. As the colony continues to expand to meet the increasing number of animal requests for AIDS-related studies, U24 program income will ensure sustainability of our AIDS-designated colony. All rhesus monkey breeding groups at the Yerkes Field Station have been SPF since April 2014, allowing us to optimize growth of this colony. For the 2016 birth season, the colony produced 419 offspring. Of these, 386 (92%) survived to at least four months of age. Over the past year of SPF funding, the Virology Core has made significant progress toward transitioning the simian betaretrovirus (SRV) diagnostic quantitative PCR test to in-house assays. Additionally, the Virology Core has continued to provide rapid and reliable serological and molecular testing for Herpes-B, SIV, STLV, and SRV. Furthermore, the expertise of the Virology Core has been utilized in developing a serotype-specific Adeno-Associated Virus (AAV) neutralizing antibody assay to screen rhesus macaques for

pre-existing immunity to this powerful genetic engineering tool currently being used by multiple groups at the YNPRC. Progress made during the current year will enable us to transfer all SNP-based parentage analyses at Yerkes to the Fluidigm EP1Genotyping Platform. Samples have been collected from every animal in the SPF breeding colony. DNA for pedigree and MHC analyses has been extracted, with all potential sires and dams identified. Further, all subjects through the 2014 birth cohort and close to one-half of the 2015 birth cohort have been genotyped for alleles important for HIV/AIDS studies at Yerkes. Notably, the Mamu-*A01, Mamu-*B08 and Mamu-*B17 MHC alleles.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIH-OD

NIH/ORIP P51OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Yerkes Biomarkers Core

SPID#: 0360

UNIT/DIVISION: Animal Resources

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 13%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	

PROJECT DESCRIPTION:

The primary mission of the Yerkes Biomarkers Core is to develop, validate and execute steroid, protein and other biologically relevant assays in support of translational and clinical research performed at the Yerkes National Primate Research Center and by outside investigators. The Core currently provides assays for reproductive function, stress physiology, growth, metabolism, circadian physiology, pituitary function, neuropeptides and neurotransmitters through the use of ELISA, radioimmunoassay (RIA), and liquid chromatography mass spectrometry (LC MS) assays in multiple species. Assays are done for investigators and clinicians on a per sample basis in which the Core bills the cost for personnel, reagents, service contracts, and miscellaneous supplies. The facility is housed at the Yerkes Main Station and contains Thermo Fisher HPLC coupled to Orbitrap Classic mass spectrometer, Shimadzu UPLC system in tandem with an AB Sciex 6500 triple quadrupole mass spectrometer, and multiple gamma and plate readers. We perform all necessary sample processing and data analysis to provide investigators with usable data. In addition to performing assays, the Core also consults with the scientific community to provide up-to-date methodology for the development, implementation, and validation of new assays with lower sample size requirements, quicker assay turnaround, improved sensitivity and higher accuracy to meet their research needs. Furthermore, we strive to lower the cost and turnaround time of existing assays by validating ELISA and RIA assays on our multiple LCMS platforms whenever possible.

PROGRESS REPORT:

Over the past year of funding, the Core has provided 4790 immunoassay and LC/MS tests using our standardized assays in support of research with our collaborators at Yerkes, Emory University and throughout the United States. We have validated several new imunoassays for use with rhesus and cynomologues monkeys and as well as validating our Angiotensin II asssay for urine. Additionally, we have modified our Angiotensin II, oxytocin, and vasopressin plasma/serum assays to be capable of reliable extraction from 1000ul to as little as 200ul. Further, the Yerkes Biomarkers Core has validated several new LC/MS methodologies for our collaborators at Yerkes. We have re-developed and validated our glucocorticosteroid LC/MS panel. The new method now uses only one-fifth of the sample volume and has a ten-fold increase in sensitivity relative to our previous protocol. By improving the extraction process, our new glucocorticosteroid LC/MS method was not limited to analysis of plasma and serum, but also can be used to analyze several new substrate types (i.e. breastmilk, hair, cerebro-spinal fluid[CSF]) with much less sample volume and lower cost than traditional methods. Our primary focus for the past year has been the development of an assay to quantify oxytocin in plasma and CSF with less sample volume and higher sensitivity and specificity. This critical and difficult-to-quantify biomarker is a high priority for several researchers at Yerkes and Emory. Once the Core overcomes several structural barriers to development of this assay (e.g. scarcity of stable reference control

molecules for oxytocin), we will have reliable access to a large number of samples for oxytocin quantification through researchers at Yerkes and Emory at large.

PUBLICATIONS:
None

FUNDING SOURCES:
P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: PRIMATE GENETIC ANALYSIS AND PEDIGREE MANAGEMENT

SPID#: 0390

UNIT/DIVISION: NPRC/Animal Resources

TYPE (indicate): Management

Percent P51 $: 29%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester		
Prin. NPRC Core Sci.			
Other Core and Affil.			

PROJECT DESCRIPTION:
Samples have and continue to be collected from all rhesus macaques for parentage and MHC and sooty mangabeys for parentage within the Yerkes' breeding colony. This includes animals from both the SPF colonies dedicated to AIDS research and the SPF colony that is not AIDS designated. Yerkes has worked with the Genetics and Genomics Working Group (GGWG) of the NPRCs to identify a large set of polymorphic SNPs, and establish a set of 96 unlinked, bi-allelic SNPs with a high degree of heterozygosity within NPRC colonies. The panel of SNPs has been validated for accuracy at assigning paternity across a set of 30 trios (offspring, dam, and sire) in independent tests at three different NPRCs as part of a GGWG collaboration. These data are used to determine parentage, pedigree and selected genetic markers for all of our macaques maintained at the Field Station. The ability to characterize specific genetic components has enabled us to better meet specific investigator needs to develop more diverse research endeavors, to selectively breed for specific genetic traits, to more efficiently manage our breeding colony to enhance genetic diversity, and to undertake specific phenotypic comparisons. To manage this data set, we are establishing a full-scale database system that will be able to assimilate genetic, parentage, pedigree, and demographic variable on all the animals.

PROGRESS REPORT:
The newly developed SNP assay was used to genotype all Yerkes SPF colony animals in the 2014-2015 birth years, for a total of 714 animals over the past year. The birth cohort of 2016 animals (n=450) will also undergo MHC and parentage analyses in the coming year. The MHC and parentage data is currently being incorporated in the ARMS record system.

PUBLICATIONS:
None

FUNDING SOURCES:
SPF grant / ORIP P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Imaging Center

SPID#: 0519

UNIT/DIVISION: Admin.

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 11%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

Name	Dept	Non-host Affiliation (if applicable)
Excluded by Requester	D	NND
	DCN	
	DCN	EMORY SOM/RADIOLOGY
		EMORY SOM/RADIOLOGY
		MOREHOUSE SOM, GA
		EMORY/PSYCHIATRY & BEHAV SCI
	EVC	
	NND	
	NND	
	DCN	
	BNPD	
		EMORY COLLEGE/ANTHROPOLOGY
		EMORY SOM/PHYSIOLOGY
		UNIV OF VERMONT, VT
	NND	
		EMORY SOM/NEUROLOGY
		EMORY SOM/ ANESTHESIOLOGY
Excluded by Requester	NND	
	DCN	
	NND	
	NND	
	DCN	
	NND	
	DCN	
	NND	
	DCN	
	BNPD	
Other Core and Affil.	None	

PROJECT DESCRIPTION:

PROGRESS REPORT:

Project Description: The Yerkes Imaging Center is part of the Yerkes National Primate Research Center at

Emory University and focuses on the development of *in vivo* magnetic resonance imaging (MRI) and positron emission tomography (PET) to study anatomy, physiology and function non-invasively to address questions in neuroscience, neruopharmacology and neurodegenerative diseases. Research at the Imaging Center includes high-resolution structural, perfusion and functional imaging of nonhuman primates, diffusion-tensor imaging (DTI), awake monkey fMRI, quantitative perfusion imaging, quantitation of monoamine transporters and receptors, brain metabolic mapping, diffusion, perfusion and functional imaging of stroke, and image data analysis and visualization.
Project Progress: The Imaging Center continues to support internal and external investigators with MRI and PET imaging as part of their individual research programs. In addition, we continued to commit significant resources to the development of a nonhuman primate model of ischemic stroke. A newly appointed endowed chair of stroke imaging joined the Imaging Center this year. We have expanded our use of diffusion tensor imaging DTI to characterize brain development in longitudinal studies conducted at the Yerkes Field Station.We have also made significant progress in establishing technical approaches that will be applicable to research programs in immunology and vaccine development. With the implementation of PET imaging, we have quantiifed the distribution of SIV virus *in vivo* and have validated biomarkers of neuroinflammation.

PUBLICATIONS:
See Scientific Divisions

FUNDING SOURCES
Howell, L / NIH/ORIP P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Genomics Core Laboratory

SPID#: 13030

UNIT/DIVISION: Admin.

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 6%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

Name	Role	Dept.	Non-host Affiliation
Excluded by Requester	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Genetics	Emory University
	Primary Investagator	Pathology	Emory University
	Primary Investagator	Pathology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Pediatrics	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Medicine	Emory University
	Primary Investagator	Neuroscience	Emory University
	Primary Investagator	Cardiology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Rheumatology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Medicine	Atlanta VA
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Medicine	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Neuroscience	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Biochemistry	Emory University
	Primary Investagator	Neuroscience	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University

Yerkes National Primate Research Center
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Excluded by Requester	Primary Investagator	Pediatrics	Emory University
	Primary Investagator	Microbiology and Immunology	Emory University
	Primary Investagator	Infectious Disease	Emory University
	Primary Investagator	Radiation	CDC
	Primary Investagator	Biochemistry	Emory University
	Primary Investagator	Pediatrics	Emory University
	Primary Investagator	Pediatrics	Emory University
	Primary Investagator	Surgery	Emory University
	Primary Investagator	Immunology and Molecular Pathogenesis	Emory University
	Primary Investagator	Pediatrics	University of Washington
	Primary Investagator	Biomedical Engineering	Emory/Georgia Tech
	Primary Investagator	Pathology	Emory University
	Primary Investagator	Pediatrics	Emory University
	Primary Investagator	Pathology	Emory University
	Primary Investagator	Gastroenterology	Emory University
	Primary Investagator	Infectious Diseases and Microbiology	University of Pittsburgh
	Primary Investagator	Infectious Diseases & Pathology	University of Florida
	Primary Investagator	Biomedical Engineering	Emory University
	Primary Investagator	Digestive Diseases	Emory University
	Primary Investagator	Psychiatry and Behavioral Sciences	Atlanta VA

Unique Species	Scientific Name
Rhesus Macaque	*Macaca mulatta*
Sooty Mangabey	*Cercocebus atys*
Pigtail Macaque	*Macaca leonina*
African Green Monkey	*Chlorocebus sp.*
Mouse	*Mus musculus*
Rat	*Rattus rattus*
Human	*Homo sapiens*
C. Diff	*Clostridium difficile*
Plasmodium Vivax	*Plasmodium Vivax*
Plasmodium Brazi	*Plasmodium Brazi*
Plasmodium Coatneyi	*Plasmodium Coatneyi*
White-throated sparrow	*Zonotrichia albicollis*
Rhizopus spp(fungi)	*Rhizopus*
Fly	*Drosophila melanogaster*
Enterobacter cloacae	*Enterobacter cloacae*

PROJECT DESCRIPTION: The primary mission of the Yerkes Genomics Core (GenCore) is to provide researchers in the Yerkes, Emory community, and NHP researchers nation-wide with access to cutting-edge

high throughput genomic technologies and bioinformatics. The primary users of the GenCore are monkey-model researchers at the Yerkes Center and immunologists within the Emory Vaccine Center; however, the GenCore is also utilized by members of the greater Emory community. The main services offered by the GenCore include RNA-Seq and array-based transcriptomics, DNA-Seq, miRNA-sequencing, microbiome 16s rRNA sequencing and sample preparation.

PROGRESS REPORT:

In the current reporting period, (5/1/2016 – 04/30/2017) we have accomplished the following goals:

Decreased Turn Around Time. To meet the increase in demand for GenCore services, we obtained a new high throughput sequencing instrument: an Illumina HiSeq3000, which became operational in March 2016. This replaced our previous "work-horse" machine, which was the HiSeq1000. The HiSeq3000 was obtained through a lease. We have also hired a 3rd laboratory technician, and have a fourth technician on staff on an interim basis to deal with our current workload. We also hired an additional 50% FTE bioinformaticist to improve the turnaround time on analyses. These have reduced average time to return sequence data to 20 days, less than half our previous turnaround time. We also instituted LIMS sample/project management software, GenoLogics, to streamline project submission and maintenance of pre-sequencing metadata. Despite these additions, the GenCore recharge recovery increased by 40% from the previous year (FY2016 recharges = $1.02 M), and our total cost recovery rose to nearly 91% over the previous two years.

Developed a low cost single-cell RNA-Seq assay and validated it NHPs. We developed an in-house single-cell RNA-Seq assay that sequences full-transcript RNA from single-cells in a cost effective manner. This assay can also extract the sequence data for the variable gene segments (VJ, VDJ) for individual B cells and T cells. We have also developed a computational algorithm to reconstruct these VJ/VDJ sequences correctly, and we have validated this assay to sequence the paired antigen receptor in rhesus macaque B cells.

Established a repertoire assay for NHP B cell Receptors/Antibodies We validated a non-commercial assay to sequence the B cell repertoire of either heavy or light chain from RNA samples, and validated it for human and rhesus samples.

Established a microbiome assay for NHPs We tested and validated a 16S amplicon sequencing assay for microbiome population sequencing in NHP samples. This has been performed on 3 NHP projects, and is now offered as a listed service.

Improved Bioinformatics Availability to Yerkes/Emory In addition to hiring another 50% FTE bioinformaticist to handle fee-for-service projects, we installed a user-dedicated workstation so that users can have access to our software licenses and analyze their own dataset under the in-person guidance of GenCore analysts. This has reduced the time to publication for projects involving the Core, as shown by Core Co-authorships on 10 published manuscripts in the last reporting period.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

NIH/ORIP P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Yerkes Virology Core

SPID#: 13031

UNIT/DIVISION: Admin.

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 37%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	

PROJECT DESCRIPTION:

The Yerkes Virology Core is provides serological and molecular viral diagnostic testing in support of Yerkes Research Services and Colony Management. The Core has developed a pipeline of diagnostic screens and tests which provide definitive diagnoses for the presence of infection by Simian Immunodeficiency Virus (SIV), Simian T Lymphotropic Virus (STLV), Simian type D retroviruses (SRV), and Simian Herpes B virus (Herpes-B). The presence of these viruses in rhesus macaques could confound the results of HIV vaccine and pathogenesis studies, present critical risks to human investigators accidentally exposed to rhesus macaque tissues, and could present significant health risks to the rhesus macaque colony as well. In addition to supporting the Specific Pathogen Free colony with viral testing services, the Yerkes Virology Core performs both custom virological assays (virus titration and growth) and kit-based CBA assays (e.g. rhesus cytokine assays) for clients across Emory University. The Core has also begun implementing methods to screen for pre-existing immunity to Adeno-Associated Viruses and is conducting preliminary experiments to begin screening for Zika infection in the rhesus macaque colony at Yerkes. Through the combined expertise of the leadership and technicians within this lab, and a close collaboration with the CFAR Virology and Molecular Biomarkers Core pre-clinical laboratory, the Yerkes Virology Core is extremely well-positioned to be the primary hub of virological and molecular diagnostic services across Emory University.

PROGRESS REPORT:

During the last year of funding, we have continued the validation process for our SRV-specific qPCR. We have constructed plasmids containing the PCR target sequences for SRV1-4 to use as copy number standards. Using highly accurate dilution series of linearized versions of these plasmids, we have tested the efficiency of the SRV qPCR protocol (slope = ~3.3) and the ability of the primers and probe to detect each SRV subtype with similar efficiency. Our initial experiments are promising with copy number over cycle threshold (Ct) slopes ranging between 3.32 – 3.47. Additionally, our lowest standard (~10 copies per reaction) is detectable around a Ct of 37 suggesting that our qPCR protocol is capable of detecting a single copy per reaction within a 40-cycle PCR. Further iterations on our standard dilutions are needed to verify equivalent efficiencies and detection limits. Once validated we will begin a yearlong process of external validation, comparing the results of our assay with those obtained from the Pathogen Detection Laboratory at the California National Primate Research Center. the Yerkes Virology Core has been providing services to screen rhesus macaques for pre-existing immunity to AAV5 by neutralization titer. While the Yerkes Virology Core has yet to identify animals with naturally occurring AAV5-specific neutralization titers lower than 1:40, we have identified several animals that have developed AAV5-specific antibody responses after intracranial exposure to a single high titer bolus of AAV5. The Core is currently validating our assay using AAV1, 2, 7, and 8.

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

PUBLICATIONS:
None

FUNDING SOURCES:
Mark Wilson, NIH, U24 OD011023
NIH/ORIP P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: BIOLOGICAL MATERIAL PROCUREMENT PROGRAM

SPID#: 0291

UNIT/DIVISION:

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 32%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Animal Resources	
Prin. NPRC Core Sci.		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Animal Resources	
		Pathology	
		Pathology	
		Pathology	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The provision of various biological specimens to Yerkes and non-Yerkes investigators is an important contribution to biomedical research at the host institution as well as other regional, national, and international institutions. Specimens provided to investigators result in a number of publications each year. These specimens have proven to be extremely valuable for educational purposes when used in undergraduate or graduate courses in anatomy, anthropology and will provide data to provide further support for future biomedical, and particularly HIV, studies. Specimens provided to these investigators included a variety of tissues; for example, bone marrow, blood, eyes, brain, biopsies, liver, kidney, semen, and urine from two nonhuman primate species.

PROGRESS REPORT:
During the reporting period, the Yerkes Center processed 42 specimen requests that resulted in the collection and provision of 279 samples. The samples collected were provided to 24 investigators of which 12 were located at Yerkes, 3 at Emory and 8 investigators at other institutions within the U.S. The Center has experienced a decrease in specimen requests. During this time period, 34 articles were published in peer-reviewed journals, all resulting from the receipt of specimens from the Yerkes Center.

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
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Excluded by Requester

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Excluded by Requester

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Excluded by Requester

FUNDING SOURCES:
NIH: ORIP/OD P51OD011132

Yerkes National Primate Research Center
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Pilot Projects

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: COGNITIVE AND SOCIOEMOTIONAL DEVELOPMENT AFTER POSTNATAL ANESTHESIA – Pilot Study

SPID#: 13032

UNIT/DIVISION: DCN

TYPE (indicate): Pilot (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester		
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This is a pilot study aimed at producing key preliminary data for a larger-scale project that will determine whether cognitive and socioemotional development is normal in monkeys that receive multiple exposures to the novel neurosteroid anesthetic drug Proprietary Info in the first six weeks of life.

PROGRESS REPORT:
This compound, developed by our colleagues Excluded by Requester Excluded by Requester (at Washington University and University of Colorado, Denver) is a very attractive new candidate agent for this purpose, because it produces surgical anesthesia in infant rodents without causing substantial neuroapoptosis or cognitive impairments in adulthood. Its effects on neurocognitive development in nonhuman primates have not been tested. Establishing Proprietary Info as a safe anesthetic in rhesus monkeys, both in terms of anesthetic physiology and in terms of lack of long-term neurocognitive effects, would be of enormous translational significance for developing Proprietary Info as an anesthetic for neonatal and pediatric surgery in humans. Therefore, to maximize the chances of a successful revised application for this proposal, we propose to obtain some preliminary data in infant rhesus monkeys exposed to either Proprietary Info or propofol, on the same schedule as our ongoing sevoflurane study, and then test their emotional reactivity at 6 months of age where we see a marked effect of early sevoflurane exposure on emotional behavior. This will address the specific aim of determining whether repeated exposure to the new anesthetic agent Proprietary Info in infant rhesus monkeys produces safe surgical anesthesia without impacting long-term neurocognitive development, unlike sevoflurane and, presumably, propofol. At present, we have completed the anesthetic exposures and will conduct the 6-month socioemotional testing over the next month.

PUBLICATIONS:
None

FUNDING SOURCES:
Private Source 4/1/16 – 3/31/17

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Neurodevelopmental consequences of Zika virus infection in infant rhesus macaques

SPID#: 13033

UNIT/DIVISION: M&I

TYPE (indicate): Pilot-Research (Management/Research/Pilot)

Percent P51 $: 100%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Emory Peds.	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

PROGRESS REPORT:

Zika virus (ZIKV) infection can have devastating neurologic consequences for infants infected in utero. Little is known, however, about the impact of ZIKV infection close to the time of delivery or in the period of infancy. To address this gap, we developed a model of postnatal ZIKV infection in infant rhesus macaques (RMs). Infant RMs were infected with 10(5) PFU of ZIKV strain PRVABC59 s.c. at five weeks of age. A subset of RMs was sacrificed soon after infection to determine tissue tropism of ZIKV in infants and another subset was followed longitudinally. Six infant RMs were challenged with ZIKV with peak viral loads in plasma at day 2-3 that cleared by day 10 after infection. Infant RMs developed anti-ZIKV binding IgG and IgM antibodies as well as neutralization titers in plasma. In two infant RMs sacrificed at the peak of viremia, ZIKV RNA was detected in multiple lymph nodes and the spleen. In two infant RMs sacrificed two weeks after infection, ZIKV RNA was additionally detected in the frontal cortex, parietal cortex, occipital cortex, cauda equina, and trigeminal ganglion. Structural T1-weighted magnetic resonance imaging (MRI), resting-state functional MRI, and Diffusion Tensor Imaging (DTI) performed at three and six months of age revealed increased size of the lateral ventricles, microstructural alteration in the corpus callosum, and reduction in the functional connectivity of the primary motor (M1) and somatosensory (S1) cortices in ZIKV-infected infant RMs as compared to age-matched controls. ZIKV-infected infants also showed emotional dysregulation during the Human Intruder task, failing to demonstrate the species-typical freezing behavior in response to an acute social stressor as compared to similarly reared controls. In summary, we demonstrate for the first time that postnatal ZIKV infection of infants disseminates into the central nervous system and has persistent structural and functional neurologic consequences.

PUBLICATIONS:

None

FUNDING SOURCES:
NIH P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Developing a novel optogenetic monkey model

SPID#: 13034

UNIT/DIVISION: NND

TYPE (indicate): Pilot (Management/Research/Pilot)

Percent P51 $: 100%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.			
Other Core and Affil.		NND	
		NND	
		NND	

PROJECT DESCRIPTION:

'Optogenetics', the introduction of light-sensitive channels into specific neurons that allows researchers to modulate the activity of these neurons by light in subsequent neurophysiological experiments, has revolutionized physiologic experimentation in rodents, facilitated by the availability of mature genetic tools and large numbers of transgenic rodent strains. However, the application of this technique to non-human primates (NHPs) has significantly lagged behind, in part because transgenic NHP lines are not readily available. Our ultimate goal is to develop a genetically modified NHP model to accelerate the application of optogenetic techniques in NHPs. This pilot study will allow us to develop and validate the necessary constructs and vectors, and generate preliminary data that will then enable us to apply for federal funding for this project.

We will create transgenic monkeys in which the expression of the opsins 'Jaws' (inhibitory) or 'Chronos' (excitatory) occurs only in catecholaminergic neurons, using a Cre-lox approach. To this end, we will create lentiviral vectors that carry the opsin sequences flanked by the loxP sequence, regulated by the ubiquitously expressed human polyubiquitin-C (Ubi) promoter, as well as vectors that carry Cre-recombinase (Cre), regulated by the tyrosine hydroxylase promoter (TH-Cre; TH is a marker of catecholamine neurons). The vectors will be validated in tissue cultures, and in monkeys that will be transgenic for both constructs (double transgenic, DTg). In these animals, opsin expression will only occur in those brain cells that also express Cre-recombinase, and will therefore be limited to TH-expressing catecholamine neurons.

PROGRESS REPORT:

We have created a conditional expression constructs for expressing opsin expression. cDNA for two constructs were cloned into lentiviral vectors (LVs), both under the regulation of the Ubi promoter. These include (1) a construct for red fluorescent protein (DsRed) with a STOP codon flanked with two loxP sequences and a fusion gene containing the sequence for green fluorescent protein (GFP) and Jaws (Jaws/GFP) named "LV-floxed-Jaws", and (2) a construct for yellow fluorescent protein (YFP) with a STOP codon flanked with two loxP sequences and a fusion gene containing the td-Tomato (tdT) and Chronos (Chronos/tdT) sequences, named "LV-floxed-Chronos". To create LVs for expressing Cre-recombinase under tyrosine hydroxylase (TH) promoter control, cDNA of Cre-recombinase and mOrange fluorescent protein (mO) was co-expressed by 2A peptide and cloned into the LV under the regulation of the TH promoter, generating the "LV-TH-Cre/mO" vector. All vectors have been created and currently assessing conditional expression of opsins. Two monkeys have been

assigned and currently preparing for identifying stereotaxic targets and surgical procedures for placing recording chamber.

PUBLICATIONS:

None

FUNDING SOURCES:
NIH ORIP P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Biological signatures of stress in mice and macaques

SPID#: 13035

UNIT/DIVISION: BNPD

TYPE (indicate): Pilot (Management/Research/Pilot)

Percent P51 $: 100%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	BNPD	
Prin. NPRC Core Sci.		DCN	
Other Core and Affil.		DCN	

PROJECT DESCRIPTION:

Adverse natural and anthropogenic events contribute to the development of neuropsychiatric disorders not only in individuals directly exposed to these events, but also in descendant generations, as reflected in recent studies of offspring of Holocaust survivors. Identifying and reversing biological mechanisms that underlie the development of neuropsychiatric disorders in these vulnerable populations requires an understanding of the biological signatures of stress exposure within somatic and germ cells of the population directly experiencing stress. Using a mouse model of paternal stress (Excluded by Requester Laboratory), two models of social stress in the non-human primate (Excluded by Requester Laboratories), and in collaboration with the Yerkes Genomics Core, the goal of this proposal is to examine how stress experienced by mice and rhesus macaques alters miRNA in circulating exosomes, cerebrospinal fluid (CSF) and sperm.

PROGRESS REPORT:

We exposed mice to olfactory stress and sequenced RNA present in circulation and sperm. In addition, we are in the process of isolating RNA from the non-human primate samples and will be sequencing this RNA within the next few months. Once these data are collected we will be using bioinformatics approaches to ascertain RNAs that are altered across these species as a function of stress. In so doing, we will illuminate conserved signatures of stress across species.

PUBLICATIONS:

None

FUNDING SOURCES:

NIH ORIP P51 OD011132

Yerkes National Primate Research Center
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Division of Developmental and Cognitive Neuroscience

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Sex Differences in the Social Brain

SPID#: 13036

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Psychology	Georgia State Univ
Prin. NPRC Core Sci.		DCN	
Other Core and Affil.		DCN	None

PROJECT DESCRIPTION:

In most mammalian species, social interactions among individuals of the same species are governed by dominance relationships. These hierarchical relationships are established and maintained by agonistic behaviors, including aggression. Importantly, data indicate that the mechanisms in the brain underlying aggression and attaining dominance also make individuals resilient to social stress while the mechanisms underlying subordinate status increase susceptibility to social stress. Despite the relation between social status and stress, the mechanisms that underlie dominance have received only limited attention in males and almost no attention in females. This project will fill this critical gap in our knowledge using rhesus monkeys to test an integrated series of hypotheses using rhesus monkeys that the agonistic behaviors responsible for the formation and maintenance of dominance relationships are regulated in dramatically different in males and females. Specifically, we propose that inhibition of serotonin (5-HT) promotes dominant status and a stress resistant phenotype in males while activation of 5-HT promotes dominance and a stress resistant in females. Positron Emision Tomography (PET) imaging will assess sex diffeences in 5-HY receptor !A binding to be used as predictors of stress physiology and behavior. Together, these data will significantly expand our knowledge of sex differences in brain chemistry that define social phenotypes and will provide innovative gender specific strategies for promoting resistance to social stress. The data obtained in this project could have an almost immediate clinical impact by guiding drug treatments for stress reduction in men and women.

PROGRESS REPORT:

None

PUBLICATIONS:

None

FUNDING SOURCES:

Excluded by Requester funded by NIMH

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: COGNITIVE and SOCIOEMOTIONAL DEVELOPMENT AFTER POSTNATAL ANESTHESIA

SPID#: 0683

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci			
Other Core and Affil.		None	Mt. Sinai SOM, New York, NY

PROJECT DESCRIPTION:
This project provides a critical translational model for assessing potential risks of anesthesia in pediatric populations, and for testing potential agents that may mitigate or eliminate this risk.

PROGRESS REPORT:
Using infant macaques, we evaluated the long-term consequences of exposure to sevoflurane, a common pediatric anesthesetic. Because general anesthetics may act as neurotoxins when given early in mammalian development, a critical question in anesthesiology is the long-term cognitive consequences of such exposure. This was Year 5 of this project. The animals in Cohort 2 have completed their testing and histological evaluations are in progress for all 20 subjects. A renewal for the project was submitted and we will submit an A1 in April. In addition to the peer-reviewed publications listed below, this work was presented by invitation at 3 conferences and 1 abstract presentation:

Excluded by Requester

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
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FUNDING SOURCES:

Excluded by Requester funded by NICHD

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ONTOGENY AND NEURAL BASES OF SOCIAL VISUAL ENGAGEMENT IN MONKEYS

SPID#: 13037

UNIT/DIVISION: Developmental and Cognitive Neuroscience

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	MPI	
Prin. NPRC Core Sci.	Excluded by Requester		
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Autism Spectrum Disorder (ASD) is a disorder defined by altered engagement with the social world that is already apparent at early stages of the disorder. Thus, increased knowledge on the critical periods of typical development during which these early social skills emerge and mature and on the underlying neurobiological systems that underlie these skills will give unprecedented opportunity to further understand the neurobiological source of the early diagnosis markers of ASD and develop new treatments. Research examining the precursors of human social abilities during early infancy has significantly increased in the last few years, yet critical information on the causes and neural bases of these early developing social skills is still lacking; the main limitations being neuroimaging the human brain in infancy, and to longitudinally follow brain-behavior relationship across development. Thus, knowledge in this domain must emerge from **translational research** examining both human populations and animal models. Thus, the **overarching goal of this proposal** is to follow longitudinally the maturation of social visual engagement processes, including attention to, detection and integration of social signals in normally developing rhesus monkeys, using "marker" tasks similar to those employed in the human populations to facilitate cross-species comparisons. At the same time, to investigate the potential brain networks responsible for the maturation of these basic social processes, the same animals has undergo a series of noninvasive neuroimaging procedures at the time they were behaviorally tested.

PROGRESS REPORT:

We have collected longitudinal behavioral and neuroimaging data on 16 additional infants from postnatal day 5 through 6 months. Behavioral and neuroimaging data analyses are ongoing and were performed using the data collected in the previous funded years. A comparison of how infants visually track faces of conspecifics or heterospecifics indicates that attention to conspecifics' faces decreased over time, whereas attention to heterospecific's faces increased over time. A second experiment examined developmental changes in the infants' preferences to look at faces with direct versus averted gaze. The results revealed that subjects attention to direct gaze faces increased sharply after birth and then returned to match the level of averted gaze faces after 3 months of age. Also, infants showed an overall preference to look at direct versus averted gaze faces. Preliminary analyses of the structural MRI data indicated significant structural developmental changes

in cortical white matter (WM) volumes in some of our networks of interest (e.g. right & left temporal visual cortex). The data, if confirmed, could represent axonal pruning followed by an increased WM volume due to myelination. Our preliminary DTI analyses also show developmental changes in structural connectivity in tracts of interest, i.e. object perception, motion and visuospatial attention pathways (as measured by increased structural integrity, measured as fractional anisotropy –FA). Finally, preliminary analyses focusing on the object perception and motion pathways suggest that functional connectivity (FC) between regions of interest along these pathways shows a nonlinear developmental pattern that differ between networks. For example, the ventral visual pathway from posterior V1 to anterior V3 shows an interesting inflection point between 4 and 8 weeks of age, reminiscent to that shown for the eye tracking and structural MRI data (see above). This developmental pattern seems specific to these visual pathways, as it is different in other pathways.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester PhD / NIMH

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: FUNCTION AND EVOLUTION OF COGNITIVE MONITORING AND COGNITIVE CONTROL

SPID#: 12012

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The proposed work will determine the functional role of cognitive monitoring for cognitive control in primates and will identify cognitive systems are accessible to cognitive monitoring and those that are not, across lemurs, monkeys, and apes. This work will extend studies of the role of monitoring in cognitive control using converging approaches. First, the extent to which monkeys regulate the amount of information they acquire prior to taking tests will be determined. Second, these studies will determine the extent to which monkeys strategically exercise cognitive control only when necessary and adaptively allocate monitoring among competing tasks. Third, the work will leverage access to a unique, language trained orangutan to evaluate the extent to which language-like mental representations contribute to cognitive monitoring and control. Fourth, the work will assess what information monkeys monitor when making metacognitive judgements. Cognitive systems accessible to cognitive monitoring in monkeys will be distinguished from those that are not by testing for dissociations between accuracy and confidence in tasks in which multiple memory systems contribute to accuracy, and in psychophysical tests that dissociate motor and perceptual processes. Comparative studies of lemurs, monkeys, and apes will determine the extent to which there have been changes in cognitive control through primate evolution.

PROGRESS REPORT:

We have initiated some experiments on cognitive control and completed others. We have found and reported shifting cognitive control throu the process of reversal learning. We have discovered post-encoding control of memory in monkeys. We have most recently completed a study suggesting that while monkeys can introspecitively monitor the decay of memory due to delay interval, they are unable to introspectively monitor the strenthg of habits.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES:

Excluded by Requester funded by National Science Foundatinon

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Stress and pubertal timing affect amygdala functional circuitry in females.

SPID#: 13040

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester		NYU
Prin. NPRC Core Sci.	Excluded by Requester	DCN	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Psychosocial stress during childhood is a risk factor for psychopathology, which increases dramatically during adolescence. One potential explanation is the interaction effect of stress and increased levels of gonadal hormones on drastic neurodevelopmental changes that take care around puberty. We propose to investigate the neurobiological bases of these links by examining the effects of psychosocial stress and the timing of puberty on intrinsic brain functional organization in a female rhesus macaque model. Socially housed female macaques organize into a dominance hierarchy in which subordinates are subject to frequent harassment in an environment that mimics the unpredictable nature of human social environments, providing an ethologically valid model for studying long-term neurobehavioral effects of psychosocial stress. More important, the model permits experimental manipulations to disentangle the effects of stress, chronological age, and puberty. Using a unique set of resting state fMRI (rsfMRI) data already collected from 67 adolescent females from all social hierarchies (dominant, subordinate and middle-ranking) we are studying both the impact of social subordination stress and pharmacological pubertal delay on functional connectivithy of prefrontal-amygdala circuits, critical for emotional and stress regulation. We focus on amygdala circuitry, particularly connections with ventromedial prefrontal cortex, based on neuroimaging evidence of stress-related alterations in this circuit as well as its sensitivity to gonadal steroids. This study in females is timely, given the steep drop in the age of the onset of puberty in the US, the high rates of psychopathology during adolescence and the public health burden. Our aims focus on the identification of mechanisms linking psychosocial stress and puberty-related increases in gonadal steroids to emotional dysregulation, as well as targets for interventions aimed at ameliorating the long-term effects of psychosocial stress and reducing women's psychopathology burden.

PROGRESS REPORT:

Our project is focused on the analysis of rs-fMRI data from scans that were already collected in all animals post-puberty (either spontaneously -in the control group-, or 3 months after cessation of Lupron treatment - GnRH analog used to delay puberty by suppressing estradiol [E2] secretion- in the group of females with pubertal delay). This experimental design allows us to determine how social stress and delayed puberty (i.e. shorter exposure to E2) affects neurobehavioral development in Lupron-treated compared with Control females, who have similar chronological age but who experienced a more prolonged exposure to E2.
After optimizing the pre-processing and analytical methods and pipelines for the rsfMRI data, resulting in increased image quality,y preliminary findings in small subset of animals suggest that subordinate animals have weaker prefrontal-amygdala functional connectivity than dominants during adolescence, at least at the

post-pubertal age. Pubertal delay induced by Lupron treatment also reduced prefrontal-amygdala functional connectivity, particularly in dominant animals. Thus, the dominant, untreated group showed the highest functional connectivity in these corticolimbic circuits, which was associated with better emotional and stress regulation than the rest of groups. An additional social rank x Lupron treatment interaction was detected, with only the dominant group being affected by delayed puberty could be explained by the fact that subordinate control animals (i.e. non-treated with Lupron) have delayed puberty onset anyway. It is possible, then, that the weaker prefrontal-amygdala connectivity in Subordinates than dominants is due to their natural delayed pubertal onset. We have now completed the preprocessing of all the 67 animals in the study and are performing statistical analysis for final manuscript preparation this Spring/Summer 2017.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NICHD

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: CONTE CENTER FOR THE STUDY OF MENTAL DISORDERS, PROJECT 3 "EFFECTS OF OXYTOCIN ON SOCIAL COGNITION IN MALE RHESUS MONKEYS"

SPID#: 13041

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Psychobiology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This project is part of a larger center grant (a Conte Center grant) in collaboration with Excluded by Requester Center for Translational Social Neuroscience, Yerkes NPRC, Emory University. It is currently in its final year.

PROGRESS REPORT:
The project examined the effects of oxytocin on social cognition, social reward, and stimulus salience in rhesus monkeys. We have completed several computerized tasks including a sequence learning memory task and a task examining the ability of monkeys to process gaze direction. In the final year, will perform eye tracking on monkeys after receiving either oxytocin or placebo to determine how these compounds affect social information processing. We are also conducting resting state functional neuroimaging to determine how oxytocin vs placebo affects the strength of connectivity between social brain regions.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIMH

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: EFFECTS OF CHRONIC OXYTOCIN ON THE DEVELOPMENT OF BRAIN AND SOCIAL BEHAVIOR IN INFANT RHESUS MONKEYS

SPID#: 13042

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Psychobiology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This is the second year of an R01 to examine the effects of chronic oxytocin administration on the development of behavior and neural functioning in infant rhesus monkeys.

PROGRESS REPORT:
Major activities during this period included continued dosing of our infant cohort, 3x per week with the three doses of intranasal oxytocin (IN-OT), high dose (3x per week), low dose (1x OT and 2x saline per week) and the placebo (3x saline per week). Around 17 weeks of age, we switched from hand holding the infants and using a aerosol cone to placing the infants inside a custom built box into which we streamed the aerosolized OT. To facilitate the distribution of the aerosol, we incorporated 2 nebulizers and halved the dose of OT in eachosing will continue until the infants are 2 years of age. The oldest infants, born in March of 2015 are nearing this milestone.
Behavioral observation data have been collected weekly for infants from their first week of life. These analyses are continuing and will be the focus on data collection in years 2 and 3. All of the behavioral data from the first 6 months of life has now been coded and data are being summarized for analyses, which will take place early in 2017.
Imaging analyses have begun. All infants have received their 2, 8 and 14 month scans and a few of the 20 month scans have been completed. All 2, 8 and 14 month scans have been pre-processed. This includes the following steps, performed using FSL and custom scripts.

PUBLICATIONS:
Excluded by Requester

FUNDING SOURCES:
Excluded by Requester funded by NIMH

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: EARLY LIFE STRESS AND ADOLESCENCE COCAINE ABUSE: Neurobiological vulnerabilities

SPID#: 13043

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci.			
Other Core and Affil.	Excluded by Requester	NND	

PROJECT DESCRIPTION:

Although adolescence is a period of high vulnerability for the development of lifelong drug addiction, including cocaine, with tremendous health and societal costs in the US, the neurobiological mechanisms are not understood. Here we examine this question in a highly translational nonhuman primate (NHP) model during adolescence testing the hypothesis that exposure to early life stress (ELS) is an important risk/vulnerability factor. The premise is that ELS increases emotional/stress reactivity in primates, particularly in females, making them particularly vulnerable to cocaine addiction and relapse. We use a highly translational macaque model of early life stress (adverse maternal care), building on ongoing longitudinal studies of developmental alterations exhibited by the animals with ELS experience, which have been characterized by our group since birth using a unique crossfostering design that rules out confounding effects of heritability on outcome measures. We have evidence that the adverse experience leads to increased emotional reactivity and alterations of prefrontal connectivity during the infant period, and we are now examining whether these alterations (1) persist during adolescence and (2) underlie increased risk to cocaine abuse. The focus is on alterations in the dopaminergic and serotonergic systems and prefrontal connectivity with the striatum and amygdala. We hypothesize that the increased emotional reactivity and poor stress regulation characteristic of ELS individuals exacerbates cocaine self-administration and reinstatement, and that females will be more vulnerable than males. The study also uses a pharmacological intervention, through pharmacological blockade of the $5HT_{2A}$ receptor during cocaine abstinence to reduce the risk of relapse. A critical aspect of this proposal is its focus on adolescence, as it is the developmental period when humans initiate drug consumption and has been rarely examined in NHP models.

PROGRESS REPORT:

We have examined in most of the animals (20 out of 25; the additional 5 youngest ones are undegoing initial testing right now) the following: (1) baseline measures of emotional and stress neuroendocrine reactivity to a novelty challenge, (2) baseline and fear-potentiated acoustic startle using an AX+/BX- paradigm, plus modulation of fear responses using safety signals, (3) neurobiological measures of dopaminergic (DA) and serotonergic (5HT) systems via colletion of cerebrospinal fluid and *in vivo* positron emission tomography (PET) to examine binding potential of $5HT_{1A}$, $5HT_{2A}$ and D2 receptors, as well as (4) prefrontal connectivity with the

striatum and amygdala using resting state functional connectivity MRI. Since last report period we have also made significant progress in the (5) cocaine self-administration studies, where almost half of the animals have now progressed through the studies of acquisition, escalation, extinction and reinstatement. Alhough we are still collecting, processing and analyzing data, our preliminary findings using the AX+/BX- *Acoustic Startle paradigm* suggest that the animals with early life stress (ELS) experiences, particularly females, have exaggerated fear-potentiated startle responses and show impaired ability to discriminate fear from safety signals during testing, which is one of impairments exhibited by humans with PTSD and other anxiety disorders. Interestingly, our preliminary data also suggests that females with ELS history show higher cocaine intake than controls during the self-administration studies, supporting our initial hypotheses. We will keep on collecting data as planned in the grant.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester and Excluded by Requester funded by NIDA

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Stress and the genome: testing the impact of social effects on gene regulation

SPID#: 12034

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester		Duke University
Prin. NPRC Core Sci.		DCN	
Other Core and Affil.		None	University of Montreal

PROJECT DESCRIPTION:

The social environment has a profound impact on human health. Chronic social stress and reduced access to social support lead to dysregulation of the immune system, increase the risk for diseases ranging from cardiovascular disease to the common cold, and, through these effects, influence mortality risk itself. Understanding the basis for these effects and how best to address them are important priorities for improving human health. However, the mechanistic relationships linking social stress to disease risk are still poorly understood, particularly on the level of genome regulation. A major obstacle in studying this relationship is the sheer complexity of the human social environment. An individual's exposure to social stress at work may differ substantially from the same individual's exposure to social stress in the family or community. Additionally, the effects of social stress, especially that induced by socioeconomic status, may be complicated by associated differences in access to resources, occupation, and other health risk factors. Isolating the direct biological effects of social stress *per se* therefore presents a substantial challenge. However, the social environment is also of demonstrated importance in other highly social species, including many nonhuman primates. Using a well characterized, translation model, this project is assessing the impact of social status to investigate the genomic mechanisms underlying the biological effects of dominance rank-induced chronic social stress in female rhesus monkeys. Our study is focusing on captive macaque females organized into social groups in which individual social status is experimentally manipulated. This design allows us to establish causal relationships between social status and gene regulation and test the degree to which an individual's history of exposure to social stress continues to influence gene regulation if stress is resolved or newly imposed.

PROGRESS REPORT:

The data set includes: (i) RNA-seq data for purified helper T cells, cytotoxic T cells, B cells, monocytes, and natural killer cells; (ii) RNA-seq data for control, lipopolysaccharide -treated (to mimic bacterial infection), and Gardiquimod-treated blood samples (to mimic mimics viral infection); and (iii) reduced representation bisulfite sequencing data to profile genome-wide DNA methylation levels for natural killer cells and helper T cells. To understand the mechanisms that contribute to rank effects on gene expression, we have also generated complementary chromatin accessibility data using ATAC-seq and RNA-seq data to identify glucocorticoid responsive genes for a subset of females. This information has been essential for identifying major transcription factors that mediate social status-related differences in gene regulation, such as NFkB and several interferon regulatory factors. The cell type-specific data set and part of the LPS response and ATAC-seq data sets are incorporated into a manuscript, so have already been deposited into NCBI's Gene Expression Omnibus (GSE83307). Our analyses indicate that

low ranking females have more exaggerated pro-inflammatory responses to infection due to increased activity of the MyD88-dependent arm of the Toll-like receptor 4 signaling pathway (TLR4 is the primary receptor for LPS). In contrast, the TLR4 response in high-ranking females is polarized towards the TRIF-dependent arm, which is important in the anti-viral response. We predict that these differences may affect the disease conditions most closely associated with social status. In addition, we showed that high social status predictes increased engagement in positive social relationships, and that status, rather than stable individual tendencies, drove this pattern. We also found that social status influences both temperament and HPA axis regulation. Further, we showed that improvements in dominance rank across the two phases of our study increased experimentally induced cortisol suppression and glucocorticoid negative feedback.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester unded by NIGMS

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Automated tracking of monkey groups:recognition of social structure and behavior

SPID#: 13044

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci.			
Other Core and Affil.	None	None	

PROJECT DESCRIPTION: Develop an RfID automated tracking system to track multiple monkeys in a complex social group at the Yerkes Field Station. Develop a customized monkey collar containing multiple active RfiD tags. Instrument an outdoor compound to detect and use RfiD signals to located and identify individuals 24hrs per day, 7 days per week. Develop a behavioral inference engine to extract social behavior from tracking data. Develop and RfiD guided video system that will allow collection of video snips of individually identified animals. Develop computer vision programs that can automatically identify individuals and patterns of social behavior.

PROGRESS REPORT: Developed prototype RfiD collars. Developed and indoor test arena with precisely described dimensions to prototype tracking system (this doesn't use monkeys, but is use to verify accuracy of tracking data). Developed software to identify social structure of a monkey group using pilot data on a 6member monkey group previously collected. Developed software pipeline for processing tracking data to make it amenable to using for the identification of behavioral patterns. Initiste design of instrumentation of outdoor compound.

PUBLICATIONS:
None

FUNDING SOURCES:
Wallen, K / 1R24 OD020174-01A1

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Stress and obesity synergize to impair neurobehavioral development

SPID#: 13019

UNIT/DIVISION: DCN

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci.		DCN	
Other Core and Affil.			

PROJECT DESCRIPTION:

Studies of both animals and children show that postnatal stress may have lasting effects on brain structure and function, resulting in behavioral and cognitive impairments, particularly for females. What is unclear, however, is how these effects emerge during childhood and whether social stress experienced by the mother during gestation synergizes with postnatal stress experienced by her offspring to produce these phenotypes. Importantly, other environmental factors that may interact with stressor exposure to affect brain development during childhood are often overlooked, most notably the consumption of calorically dense diets (CDDs) and emerging obesity. Not only may increasing fat mass accelerate the tempo of puberty but limited data in children suggest the developing brain is vulnerable to these metabolic insults, as increased body fat is associated with altered brain structure and deficits in cognition and emotional processing. Understanding the impact of obesity on neurodevelopment is critically relevant, given alarming rates of obesity in children, likely due to the consumption of CDDs - a dietary environment quite unlike the typical low caloric diets (LCD) fed animals used as models for children. Key biological signals in this synergistic stress-obesity effect could be stress and diet-induced elevations in cortisol and proinflammatory cytokines. Prospective studies of the developmental origins of health and disease are difficult to do in children. However, socially housed rhesus monkeys provide a unique translational model, as social subordination is a naturalistic stressor that produces distinct stress-related phenotypes; pre- and postnatal exposure to this stress can be controlled through cross-fostering at birth; juvenile females are susceptible to diet-induced increased fat mass; and innovative neuroimaging protocols and bio-behavioral assessments can be applied longitudinally from birth. Importantly, this model allows the identification of the biological signals mediating the synergistic impact of chronic social stress and fat mass on neurobehavioral development.

PROGRESS REPORT:

A complete data set will not be available until all subjects, recruited over 3 years, reach the target ages. Our current data suggest animals start eating solid food at ~ 2 mo, with a developmentally progressive increase in kcal consumed with age. Subjects in the dietary choice condition are consuming significantly more kcals than females restricted to the chow diet and the majority of calories in the choice condition are from the CDD. Importantly, menarche has occurred in the oldest cohort, and was advanced in females in the choice dietary condition, even in subordinates. We are in the process of completing neuroimaging analyses for the cohort recruited in 2014 through 16 mo of age. We examined changes in functional connectivity (FC) between the prefrontal cortex (PFC), amygdala (AMYG) and Nucleus Accumbens (NAcc) using rsfMRI, to test the hypothesis that stress and access to an obesogenic diet during infancy results in weakened FC in PFC-AMYG

and PFC-NAcc circuits, leading to impaired emotional regulation and "top-down" control of behavior. Data suggests that orbitofrontal cortex connectivity with both AMYG and NAcc is stronger in subordinate animals, and associated with increased infant behavioral reactivity (e.g. tantrums, screams) and daily Kcal consumption at 6 mo of age. In contrast, medial PFC connectivity with NAcc was affected by both diet condition and rank, so that females in the choice diet condition had weaker FC; however, this was only seen in dominant females as subordinates had stronger FC than DOM overall. This suggests that even during infancy the effects of social subordination and an obesogenic diet are detectable in PFC-AMYG-NAcc neurocircuits involved in the control of emotional reactivity, impulsivity and reward. Further analyses are necessary to assess the impact of social subordination and diet on neurobehavioral development and what biological signals mediate the effects of stress and diet and neurobehavioral outcomes.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NICHD

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Sustaining factors and interventional strategies for emotional feeding in females

SPID#: 13020

UNIT/DIVISION: DCN

TYPE (indicate): RESEARCH (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	DCN	
Prin. NPRC Core Sci.			
Other Core and Affil.			

PROJECT DESCRIPTION:

Data indicate that more women than men in the US are obese and are at increased risk for a number of adverse health outcomes. Because some individuals regulate intake even in a rich dietary environment where both a low caloric (LCD) and high caloric diet (HCD) are available, identifying factors that increase vulnerability to overeating is critical. Indeed, emotional feeding resulting from chronic exposure to psychosocial stressors, is likely a precipitating factor for overeating. It is probable that stress-induced feeding involves the dopamine (DA) reward pathways. Indeed, exposure to chronic psychosocial stress increases susceptibility to an addictive phenotype, reducing DA 2 receptors (D2R) in mesolimbic regions resulting in a hypo-dopaminergic condition. Furthermore, simply eating a HCD reduces D2R in these same regions but only in some animals. Thus, exposure to psychosocial stressors coupled with eating HCD may impair DA pathways and promote emotional feeding to compensate for a stress-induced dysfunctional DA system. Clearly, this is not a healthy coping strategy for unresolved stress. An issue particularly important for people attempting to lose weight is whether these stress-induced changes, including impaired DA function, persist in the face of healthier dietary choices and life style changes. Attempts to lose weight often fail, as people overeat in response to emotional states. In addition, it is unknown if the alleviation of chronic psychosocial stress will restore caloric restraint, or if changes in systems regulating appetite, including DA, persist after stress is resolved. Longitudinal studies systematically varying diet and repeatedly assessing behavior, stress responsivity, and central DA function are not possible women. Thus, this project is using socially housed female rhesus monkeys as a translational model for women to identify mechanisms that sustain emotional feeding in diverse dietary environments and to identify possible intervention strategies to reduce the health burden imposed by excess eating.

PROGRESS REPORT:

Data from previous years showed accumulative harrassment of subordinate females by higher ranking group mates predicts greater caloric intake but only for females in a dietary choice environment where both a LCD and HCD were available. Furthermore, data showed that elevated morning cortisol predicted increased caloric intake for females in a dietary choice environment and this was mediated by reduced D2R binding potential in the orbitofrontal cortex (OFC). During the current funding period we expanding our undertsnding of stress and diet induced neuroadaptations that account for greater caloriv intake. Using resting state functional MRI, the data show that reduced D2R BP in the right OFC and left dorsal lateral PFC is also associated with reduced functional connectivity FC between the left insular cortex and the anterior cingulate cortex (ACC) and reduced FC between these two regions predicts more caloric intake. Furthermore, increased diurnal concentrations of plasma cortisol also predicts reduced FC between the right and left nucleus accumbens and ACC. Reduced

FC between these two regions predicts greater total caloric intake. These patterns of FC between the PFC, insula, and striatum were not observed in females maintained on the laboratory chow diet (LCD), indicating that the dietary environment interacts with stress hormone signaling to compromise circuits that regulate cognitive control of behavior. Importantly, that data show that, in addition to plasma cortisol, elevations in the proinflammatory cytokine,elevated IL-6, and greater subordinate status are associated with reduced mPFC – NAcc FC that, in turn, predicts greater calorie intake. These associations are not observed in females maintained on a healthier LCD, underscoring the importance of an obesogenic diet on these pathways.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIDDK

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Division of Behavioral Neuroscience and Psychatric Disorders

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Ontogenic factors in adolescent-emergent depression and decision-making

SPID#: 13004

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes X No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Pediatrics	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Depression symptom onset in adolescence increases the rate of depression *recurrence* and *treatment-resistance* across the lifespan, and treatment options for adolescents are increasingly limited since the FDA issued a black box warning in 2007 for common antidepressant medications for individuals aged 25 and younger. A history of stressor exposure is the primary predictor of depression, begging the questions: Are adolescent populations uniquely impacted by exposure to stressors and adversity? And if so, why? The answers may relate to the impact of stressor exposure on the prefrontal cortex, which reaches full structural maturity only at the end of adolescence.

This proposal aims to: ***1)*** delineate critical periods during which exposure to corticosterone or social isolation — both of which confer long-term depressive-like behavior — impact dendritic spine pruning and refinement during adolescence. These experiments will chart the developmental trajectory of deep-layer dendritic spine remodeling during adolescence under both normal and pathological circumstances.

We will then ***2)*** test the antidepressant-like utility of pharmacological compounds that act on neurotrophin systems and Rho-kinase, both of which regulate structural maturation. Finally, ***3)*** we will identify neuroanatomical and neurophysiological mechanisms of goal-directed decision-making. This is critical because goal-directed action is diminished in depression, resulting in cyclical patterns of malaise, unemployment, and social withdrawal.

PROGRESS REPORT:

This year, we have made considerable progress, in particular on: ***1)*** Mapping the developmental trajectory of deep-layer neurons exposed to exogenous corticosterone (CORT);
2) determining whether the novel trkB agonist, 7,8-DHF, has antidepressant-like effects;
3) determining the role of BDNF-trkB in the orbitofrontal cortex (oPFC) in regulating actions and habits;
4) characterizing the antidepressant-like effects of fasudil and their neurobiological mechanisms;
5) publishing our key findings to date.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIMH

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Application of ifenprodil following adolescent cocaine exposure

SPID#: 13045

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes X No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Pediatrics	
Prin. NPRC Core Sci.			
Other Core and Affil.			

PROJECT DESCRIPTION:

Adolescent cocaine abuse increases the risk and severity of lifelong addiction and decreases the likelihood that cocaine-abusing individuals will seek treatment. Developing and understanding therapeutic approaches that mitigate maladaptive decision-making and cocaine-seeking behaviors in organisms with a history of cocaine exposure during adolescence could reduce the high societal cost of cocaine addiction.

In **Aim I**, we will test the hypothesis that individual differences in cocaine self-administration in adolescence determine effects on orbitofrontal cortex (oPFC) dendritic spines, such that mice that escalate are more susceptible to spine deficiencies in adulthood. We will then assess whether ifenprodil, an NR2B-selective NMDA receptor antagonist that blocks the reinstatement of heroin-, nicotine-, and alcohol-seeking behaviors in rodent models will also have therapeutic-like effects after adolescent cocaine exposure, *occluding* cocaine-induced habits.

In humans, adolescent cocaine exposure increases the risk of substance use, dependence, and relapse in adulthood. In **Aim II,** we will examine whether individual differences in cocaine self-administration in adolescence are associated with individual differences in cocaine self-administration and the reinstatement of cocaine seeking in adulthood. We expect that mice with a history of escalating cocaine exposure will respond more for cocaine as adults and be more likely to reinstate responding after extinction conditioning. In these experiments, ifenprodil will be paired with extinction training in an attempt to mitigate the reinstatement of cocaine seeking. This approach models the use of ifenprodil as a therapeutic adjunct to behavioral therapy in humans and is strongly supported by our preliminary findings.

PROGRESS REPORT:

This grant just began last summer. We have initiated several experiments, and our preliminary data indicate that adolescent mice with a history of cocaine exposure: ***1)*** better discriminate between cocaine and saline, and ***2)*** are more prone to cue-, but not context-, induced reinstatement of drug seeking following abstinence.

PUBLICATIONS:

None; project just began

FUNDING SOURCES:

Excluded by requester funded by NIDA

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Selective targeting of PI3K to restore higher cognitive function in FXS

SPID#: 13046

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes X No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Pediatrics	Cincinnati Children's Hospital
Prin. NPRC Core Sci.		Pediatrics	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

In this project, my lab has been responsible for the administration of rodent behavioral work pertaining to assessing complex decision-making in mice lacking *Fmr1* selectively within the prefrontal cortex. As such, my lab performed surgical procedures to generate knockdown mice for behavioral characterization, as well as additional surgeries to generate critical brain tissue for [redacted] lab. Next, we assessed whether a novel inhibitor of the PI3-kinase (PI3K) would be sufficient to rescue decision-making abmormalities following *Fmr1* knockdown and knockout.

PROGRESS REPORT:

The key outcomes from this subcontract are that we discovered that a novel inhibitor of PI3K was sufficient to correct cognitive abnormalities following prefrontal cortex-selective *Fmr1* knockdown, and additionally, in *Fmr1-/-* mice. These findings suggest that such pharmacotherapies could alleviate certain symptoms of fragile x syndrome. We also discovered in the course of these experiments age-dependent consequences of *Fmr1* knockdown in the orbitofrontal cortex. Our primary findings are being prepared for peer review currently, as are our age-dependent findings (in an independent report).

PUBLICATIONS:

None; manuscripts in preparation

FUNDING SOURCES:

Excluded by Requester funded by NIMH

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Rolipram revisited: New roles for PDE4 and AMPK in the etiology of affective disorders

SPID#: 13047

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	BNPD / Psychiatry	
Prin. NPRC Core Sci.			
Other Core and Affil.			

PROJECT DESCRIPTION:
The goal of this proposal is to investigate the effects of metabolic challenge on the physiology of principal neurons in the basolateral amygdala and subsequent affective behavior.

PROGRESS REPORT:
In this reporting period we have continued to push forwards in our examination of the deleterious effects of metabolic disruption on the properties and function of principal neurons in the basolateral amygdala (BLA). In

Submitted

Submitted

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
R01 MH069852-A2 (Rainnie, PI) 04/01/2016 – 03/31/2021 EFFORT
NIH/NIMH $250,000
Rolipram revisited: New roles for PDE4 and AMPK in the etiology of affective disorders.

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Novel Approaches to Enhance Social Cognition by Stimulating Central Ox

SPID#: 12035

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	BNPD	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The goal of this project is to investigate how a melanocortin receptor agonist, Melanotan II (MTII), alters neuronal activation to facilitate changes in social cognition. It is known that stimulation of the melanocortin 4 receptor (MC4R) enhances oxytocin release, and oxytocin improves social cognition in patients with autism. We therefore propose that MC4R agonists such as MTII could be useful for improving social functioning in clinical populations. Using the highly social prairie vole as our rodent model, we sought to identify how neuronal activity across the brain is altered following administration of MTII in the context of social interaction.

PROGRESS REPORT:
We have previously published results showing that MTII facilitates the formation of partner preferences in prairie voles, and enhances oxytocin release in the nucleus accumbens, one of the known oxytocin-sensitive regions of the social salience network. Activity within the social salience network is critical for social cognition, and may be impaired in persons with autism. Here we investigated the effect of MTII-enhanced oxytocin release on patterns of neuronal activation within multiple brain regions, including the nucleus accumbens (NAcc), prefrontal cortex (PFC) and the paraventricular nucleus of the hypothalamus (PVN) using immunohistochemistry. We have shown that in the absence of social stimuli, neither peripheral nor central administration of MTII increase neuronal activation within the social salience network. In contrast, adding 30 minutes of social exposure with a novel conspecific after drug treatment significantly increases the number of activated cells within multiple regions of the social salience network. This includes the PVN, a site where oxytocin is produced, and the NAcc and PFC, two brain regions where oxytocin acts to affect social cognition. These early results were gathered from experiments in female prairie voles, and we are in the process of replicating all findings in males. The demonstration that peripheral MTII crosses the blood brain barrier and alters neuronal activation patterns in a manner almost identical to the results observed with central

administration is of considerable significance. No pharmaceutical treatments currently exist which can be administered peripherally to affect oxytocin activity within the brain. Enhancing oxytocin release, and therefore neuronal activation, within the social salience network in a context-dependent manner makes melanocortin agonists a highly attractive potential therapeutic in the treatment of social deficits.

PUBLICATIONS:
None

FUNDING SOURCES:

Larry J. Young, PhD and Kara Kittelberger. Funded by NIMH (1F31MH106298)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: SILVIO O. CONTE CENTER FOR OXYTOCIN AND SOCIAL COGNITION

SPID#: 13006

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	BNPD	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		BNPD DCN DCN	

PROJECT DESCRIPTION:

The goal of this project is establishe an interdisciplinary to explore the effects of oxytocin on functional connectivity and social cognition using prairie voles, rats, rhesus macaques, healthy human subjects and individuals with autism. The Conte Center uses a highly collaborative, coordinated and integrative approach across all models to discover general principles of oxytocin function and mechanisms of action.

PROGRESS REPORT:

Using electrophysiology we have simultaniously recorded from the prefrontal cortex (PFC) and the nucleus accumbens (NAcc) of prairie voles during social bond formation and found that theta oscillations in the PFC modulate gamma oscilations in the NAcc. Under Review

Under Review

Under Review Using oxytocin antagonist infused ICV or directly into the NAcc of prairie voles we demonstrated that oxytocin facilitates the coordinated neural activity in a network of brain regions involved in processing social information and reward. We have identified a polymorphism in the vole oxytocin receptor that predicts 80% of the variation in expression of the oxytocin receptor in the NAcc. In rats we have demonstrated that prenatal valproic acid treatment recapitulates several behavioral phenotypes associated with autism. !0 rhesus macaque males have been trained to self administer oxytocin and have been trained in a touchpad social cognition task. We have developed a small molecule antagonists that is highly selective for he primate oxytocin receptor and demonstrated that it penetrates the blood brain barrier in NHP. Finally, we have completed social cognitive testing in healthy human subjects and subjects with autism. We have submitted the IND to the FDA and the IRB in order to begin the intranasal oxytocin administration in conjuction with fMRI to examine the effect oxytocin on functional connectivity in human subjects.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Larry J. Young, PhD. Funded by NIMH (1P50MH100023)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: OXYTOCIN RECEPTORS AND SOCIAL BEHAVIOR

SPID#: 12036

UNIT/DIVISION: BNPD

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	BNPD	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The goal of this project is to explore the relationship between genetic polymophisms in the oxytocin receptor gene, oxytocin receptor gene expression in the brain, and social behaviors in prairie voles. In addition, we explore the effect of early-life social deprivation on later life social behaviors. Finally, we explore the effect of oxytocin on neural communication between brain regions involved in social information processing and reward.

PROGRESS REPORT:

We have identified a set of 14 single nucleotide polymorphisms (SNPs) that robustly predicts the density of oxytocin receptor (OXTR) in the striatum, but not in other brain regions, of prairie voles. These SNP's explain 80% of the variation in nucleus accumbens (NAcc). This work was published in *Biological Psychiatry*. Since the 14 SNPs are in perfect LD in our Yerkes, we have obtained approximately 100 animals, 30 of which are wild caught, that we will genotype and analyze OXTR expression to help narrow down which SNPs are most likely functional. We have found that a single prolonged stressor, potentially modeling PTSD, results in an impairment of social bond formation. This impairment is rescued with a treatment of paroxetine. Using oxytocin antagonist infused ICV or directly into the NAcc of prairie voles we demonstrated that oxytocin facilitates the coordinated neural activity in a network of brain regions involved in processing social information and reward. Thus endogenous oxytocin enhances neural communication across a social salience network, and the Nacc is an important hub in that network. Blocking oxytocin receptors in the NAcc resulted in reduced coordinated activity with the prefrontal cortex. This work paralells nicely recent human imaging work examining the influence of genetic polymorphisms or intranasal oxytocin on functional connectivity in the brains of healthy subjects or individuals with autism.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center

Excluded by Requester

FUNDING SOURCES:

Larry J. Young, PhD. Funded by NIMH (R01MH096983)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Division of Neuropharmacology and Neurologic Diseases

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: A GENE AND PROGENITOR CELL THERAPY IN HUNTINGTON'S DISEASE MICE

SPID#: 13023

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excl udedby Requester	NND	
Co-Investigator	Exc luded by Requester	BNPD	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The goal of this project is to investigate if genetically corrected nonhuman primate neural progenitor cells derived from transgenic Huntington's monkeys (rHD-NPCs) provoke a therapeutic impact when implanted into HD mouse brain, determined by clinical assessments including behavioral tasks, neural pathology and molecular analyses. We will reduce the expression of mutant huntingtin in rHD-NPCs by expressing small hairpin RNA specifically targeting the huntingtin gene (shRNA-htt), followed by intracranial implantation in HD transgenic mice.

PROGRESS REPORT:
We have demonstrated that the knock-down of HTT levels by shRNA in HD-NPCs does not affect neural and astrocyte differentiation but significantly reduce the expression of HTT and the accumulation of oligonmeric mHTT, reverse apoptosis and enhance tolerance of oxidative stress in vitro. However, when grafting in HD mice, HD-shRNA-NPCs did not benefit motor deficit when compared to WT-NPC graft but was similar to HD-NPC grafts. One possible explanation is the low survival rate of the HD-shRNA-NPC grafts in HD mouse brains compared to WT-NPC grafts while HD-NPC grafts were largely undetectable. Comparing to NPC grafts in WT-mouse brain, all cell grafts shown better survival. These results suggest the micro-environment of the recipient brain might influent HD-NPC graft survival even mutant HTT level was reduced and WT-NPC did not seem to be affected. However, the low survival of HD-shRNA-NPC in HD mouse brain may also suggest if mHTT expression was effectively suppressed. Nonetheless, grafting with WT-NPC was able to improve motor performance of HD mice which suggest the potential benefit of cell replacement therapy in HD.

PUBLICATIONS:

Excl udedby Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:
Anthony Chan, DVM, PhD; 1R21NS084163-01

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: A NOVEL TRANSLATIONAL MODEL OF AUTISUM SPECTRUM DISORDER

SPID#: 13024

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Co-Investigator			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

A fundamental roadblock in primate research and primate modeling of human diseases has been the development of genetic knockdown or knockout strategies. In this proposal, we will incorporate recent successful technology for genetic manipulation in rodents and apply that to a groundbreaking new effort in non-human primates. Specifically, we will exploit exciting new and compelling reports regarding SHANK3 genetic associations in patients with Autism-spectrum disorders (ASD) to develop the first-ever transgenic primate model for ASD. The aims of this grant strongly complement the expertise of our group in transgenic monkey technology, thus suggestive of a highly successful and very high-impact outcome.

PROGRESS REPORT:

We have demonstrated that all SHANK3-gRNA candidates can successfully target the SHANK3 gene by creating indel mutation and resulted in sifnificant reduction of the SHANK3 protein using CRISPR/Cas9 technology. This result provide strong evident to further evaluate targeting efficiency of SHANK3-gRNA candidates in rhesus macaque early embryos. This is a critical step toward our ultimate goal of developing SHANK3 gene targeted rhesus monkey model studying autism spectrum disorder.

PUBLICATIONS:

None

FUNDING SOURCES:

Anthony Chan, DVM, PhD; 1R21MH100670-01

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Using Non-human Primate Pluripotent Stem Cells to Treat Male-factor Infertility

SPID#: 13049

UNIT/DIVISION: NND

TYPE (indicate): Research

Percent P51 $:

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	-------
Prin. NPRC Core Sci.	None	None	
Other Core and Affil.	None	None	

PROJECT DESCRIPTION:

Spermatogenesis is a critical process that ensures transmission of the paternal genome to offspring during fertilization. However there are a number of external factors that can affect spermatogenesis even resulting in sterility. Males, who would normally be fertile, are rendered sterile by exposure to environmental and industrial toxicants, medical interventions such as chemotherapies and immune suppressant treatments, and injury. While advances in fertility preservation during cancer therapies has improved fertile outcomes after treatment cessation, there still exists a number of male patients that have survived cancer but are permanently sterile. In cases where a sperm sample is not available or provided before the onset of sterility, these males are unable to ever father a child with their partner due to a lack of production of functional gametes. To date, there are no treatment options for these individuals and they are permanently sterile. Stem cell treatment options resulting in in vitro derived functional gametes represent one potential solution to enable these male patients to produce offspring with their partner. Thus an in vitro model for spermatogenic differentiation culminating in functional spermatids is essential for advancing stem cell treatments to treat infertility. This proposal seeks to build upon our recently published model that shows the ability of human pluripotent stem cells to differentiate into advanced germ cell lineages, including spermatogonia, spermatocytes, and spermatids. Using rhesus pluripotent stem cells, we propose to examine whether in vitro derived spermatids generated by our protocol are capable of fertilizing an oocyte and developing to the blastocyst stage in culture. In order to perform this research, we propose to stimulate female rhesus macaques and collect follicles for fertilization by ICSI.

PROGRESS REPORT:

We generated several key outcomes in this first experiment: 1) our *in vitro* spermatids are NOT capable of activating an oocyte on their own. This speaks to the maturity of our *in vitro* products. 2) Our *in vitro* spermatids are capable of undergoing early fertilization events including DNA decondensation and pronuclear formation. 3) Because we obtained pronuclear apposition in one embryo activated by co-injecting fertile rhesus sperm, we can deduce that our spermatids are capable of sperm aster formation. 4) *in vitro* spermatids are capable of contributing to zygotic DNA. The outstanding progress we have made on the first run leaves us very optimistic about successfully completing our project

PUBLICATIONS:

None

FUNDING SOURCES:
OD020182 (ORIP/NIH)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Transgenic Huntington's Disease Monkey Resource

SPID#: 13050

UNIT/DIVISION: Div Neuropharm Neurologic Dis

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	-------
Prin. NPRC Core Sci.		DCN	
Other Core and Affil.	None	None	

PROJECT DESCRIPTION:)

The proposed study has evolved based on our success in the creation of a transgenic Huntington's disease (HD) monkey model sponsored by the ORIP. Transgenic HD monkeys recapitulate disease progression and develop clinical features similar to HD patients. In order to facilitate the preclinical application of the HD monkey model, a *Transgenic Huntington's Disease Monkey Resource (THDMR)* will be established to provide a high quality HD monkey model for investigators. In addition, a biomaterial repository will also be established and served as a resource for HD research. To further safeguard the unique genetics of the HD-NHPs and availability of the HD-NHPs, HD sperm cryopreservation methods will be developed and optimized. Sperm cryobank will be established for future distribution and reanimation of the HD monkeys.

PROGRESS REPORT:

We have been focused on getting back to the original status of the project prior to the award of the Administrative Supplement and the renewal grant. We have established a small breeding colony including females with prior pregnancy and normal menstruation for the production of F1 HD-monkeys. Our ongoing effort is also developing the alternative plan proposed in the project to promote the breeding of HD-monkeys because of the concern of progressive decline in fertility in HD-monkeys. Thus the unspent fund of the Administrative Supplement will be critical for this development to allow us to catch up from the delay caused by transition to the renewal grant.

Recently, two key findings were published early this year. First, a report on the progressive decline in cognitive behaviors and neuroanatomical changes in HD monkeys was published in PLoS One. Second, the production of second generation HD monkeys by artificial insemination was published in Theriogenology. Also, the establishment of the THDMR has been reported through several conference presentations including the Gordon Conference entitled "CAG triucleotide repeat disorder" in Italy.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:
OD010930 (ORIP/NIH)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Asynchronous Distributed Microelectrode Neuromodulation for Epilepsy

SPID#: 13051

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	SOM / NND	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Epilepsy, occurring in 1 percent of the world's population, of this population, 30 percent of epilepsy cases are medically intractable, leaving surgical interventions as the only option for treatment. Whereas open resection, the current surgical standard of treatment, can yield seizure freedom rates as high as 60-80 percent, these are often associated with cognitive dysfunction. Particularly, patients with dominant hemisphere mesial temporal lobe epilepsy (MTLE). We have recently found in a rodent MTLE model, that delivering asynchronous pulses distributed across a multielectrode array, at low frequency, is more effective than macrostimulation. The objective of this project is to optimize asynchronous distributed multielectrode stimulation (ADMES) on a non-human primates (NHP) model.

In aim1, we implement ADMES in our NHP model and quantify effects on seizure and adverse effects on memory. In parallel, we will characterize the response of physiological biomarkers such as synchrony to allow us to develop both open-loop and closed-loop control policies to optimize these biomarkers as a proxy for seizure control.

In aim 2, the most effective stimulation parameters will be implemented in 8 NHPs using the RC+S neurostimulator and benefit on seizure frequency and memory will be evaluated. If seizure reduction is ≥50% then we will advance to an early clinical study.

In aim 3, we will identify electrophysiological biomarkers and characterize the effects of stimulation parameters informed from our NHP study on those biomarkers during invasive monitoring of MTLE patients and then move to an early feasibility trial of ADMES in 6 patients.

In aim 4, the final stimulation parameters will be implemented in RC+S and behavioral seizure reduction and memory testing for safety will be quantified over 12 months. Positive results should lay the foundation for a larger clinical trial for MTLE, with possible application to the other epilepsies.

PROGRESS REPORT:

New

PUBLICATIONS:

None

FUNDING SOURCES:

Excluded by Requester PhD; NIH-NINDS

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Udall Parkinson's Disease Research Center at Emory University: Core B

SPID#: 0681

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Core B of the Udall Parkinson's Disease Research Center serves to primary functions: (1) to prepare and process the brain tissue from experimental animals generated by all of the Udall Center's projects, and (2) to generate and evaluate parkinsonian Rhesus macaques using systemic administration of MPTP. The Core provides standardized histology services to center researchers, which will be indispensable to interpret the functional experiments, Similarly, all MPTP-treated parkinsonian monkeys to be used are treated and evaluated using standardized procedures by core B personnel. This will help to integrate and compare data generated from these projects. By providing these services, the Core helps to free up time and resources from the research projects, and center research will benefit by the use of standardized, well-establish anatomical and behavioral assessment techniques

PROGRESS REPORT:
Our funding period started on 9/30/2016. The core has started its operation by purchasing the necessary equipment and histologic supplies. We have also optimized our techniques of standardized evaluation of animal tissue as well as developing novel video-based techniques to evaluate motor deficitis in parkinsonian animals. The first animal tissue will become available for processing in the spring of this year.

PUBLICATIONS:
None

FUNDING SOURCES:
NIH/NINDS

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: IMPACT OF SELECTION PRESSURE FOR SOCIAL BEHAVIOR ON CANID BRAIN EVOL

SPID#: 13038

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	-------	Emory SOM (Neurology)
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
In progress during the reporting period. This project studies variation in brain structure related to selection for specific social behaviors in different dog breeds and in wild vs. tame strains of silver foxes.

PROGRESS REPORT:
To date, we have scanned representatives of 27 dog breeds with in vivo MRI, and > 3 individuals each of aggressive-selected, tame-selected. and wild-type Siberian silver foxes with ex vivo MRI. Cluster analysis, carried out In collaboration with Excluded by Requester), shows that the brain morphology of different breeds reflects their relatedness. Moreover, as expected, the different silver fox morphs show differences in the sizes of brain structures involved in regulating social behavior. We are currently piloting a battery of behavioral assays to evaluate the social behavior of different dog breeds.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester
NSF IOS 145729

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Dopamine neurotransmission in a model of DOPA-responsive dystonia

SPID#: 13052

UNIT/DIVISION: NND

TYPE (indicate): Research subproject (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Pharmacology	
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION: Dopamine neurotransmission in a model of DOPA-responsive dystonia

PROGRESS REPORT:

The goal of this project is to further characterize the synaptic plasticity of the glutamatergic corticostriatal system in a mouse model of dopamine-responsive dystonia (DRD). The mutant mice used in these studies were developed in the laboratory of Excluded by Requester Based on recent findings gathered from these animals (Excluded by Requester), we hypothesized that striatal neurons undergo spine pruning and that the morphology and ultrastructural features of corticostriatal glutamatergic terminals are altered in DRD. To directly test this hypothesis, we processed striatal tissue from DRD and WT mice for the immunohistochemical localization of the vesicular glutamate transporter 1 (vGluT1), a specific marker of cortical glutamatergic terminals in the striatum, at the electron microscopic level. The Serial Block Face scanning EM (SBF/SEM) approach was used to prepare serial ultrathin images of vGluT1+ terminals and their postsynaptic targets which were then reconstructed using the RECONSTRUCT software. Preliminary data suggest that the volume of vGluT1-positive terminals and their post-synaptic targets are significantly increased in the striatum of DRD mice. The area of the asymmetric postsynaptic densities at cortical glutamatergic synapses is also increased. Thus, these preliminary data strongly suggest that the corticostriatal synapses display maladaptive pasticity that may result in abnormal strengthening of these synapses and consequent dysregulation of GABAergic striatal outflow in DRD. Combined with results of in vitro electrophysiology studies that will be achieved in this project, our electron microscopy data will provide evidence that the reduced striatal dopamine release in DRD induces permanent changes in the synaptic connectivity of the corticostriatal glutamatergic system, which may contribute to the pathophysiology of DRD in humans.

PUBLICATIONS:

None

FUNDING SOURCES:

Hess, Ellen / NINDS, R01NS088528

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Pathomechanisms of dopamine dysregulation in DYT1 dystonia

SPID#: 13053

UNIT/DIVISION: NND

TYPE (indicate): Research subproject (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Pharmacology	
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Pathomechanisms of dopamine dysregulation in DYT1 dystonia: Targets for Therapeutics

PROGRESS REPORT:
The goal of this project is to elucidate the cellular and neurochemical mechanisms that underlie the reduced release of dopamine in the striatum of DYT1 mice model of dystonia. The specific contribution of our labaoratory to this project is to determine if dopamine terminals in the striatum of DYT1 mice undergo ultrastructural changes that might account for a low release of striatal dopamine. More specifically, we use high resolution three dimensional electron microscopy immunocytochemistry to analyze in fine details the morphometry of individual dopamine terminals and compare those between WT and DYT1 mutant mice. During the previous funding period, both WT and DYT1 mice have been euthanized and striatal tissue has been processed for the immunohistochemical localization of tyrosine hydroxylase (TH-marker of dopamine terminals) at the light and electron microscopic level. Areas of striatal tissue have been embedded in resin and prepared for 3D electron microscopy analysis using Serial Block Face scanning EM (SBF/SEM). Series of serial images of TH-psoitive terminals have now been collected and ready to be analyzed and reconstructed using the software RECONSTRUCT. Following reconstruction, morphometric parameters such as the volume of terminals, number and size of synaptic vesicles, area of synaptic contacts, postsynaptic targets, etc.… will be measured and compared between the two animal groups. These findings will allow to determine if abnormal structural development of dopamine terminals may account for reduced striatal release of dopamine in DYT1 dystonia.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester / Department of Defense (DOD)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: PET IMAGING & COCAINE NEUROPHARMACOLOGY IN MONKEYS

SPID#: 0050

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Co-Investigator		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

This research program effectively integrates behavioral pharmacology and i.v. drug self-administration, in vivo neurochemistry with microdialysis, and functional brain imaging with PET and fMRI to better understand the neuropharmacology of abused stimulants. The experimental approach is highly translational in its focus on medications development and its emphasis on brain imaging techniques that can be extended directly into human studies. We are the only research group worldwide that has the capacity to integrate these approaches in nonhuman primate models of drug addiction.While the acute effects of cocaine on brain neurochemistry have been well characterized, much less is known about the long-term changes in neurochemistry and brain function associated with chronic drug use. Clearly, a better understanding of the neurobiology underlying the progression to dependence and addiction will help direct appropriate treatment strategies.

PROGRESS REPORT:

We completed an extensive series of studies evaluating the sleep-disrupting effects of methamphetamine self-administration and normalization of sleep by 5-HT2 receptor compounds. There is a high comorbidity between sleep disorders and substance abuse and we have previously shown that methamphetamine self-administration significantly disrupts sleep in rhesus monkeys. To the best of our knowledge, no study has evaluated the ability of any pharmacological intervention to attenuate the sleep-disrupting effects of methamphetamine under well-controlled conditions in laboratory animals. The objectives of this study were to examine the effects of a 5-HT2A receptor antagonist and a 5-HT2C receptor agonist, given alone and in combination. Both compounds dose-dependently improved sleep-like measured disrupted by methamphetamine by decreasing latency to sleep onset and sleep fragmentation, and increasing sleep efficiency compared to vehicle. By combining these compounds, their sleep-promoting effects significantly were enhanced. Hence, agonists at the 5-HT2C receptor and antagonists at the 5-HT2A receptor show promise as potential treatments for the sleep-disrupting effects of stimulants when used alone and in combination.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:
Leonard Howell, PhD; NIH/DA010344

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Evaluation of the novel antipsychotic SEP-363856 with fMRI in primates

SPID#: 13025

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.			
Other Core and Affil.	Excluded by Requester	None	

PROJECT DESCRIPTION:
Psychosis is a significant public health problem. In recent year, a large body of research has explored the effects of neurotransmission on the pathophysiology of schizophrenia and psychosis. Of particular interest is N-methyl-D-aspartate (NMDA)-dependent neurotransmission as a key mechanism in cognitive dysfunction. It is well known that NMDA-receptor antagonists, like ketamine, mimic the neurobehavioral correlates of psychosis. This has led to a well-established ketamine-induced NMDA receptor hypofunction model of schizophrenia-related cognitive deficits in healthy human subjects that is used to study the pathophysiology of these diseases and explore pharmacotherapeutic interventions. The general aim of this project is to fist validate a ketamine-psychosis model in nonhuman primates (rhesus macaques) using functional magnetic resonance imaging (fMRI). The second aim is to use the model to examine the efficacy of the novel antipsychotic pharmatherapeutic SEP363856.

PROGRESS REPORT:
Ketamine infusion induced extensive changes in functional connectivity. In particular, functional connectivity to the dorsolateral prefrontal cortex (dlPFC) was increased in several cortical and subcortical regions. Pretreatment with risperidone largely attenuated ketamine-induced changes in functional connectivity. The results are highly consistent with similar human imaging studies showing ketamine-induced hanges in functional connectivity, as well as a significant attenuation of these changes when ketamine infusion is preceded by pretreatment with risperdone. The extensive increases shown in functional connectivity to the dlPFC are consistent with the idea that disinhibition of the dlPFC may be a key driver of the antidepressant and psychotomimetic effects of ketamine.

PUBLICATIONS:
Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: REGULATION OF MOTOR FUNCTION IN PARKINSON'S DISEASE

SPID#: 0369

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This project is focused on the striatal mechanisms involved in the development of motor abnormalities in the evolution of Parkinson's disease. Specifically, studies in this project are concerned with the role of striatal glutamatergic transmission in the pathophysiology of abnormal motor responses to dopamine replacement therapy. The specific aims of this project are focused on characterizing the responses of striatal projection neurons to dopamine inputs in the context of chronic dopamine denervation and altered responses to dopaminergic stimulation. The goal of these studies is to identify changes in these neuronal circuits that could be targeted to develop new treatments for the long-term therapy of Parkinson's disease.

PROGRESS REPORT:
Specific aims 1 and 2 consisting of analyzing the physiologic changes of striatal projection neurons in advanced parkinsonism and testing the role of glutamatergic transmission have been completed and the data analyzed and partly published. We have demonstrated a critical abnormality in the activity of these neurons that is present in the non-human primate model and humans with Parkinson's disease.

In the past year, we have also completed the preparation of a series of studies aimed at generating preliminary data for a grant renewal application. The pilot studies of optogenetic identification of striatal neurons have produced positive results, and we are moving forward with the design of a large-scale study. Other pilot studies have also generated significant data, indicating several promising therapeutic avenues to target striatal mechanisms of dysregulation in Parkinson's disease. We have also published the human study of abnormal striatal activity that validates all our primate findings and underlies the importance of this striatal mechanisms. We also have prepapred a comprehensive report of our extensive studies of selective NMDA and AMPA receptor blockade in the striatum of advanced parkinsonian monkeys. These results demonstrated the link between ionotropic glutamate receptor signaling mechanisms and abnormal motor responses to dopamine replacement. In Preparation

Pending Support

PUBLICATIONS:
Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Stella Papa, MD; NIH-NINDS 2R01 NS045962

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: MANIPULATING GENE EXPRESSION IN THE DYSKINESIAS OF PARKINSON'S DISEASE

SPID#: 0688

UNIT/DIVISION: NND

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

This project is focused on the role of the transcription factor deltaFosB in the striatal mechanisms associated with the development of levodopa-induced dyskinesias in Parkinson's disease. The planned studies test the effects of transgenic manipulation of deltaFosB protein expression in non-human primates. The novel approach taken in this project is aimed at addressing pathophysiologic aspects and help develop new therapies. The project includes three specific aims that use viral vectors to induce or suppress gene expression in the striatum of parkinsonian primates that have developed abnormal responses to L-dopa, particularly levodopa-induced dyskinesias.

PROGRESS REPORT:

Aims 1 that consisted of the study of behavioral and molecular changes following the overexpression of deltaFosB in the striatum of parkinsonian primate using gene induction has been completed. Aim 2 that consisted of the study of physiologic changes in the same primate model using single cell recordings is also completed. All experimental work in these aims and data analyses have been completed.

In the past year, we advanced studies of Aim 3 (effects of deltaFosB down-regulation). Currently these studies are near completion of the rodent phase using gene silencing. We are also preparing the communication of all results obtained in studies of aims 1 and 2. Our data demonstrate that deltaFosb plays a major role in the development of LID and validates targeting its expression or associated molecular pathways for preventing these disabling complications of dopamine replacement therapy in Parkinsons's disease. With this objectives,

Pending Support

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:
Stella Papa, MD; NIH - NINDS 1R01 NS073994

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: A NEW PDE INHIBITOR FOR PARKINSON'S DISEASE

SPID#: 13054

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

This project is focused on the role of the cyclic nucleotide phospho-diesterase 10A(PDE10A) in the striatal regulation of motor function aiming at developing a new therapy for Parkinson's disease. PDE10A is highly expressed in the striatum where it participates in signaling mechanisms related to cognitive and motor function. Recently, selective PDE10A inhibitors have been synthesized, and preclinical tests of these agents have shown significant motor effects. However, their pharmacological profile in the context of Parkinson's disease is lacking. These studies are aimed at testing in acute and chronic trials the potential benefits of a selective PDE10A inhibitor for the treatment of motor symptoms in parkinsonian primates. We planned to study the effects of a novel, selective PDE10A inhibitor as monotherapy and co-therapy with L-Dopa. In these trials, studies comprise the potential antiparkinsonian as well as antidyskinetic effects. Also tests of co-administration with dopamine agonist are planned in order to assess the targeted mechanisms for the motor effects of PDE10A inhibition.

PROGRESS REPORT:

We completed the pilot tests of escalating doses of the PDE10A inhibitor to determine the best doses for assessment in acute and chronic trials. We also completed the tests of several doses of L-dopa to determine the adequate inidividual doses to use in co-administration tests. Subsequently, we continued with the evaluation of the new compound in acute co-therapy tests. We found significant PDE10A inhibitor effects on the motor responses induced by L-Dopa in a group of five advanced parkinsonian primates. We found positive effects of a range of doses of the drug when given in combination with L-dopa optimal and suboptimal doses. All data have been analyzed and are now being processed for the preparation of a report.
Currently, we are testing the effects of PDE10A inhibitor in co-therapy with L-Dopa in a "chronic" trial using the L-dopa suboptimal dose. Motor effects are assessed together with other effects related to sedation, autonomic dysfunction, and other behavioral changes as measured with the 'Drug Effects on the Nervous System' scale. These studies are important to determine the potential toxicity of these new agents. The next phase will be the tests of monotherapy and the test of co-administration with dopamine agonists. The pharmacokinetics of the compound in the parkinsonian primate will also be profiled in views of clinical application.

PUBLICATIONS:

None

FUNDING SOURCES: Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: NEURAL MARKERS OF COMBAT STRESS IN MILITARY WORKING DOGS

SPID#: 13055

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Military working dogs exposed to combat are reported to develop a condition similar to human PTSD. This project uses MRI to identify differences in brain anatomy and connectivity between dogs exposed to combat and control animals.

PROGRESS REPORT:
In progress during the reporting period. To date, too few dogs have been received from the military to yield meaningful conclusions.

PUBLICATIONS:
None

FUNDING SOURCES:

Excluded by Requester
Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: The Neuroendocrine & Neurobiological Bases of Complex Social Behavior

SPID#: 13056

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Anthropology	
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The purpose of this study is to investigate the role of oxytocin and vasopressin systems in explaining species-specific behaviors in baboons

PROGRESS REPORT:
Behavioral obsercations have been completed. Brain specimens have been collected. Nearly all biological samples (blood, urine, CSF) have been collected. Data analyses have not yet been completed.

PUBLICATIONS:
None

FUNDING SOURCES:
NSF

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: TRAINING IN SYSTEMS AND INTEGRATIVE BIOLOGY NEUROSCIENCE

SPID#: 0513

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This NIH training grant represents the main source of funding for students enrolled in the Emory Neuroscience program. In 2016-2017, this training grant supported parts of the stipends, tuition fees, activity fees and other training expenses for seven second year students in the neuroscience graduate program. Among those three are Personal Info Trainees nominated for training grant support are chosen based on their academic performance during their first year in the program and their general participation in program activities. In addition to financial support, trainees use some of these funds to invite a guest speaker for the weekly seminar series sponsored by the program. The trainees are in charge of inviting their guest, organize their visit and host them when they come to Emory. This has proven to be an excellent opportunity for students to interact with well-known researchers in their field of interest. All trainees also received funds to cover expenses to attend the annual Society for Neuroscience meeting (or another meeting of their choice), which provided them a unique exposure to the field of neuroscience research.

PROGRESS REPORT:
n/a

PUBLICATIONS:
None

FUNDING SOURCES:
Yoland Smith, PhD; NIH/NIGMS T32GM08605

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Udall Parkinson's Disease Center at Emory University: Circuitry to Therapy

SPID#: 0680

UNIT/DIVISION: NND

TYPE (indicate): Research subproject (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION: Anatomy and synaptic plasticity of the basal ganglia-thalamocortical loops in Parkinson's disease

PROGRESS REPORT:
The goal of this new project (since Nov 01, 2016) is to examine the anatomy and plasticity of the synaptic connections between the motor cortex and the basal ganglia-receiving regions of the ventral motor thalamus (BGMT) in control and MPTP-treated parkinsonian monkeys. To achieve this goal, we use a broad range of tract-tracing methods combined with immunocytochemical approaches at the light and electron microscopic level. Preliminary data obtained during the past funding period can be summarized as follows: (1) There is a significant thalamic denervation of deep cortical layers in the primary motor cortex (M1) of MPTP-treated monkeys, (2) Thalamic terminals target both spines of projection neurons and dendrites of putative interneurons in M1 of control and MPTP-treated monkeys, (3) The number of thalamic terminals that form multiple synapses with various targets in M1 is increased in MPTP-treated monkeys, (4) Cortical glutamatergic terminals belong to a homogeneous population of small boutons densely packed with round synaptic vesicles and a few mitochondria in BGMT of control monkeys, (5) The prevalence of cortical terminals in contact with GABAergic interneurons is increased in BGMT of parkinsonian monkeys. Together, these preliminary data suggest that the thalamocortical and corticothalamic connections undergo significant plastic changes in the parkinsonian state. These anatomical changes may underlie various aspects of the pathophysiology of the basal ganglia-thalamocortical loops in Parkinson's disease.

PUBLICATIONS:
None

FUNDING SOURCES:
NINDS, Udall Center of Excellence for Parkinson's disease

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ION: A summer research immersion for high school students and teachers

SPID#: 13058

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Biology	Georgia State Univ.
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
ION/TEACH: A summer research immersion for high school students and teachers

PROGRESS REPORT:
This project aims at supporting rising senior high school students and high school or middle school teachers interested in neuroscience to join research laboratories at the Yerkes Primate Center, Emory University and Georgia State University for a period of 10 weeks during the summer. In addition to provide students with faculty mentoring and resources to achieve their project, this grant covers the trainees' stipends and allow them to attend series of workshops and mentored activities to prepare for college education and neuroscience research. At the end of the training period, each student and teacher must present the results of their summer project orally to their peers, ION program leaders and research colleagues from the laboratories they trained in. During the past funding period, four students and one teacher joined the Yerkes Primate Center as part of this program. We expect the same number of trainees to be part of this program in summer 2017. Overall, this NIH-funded training program provides young students a unique opportunity to be exposed to the daily activities of a neuroscience research laboratory and helps them set a research foundation they can build on as they undertake their college education. Similarly, the teachers benefit tremendously from this program, not only through their gained research experience, but also the guidance provided by the ION leaders in the development of neuroscience teaching curriculum for their science classes.

PUBLICATIONS:
None

FUNDING SOURCES:
NIH, R25MH095735

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: DEFINING THE PROPERTIES OF PATHOGENIC AB STRAINS IN ALZHEIMER'S DISEASE

SPID#: 13059

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Co-Investigator		Emory University, Dept of Chemistry	
Co-Investigator		Emory University, Dept of Chemistry	
Co-Investigator			Ga Tech

PROJECT DESCRIPTION:

Excluded by Requester is the PI of Project 3 of the Emory Alzheimer's Disease Research Center (Excluded by Requester ADRC PI). The goal of the project is to evaluate the variability in the structure and function of aggregated Aβ as it relates to the pathogenesis of AD.

PROGRESS REPORT:

In the past year, we published the results of an analysis showing that aggregated Aβ in aged nonhuman primates, which has the same amino acid sequence as Aβ in humans, forms assemblies with different ligand-binding characteristics from those in humans Excluded by Requester. This finding is significant in that nonhuman primates do not develop AD, and presents clues to the particular pathogenicity of Aβ assemblies in humans. We also initiated studies of differences in binding of luminescent conjugated oligothiophenes (LCOs) which indicate that Aβ assemblies differ ("strains") in hereditary and idiopathic cases of AD. Studies are underway to characterize these diverse assemblies using electron microscopy and various biophysical methods. We also have shown that the transfection of yeast cells bearing the Aβ42-based chimeric construct (Aβ42-NR-MC) with in vitro-produced aggregates of Aβ42 produces multiple [Aβ+] prion strains, probably due to multiple nucleation sites generated during amyloid aggregation in vitro. In addition, expression constructs for studying interactions between Aβ and other proteins in yeast were prepared. In biophysical analyses, we initiated enrichment of Aβ assemblies following a range of published protocols and looking at co-assemblies with other biopolymers of the cellular matrix including RNA. Efforts to transfer our Aβ40 seeding protocols to Aβ42 were unsuccessful, indicating that these peptides form structures that seed optimally in different sets of conditions (or contexts). We also demonstrated that the nucleating core of Aβ does not cross-seed parallel and antiparallel assemblies, consistent with recently published results of propagation

Excluded by Requester

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES:
Allan Levey, MD, PhD; NIH/NIA - P50 AG025688

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: THALAMIC INTERACTIONS WITH THE STRIATUM

SPID#: 13022

UNIT/DIVISION: NND

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	N/A
Prin. NPRC Core Sci.		NND	N/A
		NND	N/A
Other Core and Affil.		NND	N/A

PROJECT DESCRIPTION:

The 'motor' thalamus is known to receive prominent basal ganglia input. Studies have demonstrated that thalamic projections do not only reach the cerebral cortex, but also project back to the basal ganglia. The most prominent of these projections arise from the intralaminar thalamic nuclei, with additional projections from other thalamic centers, including specifically the ventral anterior and ventrolateral nuclei. These projections differ anatomically, and may also be differentially affected by neurodegenerative diseases, such as Parkinson's disease. This project utilizes cutting-edge optogenetic techniques to examine the functional effect of the thalamostriatal projections in normal and parkinsonian monkeys (with electrophysiology), and to examine their anatomic patterns of termination in the striatum (using light- and electron microscopic methods). The optogenetic work utilizes AAV transfection. Transfection and the subsequent recording studies are done using MRI-based targeting approaches.

PROGRESS REPORT:

We continued the analysis of data from previously recorded animals which received injections of a viral vector solution carrying the genes for the excitatory opsin C1V1 into the CM/Pf for tests of light-evoked electrophysiological responses in the striatum. We analyzed the activity of 41 caudate and 487 putamen neurons. Activation of opsins on thalamic terminals decreased firing in approximately 40% of caudate and 20% of putamen neurons. Fewer than 10% of the recorded neurons showed light-induced increases in firing. One monkey was subsequently rendered moderately parkinsonian with systemic injections of MPTP. In subsequent putamen recordings we found that only 1 of the recorded 205 neurons responded to light stimulation in the parkinsonian state (decreasing its firing). The (unexpected) preponderance of reductions in firing of striatal neurons during optogenetic stimulation of thalamostriatal terminals in the normal state indicates that activation of thalamic terminals prominently engages intrastriatal (or other) inhibitory circuits. The absence of responses in the parkinsonian state may have resulted from the degeneration of CM/PF terminals. We are currently completing recordings in the normal state in two additional animals. These animals will then be treated with MPTP.

With regard to Aim 2, we examined whether the (known) loss of thalamus-originating vGluT2-containing terminals in the striatum of parkinsonian monkeys affects preferentially the thalamic innervation of striatal cholinergic interneurons. We found that the number of vGluT2-negative terminals forming synapses with dendrites of cholinergic interneurons greatly outnumbered that of vGluT2-positive terminals in both control and parkinsonian monkeys. The same was true for the synaptic relationships between vGluT1-positive (i.e.,

corticostriatal) or -negative terminals. The low prevalence of vGluT2-positive thalamic terminals in contact with cholinergic cells is at odds with results from tract tracing studies, perhaps suggesting that the CM/Pf-striatal fibers originate from vGluT2-positive and vGluT2-negative neurons that target specific groups of striatal neurons.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Wichmann, Thomas / NIH/NINDS NS083386

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ADMINISTRATIVE CORE (UDALL CENTER, CORE A)

SPID#: 0677

UNIT/DIVISION: NND

TYPE (indicate): Administration

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		NND	School of Medicine

PROJECT DESCRIPTION:
The Udall Center's administrative core supports Parkinson's disease-related research activities of the investigators at the Udall Center and facilitates communication between Center personnel, other Emory researchers, the Center's advisory boards, the general public, other Centers within the Udall Center network, and the NIH. The core organizes regular meetings of project leaders, quarterly meetings of the basal ganglia research community at Emory, meetings with internal and external scientific advisors, and meetings of the Center's outreach board. The core organized also the participation of center personnel at the annual Udall Center network meeting, and administers the Center's pilot grant program. Another essential function of the core is to work with the administrative staff at the Yerkes center to track the financial health of the center, and to compile progress and budgetary reports for the NIH. The Center provides educational opportunities for students, postdoctoral fellows, and clinical residents and fellows, such as lectures, journal clubs and hands-on training.

PROGRESS REPORT:
The core of the Udall Center started its activities in the late summer of 2016. It has organized the aformentioned meetings between investigators at the Center and the national Udall Center network. We also have had already 2 quarterly seminars, and are planning a third, and are busy with setting up this year's community outreach event, scheduled for May 2017. An RFA for this year's pilot grants was issued in December, and responses will be reviewed soon.

PUBLICATIONS:
None

FUNDING SOURCES:
Wichmann, Thomas / NIH/NINDS P50NS071669, now P50NS098685

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: UDALL PARKINSON'S DISEASE CENTER AT EMORY UNIVERSITY

SPID#: 13060

UNIT/DIVISION: NND

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	N/A
Prin. NPRC Core Sci.		NND	N/A
		NND	N/A
Other Core and Affil.			Emory College (Biology)
		NND	
			Emory School of Medicine
		NND	

PROJECT DESCRIPTION:

This Center helps electrophysiologists and anatomists to collaboratively study the pathophysiology of parkinsonism, and to examine and optimize the effects of existing treatments for Parkinson's disease. It receives strong internal support that helps it to fund Parkinson's disease related pilot grants, invite seminar speakers, and organize effective education and outreach programs. The Center consists of three tightly linked projects and two cores. The research sheds light on the poorly understood parkinsonism-related activity changes in thalamus and cortex which, in turn, will help us to better understand the pathophysiology of parkinsonism, and to optimize existing neuromodulation strategies and to develop new ones. Project 1 (led by Excluded by Requester utilizes brain slice and in vivo recordings in rodents, as well as a neural computational approach to develop mechanistic models of thalamocortical dysfunction in parkinsonism. Project 2 Excluded by Requester explores thalamic and cortical abnormalities in parkinsonian monkeys, using selective activation and inactivation approaches which are designed to study corticothalamic, pallidothalamic and thalamocortical information transfer. Project 3 Excluded by Requester examines morphological changes in the thalamic and cortical microcircuitry in parkinsonian primates. All projects are supported by an administrative core (Core A, Excluded by Requester Excluded by Requester, and an anatomy and behavior core (Core B Excluded by Requester which provides immunohistochemistry and electron microscopy services to all of the center projects, and standardized MPTP treatment and quantification of parkinsonism to the primate experiments in projects 2 and 3. The Center has a strong educational goal of helping young scientists to develop a career in Parkinson's disease research, and engages in significant outreach efforts.

PROGRESS REPORT:

The Center projects and cores have made excellent progress in the short time since the inception of the Center. The specific results are detailed in the descriptions of the individual components.

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

PUBLICATIONS:

(Relevant publications are listed in the descriptions of the individual center components).

FUNDING SOURCES:

Wichmann, Thomas / NIH/NINDS P50NS071669, now P50NS098685

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Udall Center Project 2

SPID#: 0679

UNIT/DIVISION: NND

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		NND	

PROJECT DESCRIPTION:
This project explores parkinsonism-associated changes in thalamic and cortical information processing. Specifically, we are comparing between the normal and parkinsonian state how cortical inputs shape thalamic output, and how basal ganglia inputs alter the cortico-thalamic information transfer. Other studies examine the impact of thalamic inputs on cortical processing, both on a single cell and a neuronal ensemble level. Specific emphasis will also be put on an exploration of the impact of deep brain stimulation of the basal ganglia output nuclei on thalamic and cortical information processing. The experiments use newly developed optogenetic techniques to study the function of the corticothalamic or thalamocortical projections in isolation.

PROGRESS REPORT:
These studies started in the fall of 2016. We were fortunate to be able to hire two excellent and highly motivated postdoctoral fellows Excluded by Requester. Thus far, we have obtained two animals, with two additional animals planned to be studied later in the spring. Both of the current animals were acclimated using positive reinforcement training to accept investigator interactions, and one of them already received two recording chambers in a surgical operation under anesthesia. The chambers will allow us to carry out subsequent optogenetic and electrical recording experiments. The second animal will be operated similarly in mid-February. We also completed the analysis on several papers that used data from work done under our previous Udall Center project. Finally, a new analysis is under way, using phase-amplitude coupling parameters, applied to cortical and subcortical local field potentials. This analysis, specifically, studying the coupling between the phase of beta-band oscillations and the amplitude of gamma-band oscillations, is frequently used in clinical patients with Parkinson's disease or dystonia, and discussed as a possible control signal for closed-loop deep brain stimulation systems. We are currently completing an analysis of parameter choices for phase amplitude analyses (using synthetic data), as well as a larger study on the temporal development of phase amplitude coupling abnormalities in the parkinsonian brain, using biologic data collected before and during the development of parkinsonism in a cohort of our animals.

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Wichmann, Thomas / NIH/NINDS P50NS071669, now P50NS098685

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ROLE OF CEREBELLO-BASAL GANGLIA INTERACTIONS IN PRIMATE DYSTONIA

SPID#: 13061

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	N/A
Prin. NPRC Core Sci.		NND	N/A
		NND	N/A
Other Core and Affil.		None	

PROJECT DESCRIPTION:

A major roadblock for progress in the development of treatments for dystonia is that the brain region(s) that generate the abnormal neural activity that underlies dystonia has/have not been identified. Over the last decade, imaging data from patients with generalized dystonia as well as data from rodent experiments have suggested that abnormal nerve cell activity in the cerebellum, a brain region not traditionally considered part of the dystonia network, may, in fact, be essential for the production of this movement disorder. In rodents, dystonia-like movements can be produced by injection of the excitatory compound (S)-AMPA into the outer cortical mantle of the cerebellum. In order to bring us closer to an understanding of the brain network abnormalities that underlie dystonia in (non-human and human) primates, studies in the current project examined whether (S)-AMPA injections would have the same effects in monkeys.

PROGRESS REPORT:

Given that different portions of the cerebellar cortex are related to different body regions, we expected that local cerebellar injections would produce dystonia specifically in the body regions related to the injected portion of the cerebellum. To test this hypothesis, we injected (S)-AMPA into different locations in the cerebellar cortex, and determined if these resulted in abnormal dystonic-like movements of specific body parts in two Rhesus monkeys. We also studied the effects of different amounts of the drug to define the conditions which would produce abnormal movements. Based on 73 intra-cerebellar injections in these animals, we found that cerebellar (S)-AMPA injections resulted in stereotypic head or trunk-turning movements (up to 6/min), starting no earlier than 15 minutes after the injection, and lasting for up to 90 minutes. These movements were strongest and occurred most quickly when the injections were placed close to the midline of the cerebellum, and were less intense and of longer latency (up to 40 minutes) when the injections were placed more laterally in the cerebellar hemispheres. Interestingly, these abnormal movements were induced after injections in different parts of the cerebellum, irrespective of the body parts represented in these regions. The success rate of the injections ranged from 50-90%. Note that the injection experiments in the last animal, as well as planned histologic studies have not concluded yet.

These studies show that (S)-AMPA injections into the cerebellum can induce involuntary posturing in monkeys. Contrary to expectations, these dystonic-appearing movements never involved the animal's limbs, even with injections that were placed into the arm- or leg area of the cerebellum. This suggests that dystonic trunk or neck posturing, but not limb posturing may involve the cerebellum.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

None

FUNDING SOURCES:

Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: GLUN2D ANTAGONISM IN SUBTHALAMIC NUCLEUS FOR TREATMENT OF PARKINSONISM

SPID#: 13062

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	NND	N/A
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	Emory School of Medicine (Pharm.)

PROJECT DESCRIPTION:
These experiments were aimed at elucidating whether microinjections of antagonists at glutamatergic GluN2D receptors (subtype of NMDA receptors) into the subthalamic nucleus would have antiparkinsonian effects in monkeys. These drugs had previously been shown to be effective in parkinsonian rodents. Under aim 1, we studied the efficacy, specificity, potential tissue toxicity of a large number of GluN2D compounds in rodents, for subsequent studies in monkeys. Aim 2 consisted of studies of the time course of GluN2D antagonism on neuronal function in awake parkinsonian primates, and aim 3 was planned as a study of the potential behavioral effects of GluN2D inhibition in the subthalamic nucleus on motor function in parkinsonian monkeys, with the expectation that the drugs would ameliorate parkinsonism contralateral to the drug infusion, and that it would act synergistically with levodopa.

PROGRESS REPORT:
This report concerns only the studies carried out in primates (additional rodent studies were carried out in Excluded by Requester Excluded by laboratory on the Emory campus). For the primate studies, we chose to evaluate two newly synthesized compounds that had shown robust effects in rodents. We carried out microinjections of these agents into the subthalamic nucleus (STN) in MPTP-treated monkeys, examining changes in spiking and bursting activity of the recorded cells. Both agents failed to produce the expected effects on spiking activity. We eventually initiated a third set of in vivo recordings, studying the effects of non-specific NMDA receptor blockade on STN activity, comparing 5 mM D-APV injections (500 nl) to saline injections. This resulted in highly consistent and robust reductions in spike firing in the animals, with no effects in the saline-injected cases.

In Preparation

In Preparation We are preparing a manuscript to communicate the results of this study.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

None (manuscript in preparation at the moment)

FUNDING SOURCES:

Excluded by Requester	Pri vætSource

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: HUMAN SPECIFIC BRAIN DNA METHYLATION AND NEUROPSYCHIATRIC DISEASES

SPID#: 13063

UNIT/DIVISION: NND

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	-------	Georgia Tech
Prin. NPRC Core Sci.		NND	
Other Core and Affil.		None	

PROJECT DESCRIPTION: This project seeks to identify human-specific changes in DNA methylation sites in adult higher-order association cortex and determine effects of these changes on gene and protein expression in human controls, humans with schizophrenia, and nonhuman primates.

PROGRESS REPORT:
In progress during the reporting period. Following up on our prelimiary results, which we have now published, we are now sorting neurons and non-neuronal cells from archival tissue, and extracting DNA and RNA. We are in the process of identifying DNA regions that are differentially methylated across species and in the human control and clinical group, as well as comparing nuclear RNA transcriptomes in the different groups to examine the effect of methylation on gene expression. We have developed riboprobes to be used in confirmatory in situ hybridization studies in frontal lobe tissue from the different species.

PUBLICATIONS:
Excluded by Requester

FUNDING SOURCES:
Soojin Yi, PhD. PI
Todd M. Preuss, PhD. PI
Genevieve Konopka, PhD. PI
NIH/NIMH 1R01MH103517-01A1

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Division of Microbiology and Immunology

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Targeting PD-1 Pathway for Functional Cure of AIDS

SPID#: 13064

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:

The overall goal of this proposal is to evaluate the safety and therapeutic potential of in vivo blockade of the PD-1 (Programmed death-1) co-inhibitory pathway to achieve a functional cure (long-term control in the absence of antiretroviral therapy) for HIV/AIDS using the SIV/macaque model. Dysfunctional anti-HIV immunity and persistence of viral reservoirs represent the two major issues that must be addressed by therapeutic approaches targeting functional cure. Combination antiretroviral drug therapy (ART) helps only to some extent. We believe that these two issues can be addressed effectively by targeting the PD-1 co-inhibitory pathway during ART. First, our recent studies showed that PD-1 blockade during chronic SIV infection (in the absence of ART) is safe and restores function of SIV-specific cellular and humoral immunity, improves gut permeability barrier function and prolongs survival. These results demonstrated that in vivo blockade of PD-1 represents a novel treatment strategy to restore anti-HIV immunity. Second, recent studies have demonstrated that the majority of HIV-1 latently infected cells express PD-1 and blocking PD-1 signaling on these cells reactivates the latent virus in vitro, suggesting that in vivo blockade of PD-1 may result in reactivation of the latent virus that can subsequently be cleared by the functional anti-viral immunity. Here we propose to achieve a functional cure for HIV/AIDS by combining PD-1 blockade with ART and therapeutic vaccination. This proposal has three specific aims. In aim 1, we will optimize conditions for enhancing anti-viral immunity and reducing the establishment of latently infected cells following the initiation of ART. In aim 2, we will optimize conditions to purge the viral reservoirs during ART. In aim 3, we will use the best condition from aims 1 and 2, and combine with therapeutic vaccination to achieve a functional cure.

PROGRESS REPORT:

Here we tested the influence of PD-1 blockade administered during the initiation of ART and under fully suppressive ART on both dysfunctional CD8 T cells and latently infected CD4 T cells using a primatized anti-human PD-1 Ab. PD-1 blockade was performed in two phases after SIVmac251 infection in rhesus macaques (RMs). In Phase I, 5 infusions were administered over 14 days at 3mg/kg dose at 10 days prior to the initiation of ART. In Phase II, 3 monthly infusions were administered at 10mg/kg starting from 32 weeks post ART. ART was interrupted at 2 weeks after the final PD-1 Ab infusion. Administration of PD-1 blockade during Phase I resulted in rapid proliferation of total CD8 and CD4 T cells, proliferation of SIV-specific CD8 T cells with higher cytotoxic potential and polyfunctionality ($p<0.05$). Impressively, the PD-1 Ab treated animals showed more rapid viral suppression (42 days in the PD-1 group versus 140 days in saline group; $p = 0.01$) and greater reconstitution of Th17 cells in the rectal mucosa ($p = 0.01$) following initiation of ART. During phase II, there

was a proliferation of total CD8 and CD4 T cells but this was much lower compared to Phase I. Interestingly, PD-1 blockade during Phase II resulted in transient but significant increases in viremia. Following ART interruption, PD-1 Ab treated animals showed up to 80-fold reduction in set point viremia compared to set point levels prior to initiation of ART. These results demonstrate that PD-1 blockade can be combined effectively with ART both to restore SIV-specific CD8 T cell function and possibly destabilizing the viral reservoir under ART, and have implications for developing potent approaches for achieving functional cure for HIV.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Rama Amara, NIAID- R37 AI0112787

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Optimizing Adjuvants and Needle Free Delivery Methods for Oral HIV Vaccination

SPID#: 13066

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The majority of HIV infections occur via mucosal routes (genital, oral or rectal) world-wide. The overall goal of this proposal is to develop a vaccination approach that induces strong HIV-specific humoral and cellular immunity in genital, intestinal and oral mucosae. We hypothesize that vaccines, which elicit strong anti-HIV immunity at these mucosal sites, will prevent infection and rapidly clear infected cells very early at the site of infection and enhance protection. Oral cavity is rich in lymphoid tissue containing antigen presenting cells, T cells and B cells, and provides an excellent opportunity for mucosal delivery of vaccines. However, this route of immunization has been under-utilized to deliver vaccines in part due to the presence of proteases in saliva that can degrade vaccines. This is particularly true for protein-based vaccines. Here, we aim to target the oral mucosa for immunization using a needle free device (Syrijet) as an oral vaccine delivery system to induce strong immune responses at oral and intestinal mucosal sites. The syrijet can deliver vaccines into the oral mucosa thus will 1) enhance the delivery of vaccine to local lymphoid tissue that will facilitate uptake by DC and 2) will maintain integrity of the vaccine by preventing degradation by oral proteases. To test our hypothesis, in Aim 1, we will first optimize the method and location of oral vaccine delivery and compare different adjuvants for protein immunogen. We will compare sublingual and buccal immunizations delivered with and without syrijet for induction of strong SHIV-specific humoral and cellular immunity in the oral and gut mucosal tissue. We will also test other mucosal adjuvants flagellin and dmLT for protein immunizations. In Aim 2, using the best delivery method and adjuvant combination that we identify in Aim 1, we will conduct an intrarectal challenge study with clade C SHIV.

PROGRESS REPORT:
This is a new project. We just started these studies. We enrolled 20 rhesus macaques. These animals received MVA immunizations either orally or intradermally. Oral immunizations compare topical delivery vs delivery using Syrijet. These animals will be boosted soon with protein either orally or subcutaneously. Measurement of systemic and mucosal responses are in progress.

PUBLICATIONS:
None

FUNDING SOURCES:
Rama Amara, NIDCR-R01DE02633

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: CD40L adjuvanted clade C DNA and MVA HIV vaccines

SPID#: 13067

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Development of an effective vaccine against HIV-1 has been an elusive goal for the past three decades. As a result it has been a major challenge to stem the tide of the epidemic caused by this virus globally. The results of the RV144 efficacy trial in Thailand have spurred a new level of excitement for the development of HIV vaccine and strongly support the development of vaccination approaches that enhance the titer and functional quality of anti-HIV Env antibody that may significantly enhance protection against HIV.

The overall goal of this program is to develop novel vaccination approaches that not only enhance the magnitude but also enhance the functional quality of anti-HIV cellular and humoral immunity. Specifically, we propose to combine two new vaccination approaches developed recently at Emory University that showed great promise in rhesus macaques. The first approach uses CD40L, a co-stimulatory molecule for dendritic cells (DC) and B cells, expressed on the surface of HIV VLPs as a genetic adjuvant for enhancing the magnitude and functional quality of HIV-specific cellular and humoral immunity leading to enhanced protection from acquisition of SIV infection. The second approach uses a new MVA that lacks 4 immune modulatory genes (MVAΔ4) as a vaccine vector that showed a significant increase in the magnitude of HIV-specific cellular and humoral immunity in rhesus macaques. In this program, we hope to combine these two new complementary approaches to develop a novel vaccination strategy against HIV. This program is a collaborative effort between scientists at the Emory University (Excluded by Requester), NIH (Excluded by Requester) and Louisiana State University (LSU; Excluded by Requester). Successful completion of the program will result in the clinical development of two new vaccine products and a novel HIV vaccine.

PROGRESS REPORT:

We completed M22 trial that tested the immunogenicity and efficacy of DNA/MVA, DNA/MVAΔ4 and DNA/MVA/Protein vaccination.

Conclusions for Cellular immunity: CD40L adjuvanted DNA/MVA vaccination induced a strong SHIV-specific CD8 and CD4 T cell response with polyfunctional properties including the CXCR5+ CD8 T cells with follicular homing potential. The SHIV-specific CD8 and CD4 T cell responses were not different between MVA and MVAΔ4 vaccine. The protein boosts did not boost CD8 T cell response but strongly boosted Env-specific CD4 T cell responses. This resulted in significantly higher CD4 T cell responses in the protein-boosted group

compared to no protein groups. This also resulted in a shift in the balance between Gag and Env-specific CD4 T cell response.

Conclusions Humoral immunity: CD40L adjuvanted DNA/MVA vaccine induced strong binding antibody responses in serum and low levels in mucosal secretions. MVAΔ4 did not enhance any of these responses. Gp140 protein boost increased serum and mucosal binding IgG responses at least by 10 fold. However, these did not bind efficiently to challenge virusinfected cells and thus failed to perform ADCC and neutralization functions.

Conclusions Protection: The vaccinations did not prevent SHIV1157ipd3N4 infection but showed enhanced viral control. These results demonstrate that although protein boosts were successful in enhancing the antibody response, they did not induce the right kind of antibody response and induced more target cells. We think a combination of this resulted in lack of protection in vaccinated animals. These results highlight the need for the use of protein boosts that predominantly present trimer specific epitopes and induce lower levels of CCR5+ CD4 T cell response.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES:
Rama Amara, NIAID- U19 AI109633

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Emory WIHS CRS-Longitudinal Cohort

SPID#: 13111

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Infectious Diseases School of Medicine	
		Microbiology Immunology	
		Microbiology Immunology	
		Infectious Diseases School of Medicine	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The vast majority of heterosexually transmitted HIV infections occur in women. While a variety of factors put women at an increased risk for heterosexual HIV infection, the immune environment in the female genital tract (FGT) plays a decisive role. Within the FGT, HIV relies upon target T cells for entry, replication, and cell-to-cell transmission and ultimately for establishing productive infection. These HIV target T cells express CD4, the primary cellular receptor for HIV entry, and C-C chemokine receptor type 5 (CCR5), one of the major HIV co-receptors facilitating HIV entry. Notably, a substantial fraction of HIV target cells within the FGT also express the integrin receptor $\alpha_4\beta_7$, which binds with high affinity to a conserved epitope on HIV-1 gp120. Therefore, $CCR5^+$ $\alpha_4\beta_7^+$ dual positive CD4 T cells represent prime cellular targets for HIV infection in the FGT. Despite having critical ramifications for HIV replication and AIDS progression, the molecular characteristics of $CCR5^+$ $\alpha_4\beta_7^+$ CD4 T cells in the FGT remain unknown. In the proposed studies we will overcome this hurdle by employing a high-throughput, highly sensitive, single-cell RNA-sequencing approach to explore the transcriptional program of HIV target cells before and after *ex vivo* HIV infection.

PROGRESS REPORT:

Under Revision

We have sorted HIV target cells from the FGT of HIV- women for RNA sequencing.
Studies to examine HIV target cells from HIV+ women on ART are underway. These data will provide critical insights into the biology of CD4 T cells in the FGT.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:
U01 AI103408 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Experimental depletion of plasmacytoid dendritic cells in SIV infection

SPID#: 13068

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The basis of this proposal is a novel reagent – a monoclonal antibody that specifically depletes plasmacytoid dendritic cells (pDCs) in rhesus macaques. This proposal will test the hypothesis that the elimination of pDCs, *in vivo*, from SIV-infected rhesus will substantially reduce immune activation. This hypothesis will be addressed by the experiments in the following Specific Aims: **(Aim1)** To test the effect of experimental pDC depletion on global IFN responses in SIV infection; and (**Aim 2)** Determine the effect of pDC depletion on immune activation, CD4+ depletion and control of viral replication. At the conclusion of these exploratory studies, we will have definitively established the role of pDCs and IFN in driving immune activation, determined if the IFN response to SIV is primarily due to pDCs, developed a novel research tool for immunological studies in NHPs, and characterized the potential of this reagent for translation into clinical trials.

PROGRESS REPORT:

In the past progress period, we have administered the monoclonal to a total of five rhesus macaques. We performed infusions with a low dose of antibody (2 mg/kg, n = 2) and with a high dose (50 mg/kg, n = 3). We also developed an assay to assess the binding of the depletion antibody on the surface of pDCs. Using this assay, we determined that the monoclonal antibody was binding to the target cells in vivo, but was not affording depletion at the low doses, and partially at high doses. To improve efficacy, we have conjugated an immunotoxin the antibody for subsequent infusions.

PUBLICATIONS:

None

FUNDING SOURCES: Bosinger, Steven / NIAID R21 AI118542

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Simultaneous antigen receptor repertoire profiling and single-cell transcriptomics in T and B lymphocytes from limited clinical samples.

SPID#: 13069

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

In the vast majority of vaccine trials, the primary readouts are empirical do not collect information about the immunological determinants of a vaccine's success or failure. In recent years, several vaccine studies have combined high-throughput transcriptomic data with measures of antigenicity. These "systems vaccinology" studies have proven invaluable insight into the determinants of efficacy and antigenicity, and have demonstrated the enormous value in mechanistic studies of human vaccination. However, one area that is particularly understudied is the composition of antigen specific receptors that arise during successful and unsuccessful vaccinations. Collection of antigen-specific clonotype information in clinical vaccine studies would provide valuable data that could be used to accelerate vaccine development. The utility of current methodology for repertoire sequencing for immunological studies has been limited due to several factors (i) high-cost and low-throughput of cloning based assays (ii) most high-throughput assays only provide information on a single gene(typically the H-chain of immunoglobulin or β-chain for TCRs), or (iii) do not link ag-receptor sequences with immunophenotypic or transcriptomic data. In preliminary work, we have developed a protocol that simultaneously queries the transcriptome and paired antigen receptor sequences in B lymphocytes derived from human bone marrow after flu vaccination using next generation sequencing. The goal of this proposal is to complete development of this combined "-Seq" assay for both B and T cells, including establishment of its limitations and benchmark against contemporary repertoire sequencing techniques.

PROGRESS REPORT:

In the past year, we have established a cohort of seasonal influenza vaccinees which provided the necessary access to plasmablasts for this study. We have performed single-cell RNA-Seq on 300 single plasmablasts, and established a dataset of 35 individual cells in which we have RNA-Seq data, and also Sanger sequence of the Heavy and Light chains of the B cell antigen receptor/antibody chains. Using this dataset, we have developed and tested an algorithm that can accurately identify the correct Heavy & Light Chain pairing in >90% of cells. These work are being written into a manuscript. We have also collected pre- and post-vaccine sorts of naïve and memory B cells in addition to the vaccine-induced plasmablasts to analyze the fate of vaccine induced cells.

PUBLICATIONS:

None

FUNDING SOURCES: Bosinger, Steven / NIAID U24 AI120134

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Neurobiology of cytokine effects on CNS glutamate in IFN-alpha-induced depression

SPID#: 13070

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Psychiatry Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
To identify novel therapeutic targets to reverse inflammatory cytokine effects on behavior, this study will explore mechanisms by which interferon (IFN)-alpha affects CNS glutamate using post-mortem brain tissue collected from a back translational model of cytokine-induced depressive-like behavior. Inflammatory cytokines and their signaling pathways are reliably elevated in a significant proportion of depressed patients, and administration of cytokines is associated with development of depressive symptoms in laboratory animals and humans. For instance, peripheral administration of IFN-alpha for treatment of hepatitis C and malignant melanoma is well known to induce clinical depression in up to 50% of patients, and has been shown to cause anhedonic and depressive-like behavior in laboratory animals. Despite the mounting evidence that inflammatory cytokines affect behavior, the CNS mechanisms by which cytokines cause depressive symptoms are only beginning to be understood. One pathway that is receiving increasing attention is CNS glutamate. Recent results from our group using magnetic resonance spectroscopy indicate that administration of IFN-alpha to patients with hepatitis C increased glutamate in the basal ganglia and anterior cingulate cortex (ACC), which correlated with depressive symptoms. Our preliminary data indicate that IFN-alpha increased perivascular macrophages and increased microglia activation in specific basal ganglia nuclei. Based on these findings from animals and humans, this proposal will test the hypothesis that chronic IFN-alpha increases glutamate and affects glutamate neurotransmission in the basal ganglia and ACC through decreasing glutamate transporters, increasing excitotoxic glutamate receptor subtypes and their signaling pathways, and increasing the production of QUIN by activated microglia and perivascular macrophages. This study will be the first to elucidate cytokine-induced changes in glutamate neurotransmission in vivo and link these changes to QUIN induction by activated macrophages and microglia in an established, back translational model.

PROGRESS REPORT:
In the past year, we have conducted RNA-Seq on 42 sections of brain obtained from rhesus macaques, and have performed differential expression analysis. We also performed immunohistochemistry on a paired section. These data have identified an enrichment of Type I Interferon Signalling in animals exhibiting depressive behaviours.

PUBLICATIONS:
None

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES: Bosinger, Steven / NIMH R21 MH106904

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: CENTER FOR HIV/AIDS VACCINE IMMUNOLOGY & IMMUNOGEN DISCOVERY

SPID#: 12029

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Scripps Research Institute Microbiology Immunology Emory Vaccine Center	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:

Infection of macaques with simian immunodeficiency virus (SIV) or simian-human immunodeficiency virus (SHIV) is a key animal model for HIV-1 infection. The Nonhuman Primate (NHP) Scientific Research Support Component (SRSC) aims to support this CHAVI-ID by providing all the expertise, infrastructure, reagents, personnel, and animals for the conduct of complex in vivo immunogenicity and challenge studies in NHPs. This SRSC leadership will work closely with the research discovery teams responsible for the studies included in Scientific Foci 1 & 2 and participate actively to the scientific mission of CHAVI-ID. The main role of SRCS is to provide leadership and technical expertise to ensure consistency and quality control in animal selection, execution of study protocols, experimental procedures, sample acquisition and distribution, immunologic and virologic studies, and data collection and analysis. The Specific Aims of the SRSC are:

1. To support this CHAVI-ID by selecting and providing rhesus macaques, providing exceptional animal care, conducting experimental studies with monoclonal antibodies and vaccines, collecting samples for immunologic and virologic testing, and performing necropsy studies. These studies will initially evaluate:
   - A. Protective efficacy of HIV-1 Env-specific monoclonal antibodies against SHIV challenge;
   - B. Immunogenicity and protective efficacy of novel HIV-1 Env immunogens;
2. To support this CHAVI-ID by providing blood and tissue samples from SIV-infected and uninfected NHPs to collaborating investigators to underpin basic research studies. These samples are especially central to the activities of Scientific Focus #2, as they will help elucidate the characteristics of HIV-specific CD4+ "follicular helper" T cell (Tfh) responses, with initial emphasis on the development of Tfh cells during a vaccine-induced immune response, and the role of these cells in providing help to B cells and promoting the critical process of affinity maturation of antibodies.

PROGRESS REPORT:

We completed several immunization studies in collaboration with Excluded by Requester to further test novel immunogens to induce broadly neutralizing antibodies. We finished an immunization study that reuses six 10E8-immunized animals from the first experiment. This study was aimed at improving VH1-2 targeting by immunizing with eOD-GT8-60mers. We concluded two other studies: (i) An 11-animal study compared three immunizations: 10E8 single-epitope with no particles, a 10E8 single-epitope

nanoparticle, and 10E8 three-epitope nanoparticle. The other trial is 16-animal study that is a comparison of the ability of several different trimers to induce neutralizing antibodies. For all of the studies we collected plasma and PBMCs for further evaluation by our lab Excluded by Requester and the Excluded by Requester lab. In addition, we evaluated the use of lymph node (LN) fine needle aspirate (FNA) in longitudinal immunization studies in collaboration with Excluded by Requester We completed a 20-animal study that directly compares collection of LN-biopsy versus LN-FNA in a SOSIP trimer nanoparticle adjuvant study. We obtained on average a million cells per FNA sampling with FNA accessing approximately 3% of the total LN. The FNA is representative of whole LN biopsies as frequencies of GC B cells and T_{FH} correlate between the two types of samplings. Further, we tracked a LN region over time using this technique. We find that the largest expansion of germinal centers (GC) occurs after the first immunization, and after subsequent immunization minor GC boosts are observed. We find that the GC center response and antibody production is equivalent in animals that had repeated FNA access compare to animals that had no FNA. The plasma and serum collected showed the production of neutralizing antibodies in the majority of animals. This study demonstrates that FNA is appropriate for longitudinal studies and repeated FNA does not affect the overall immune response.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
NIAID - UM1 AI100663

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Maximizing germinal centers and somatic hypermutation to HIV Env immunogens

SPID#: 13071

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	La Jolla Institute for Allergy and Immunology Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

HIV-specific broadly neutralizing antibody (bnAbs) are challenging to develop and have traits indicative of extensive affinity maturation. We propose that the features of germinal center biology important for developing high affinity B-cells to a Tier 2 neutralizing antibody epitope on HIV Env trimer are very different than the features for conventional antigens, such as haptens or even HIV gp120 V3 loop (a non-Tier 2 neutralizing epitope) for which a very small number of mutations suffice for maturation of high affinity B-cells and antibodies. We will use innovative slow immunogen release vaccine technologies as candidate HIV vaccines and as tools to probe the biology of germinal centers relevant to affinity maturation against the difficult HIV trimer target in non-human primates. Our innovative slow immunogen release vaccine strategies provide two advantages: (1) protection of the immunogen for sustained release of intact trimer epitopes for B-cell recognition, and (2) sustained provision of antigen to germinal centers. This study will be extremely valuable to the HIV vaccine effort because it will test novel approaches to induce high quality HIV neutralizing antibodies and assess immunological relationships between germinal center size, duration, sequence space explored, and Tfh cells to understand which parameters are most important for affinity maturation to the bnAb epitopes of HIV Env. Aim 1. Determine how sustained Env immunogen availability impacts the quality of the germinal center and nAb responses, using slow release osmotic pumps. Aim 2. Determine whether intradermal silk microneedle patches delivering immunogen in a sustained manner maximize germinal center activity and affinity maturation to HIV Env trimers. Aim 3. Determine the Env trimer immunogen kinetics that maximize germinal center quality and duration. Aim 4. Assess the relatedness and predictive capacity of immunological parameters in the blood with the actual germinal center activity present in the lymph nodes after immunization.

PROGRESS REPORT:

In the first year of this award we have received IACUC approval and assigned the animals for Aim 1 of the proposed work. This aim includes comparing a one day bolus immunization of the envelope trimer mimic, BG505 SOSIP with the adjuvant ISCOMIT, to sustained antigen delivery via osmotic pumps designed for either delivery over 2 weeks or 4 weeks. We are collecting blood and lymph node fine needle aspirates (LN-FNAs) weekly throughout the study as well as lymph node biopsies. During the second immunization the dose for the pumps was decreased by half and we added a bolus immunization of the same amount to the end of the sustained delivery time period. We have fully completed two immunization cycles. We are able to utilize the

LN-FNAs to characterize the immune response generated by the immunizations. We are phenotype of antigen-specific B cells and single cell sorting these cells to do further genotypic analysis. Further, we are able to save RNA from these cells for BCR and TCR characterization. Using blood we can assess the generation of the neutralizing antibody response that can be later correlated the phenotypic data generated with the LN-FNAs. We will continue to assess the immune response in these animals and begin work on Aim 2 shortly.

PUBLICATIONS:
None

FUNDING SOURCES: Silvestri, G / NIAID R01 AI157851

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Mechanisms of hepatitis C virus persistence

SPID#: 0510

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Persistent hepatotropic viral infections are a common etiologic agent of chronic liver disease. Unresolved infection can be attributed to non-functional intrahepatic CD8+ T cell responses

PROGRESS REPORT:
In light of dampened CD8+ T cell responses, liver disease often manifests systemically as Ig-related syndromes due to aberrant B cell functions. These two opposing yet co-existing phenomena implicate the potential of altered CD4+ T cell help. Elevated CD4+ Foxp3+ T cells were evident in both human liver disease and a mouse model of chemically induced liver injury despite marked activation and spontaneous IgG production by intrahepatic B cells. While this population suppressed CD8+ T cell responses, aberrant B cell activities were maintained due to expression of CD40L on a subset of CD4+ Foxp3+ T cells. *In vivo* blockade of CD40L attenuated B cell abnormalities in a mouse model of liver injury. A phenotypically similar population of CD4+ Foxp3+ CD40L+ T cells was found in diseased livers explanted from patients with chronic hepatitis C infection. This population was absent in non-diseased liver tissues and peripheral blood. Together these data indicate that liver disease elicits alterations in the intrahepatic CD4+ T cell compartment that suppress T cell immunity while concomitantly promoting aberrant IgG-mediated manifestations.

PUBLICATIONS:
Excluded by Requester

FUNDING SOURCES:
Arash Grakoui / NIAID-R01AI070101

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: T cell compartmentalization and antiviral response

SPID#: 13072

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	Research Inst Nationwide Children's Hospital
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Excluded by Requester we found that anatomic compartmentalization regulates TCR–pMHC interaction and fate of $CD8^+$ T cells during the early contraction phase of viral infection.

PROGRESS REPORT:

We measured the TCR–pMHC interaction by micropipette technology and found that virus-specific TCR transgenic P14 T cells within the splenic red pulp (RP) displayed significantly higher effective 2D affinity than those from the white pulp (WP). Early determination of gene expression during the initial contraction phase led memory precursors from the WP to preferentially develop into long-term memory cells as compared to their counterparts in the RP despite expression of the same memory markers ($KLRG1^{lo}CD127^{hi}$). Our results suggest a regulatory mechanism of TCR–pMHC interaction, gene expression, and generation of effector and memory precursor cells governed by cellular and cytokine microenvironmental compartmentalization of the lymphoid organ during the early contraction phase of an antiviral response.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
Arash Grakoui / NIAID-R01AI126890

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Highly-parallel PCR analysis of latently-infected reservoirs

SPID#: 13073

UNIT/DIVISION: Microbiology and Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	
Prin. NPRC Core Sci.			
Other Core and Affil.		M&I	

PROJECT DESCRIPTION:
Substantial evidence suggests HIV-1 can establish a latent infection of long-lived quiescent cells, which carry an integrated provirus that is largely transcriptionally silent, functionally invisible to immune surveillance and impervious to the activity of antiretroviral drugs. The long half-life of these cells and their capacity to be reactivated and produce infectious virions remains the primary obstacle to viral eradication. We propose a novel approach using a highly sensitive qPCR technique to analyze the lymphoid tissues most likely to harbor latent reservoirs, to identify the cellular compartments and subsets most enriched for latently-infected cells at higher resolution than previous analyses, and to use highly-parallel qPCR transcriptional analysis to identify novel cell surface biomarkers expressed on these subsets. The use of highly-parallel simultaneous genome/transcriptome qPCR represents a unique approach to address the fundamental challenges in characterizing latently-infected reservoirs and should provide essential information necessary for the development of strategies for viral eradication.

PROGRESS REPORT:
Progress over the past year included the optimization of high-throughput single cell PCR using the Fluidigm C1 platform, identification of a subset of molecules that are differentially expressed on the surface CD4+ T cells, development of a panel of PCR primers for these target molecules, development of a panel of PCR primers for integrated and latent forms of SIV, and analysis of the presence of full length and short SIV transcripts in different populations of memory CD4+ T cells from SIV-infected animals that have been treated with potent antiretroviral therapy. In addition, we are optimizing the combination of index sorting of single cells coupled with transcriptional analysis on the Fluidigm Biomark platform as an alternative approach to the Fluidigm C1 platform.

PUBLICATIONS:
None

FUNDING SOURCES: Excluded by Requester | Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Vaccine design to concentrate protective antibodies at the mucosal border

SPID#: 13074

UNIT/DIVISION: Microbiology and Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	Univ. Minnesota

PROJECT DESCRIPTION:
Recent collaborative experiments from the Excluded by Requester laboratories have suggested that the presence of antibodies against an oligomeric form of gp41 in the female reproductive tract may play a role in mediating protection against vaginal challenge induced by the live attenuated SIV vaccine, SIVdeltanef. The present experiments further extend these observations to determine the ability of antibodies directed against oligomeric gp41 to mediate protection against vaginal challenge. Initial studies will focus on a more detailed characterization of antibody responses induced by SIVdeltanef, as well as antibodies induced by immunization of macaques with oligomeric forms of gp41. Subsequent experiments will analyze the protective effects of passive immunization with rhesus antibodies that are specific for oligomeric gp41 and their ability to provide protection against vaginal challenge with SIV.

PROGRESS REPORT:
Recent studies have focused on the optimization of flow cytometric techniques to identify plasma cells and plasmablasts in macaques, as well as the development of new approaches to identify gp41-specific B cells by flow cytometry and ELISPOTs. In addition, we have analyzed the pharmacokinetics of a gp41-specific monoclonal antibody in a naïve macaque as a prelude to passive transfer experiments to examine their ability to protect against vaginal SIV infection. We have completed the vaginal challenge phase of animals that were vaccinated parentally and mucosally with a gp41 trimer; unfortunately, no effects of vaccination on either acquisition or control of viremia were observed. We are now repeating efforts at passive immunization with gp41-specific antibodies using antibodies that have a specific modification in order to enhance localization in the female reproductive tract.

PUBLICATIONS:
Excluded by Requester

FUNDING SOURCES: Johnson, RP / R01 AI102625 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Live attenuated SIV-mediated protection against mucosal SIV infection

SPID#: 13075

UNIT/DIVISION: Microbiology and Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Vaccination of macaques with attenuated SIV strains has consistently provided the most effective protection against pathogenic SIV challenge and offers the best available experimental model to define specific mechanisms responsible for protection. Recent studies from our group have demonstrated that a significant maturation of protective immunity against vaginal challenge occurs between 5 and 20 weeks after vaccination with SIVΔnef, which is associated with evolution of both cellular and humoral immune responses. Based on these observations, we hypothesize that SIVdeltanef is able to block critical stages of SIV replication and spread in first 7 days after vaginal challenge. The goal of this proposal is to apply a panel of innovative techniques to serial necropsies of SIVdeltanef-vaccinated animals before and after challenge to elucidate the roles of adaptive and innate immune responses in mediating protection induced by SIVdeltanef and to identify the sites of containment of viral replication within the female reproductive tract.

PROGRESS REPORT:

We undertook a comprehensive assessment of immune responses that protect against SIV infection through detailed analyses of cellular and humoral immune responses in the blood and tissues of rhesus macaques vaccinated with SIVΔnef and then vaginally challenged with wild-type SIV. Despite the presence of robust cellular immune responses, animals at 5 weeks after vaccination displayed only transient viral suppression of challenge virus, whereas all macaques challenged at weeks 20 and 40 post-SIVΔnef vaccination were protected. Multiple parameters of CD8 T cell function temporally correlated with maturation of protection, including polyfunctionality, phenotypic differentiation, and redistribution to gut and lymphoid tissues. We also demonstrated the induction of a tissue-resident memory population of SIV-specific CD8 T cells in the vaginal mucosa, which was dependent on ongoing low-level antigenic stimulation. Moreover, we showed that vaginal and serum antibody titers inversely correlated with post-challenge peak viral load, and we correlated the accumulation and affinity maturation of the antibody response to the duration of the vaccination period as well as to the SIVΔnef antigenic load. In conclusion, maturation of SIVΔnef-induced CD8 T cell and antibody responses, both propelled by viral persistence in the gut mucosa and secondary lymphoid tissues, results in protective immune responses that are able to interrupt viral transmission at mucosal portals of entry as well as potential sites of viral dissemination. A manuscript describing the effect of sequence variation has been published in *PLOS Pathogens*.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES: Johnson, RP / U19 AI095985 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Assessing the impact of immune checkpoint antagonists on persistent viral reservoirs, using the SIV model of HIV infection

SPID#: 13110

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	University of North Carolina at Chapel Hill	
Prin. NPRC Core Sci		M&I	
Other Core and Affil.			

PROJECT DESCRIPTION:
The goal of this proposal is to test the safety and activity in reducing SIV persistence of combined co-inhibitory receptor blockades in ART-suppressed SIV-infected RMs

PROGRESS REPORT:
Funds were very recently received. In this short period, we completed all the documents related to IACUC approval and animal assignment. We performed baseline (pre-infection) collections and infected all animals with SIVmac239. Infection was successful, with all animals showing active viral replication. At day 60 post infection, all animals will start antiretroviral therapy.

PUBLICATIONS:
None

FUNDING SOURCES:
None

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Mechanisms and correlates of post-ART treatment control in SIV-infected macaques

SPID#: 13076

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
We propose to define the immunophenotype and anatomic location of IL-10-producing cells, and how this production correlates with the size of the reservoir. We will address this question using immunohistochemistry coupled with novel in situ techniques (DNA/RNA Scope) to co-localize IL-10-producer cells, TFH cells and SIV-infected cells in LN and rectal biopsy tissues from ART-treated, SIV-infected rhesus macaques (RM).

PROGRESS REPORT:
As planned, we have determined plasma and tissue levels of IL-10 longitudinally in SIV-infected RMs, as well as how IL-10 levels impact viral persistence. Specifically, IL-10 and the levels of viral reservoirs were quantified pre-infection, during active viral replication, during ART treatment, and after ART treatment interruption. Our preliminary data suggest a strong relationship between IL-10 and viral persistence, that we are further investigating.

PUBLICATIONS:
None

FUNDING SOURCES:
Paiardini, Mirko / amfAR-109354-59-RGRI

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Central memory CD4 T cell infection: key role in ART response and HIV persistence

SPID#: 13112

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology Infectious Diseases	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:

A major obstacle to cure HIV infection is our incomplete understanding of what factors regulate the immunologic response to antiretroviral therapy (ART) and the persistence of the latent HIV reservoir. Although it is well established that HIV preferentially infect memory CD4 T cells, it is still unclear to what extent the relative distribution of HIV infection within the various CD4 T cell subsets influences: (i) the magnitude of CD4 T cell reconstitution, (ii) the extent of residual activation and (iii) the size of the persistent HIV reservoir during ART. Recent evidence generated in nonhuman primate models of HIV infection implicates the infection of CD4 T central memory (TCM) as a key factor determining the outcome of infection. In the pathogenic SIV-infection of rhesus macaques, the levels of infection of CD4 TCM dictate the tempo of progression to AIDS, and the preservation of CD4 TCM in vaccinated animals associates with resistance to SIV infection. Furthermore, in nonpathogenic SIV infection of sooty mangabeys, low level of CD4 TCM infection is a key mechanism of AIDS resistance. Based on these findings, we propose that the pattern of infected CD4 T cells is more important than the overall level of virus replication and the total number of infected cells in dictating the magnitude of CD4 T cell reconstitution and the size of the virus reservoir during ART. Here, we will test the hypotheses that, in blood and lymph nodes, CD4 TCM infection (i) critically contributes to the extent of immunologic restoration and residual immune activation and (ii) is a prognostic factor for both the size and stability of the HIV reservoir following ART. If our hypothesis is confirmed, these studies will suggest that novel strategies aimed at protecting CD4 TCM from infection should be a critical component of interventions aimed at curing HIV infection.

PROGRESS REPORT:

30 HIV-positive individuals were enrolled. Immunologic responders (IR) were defined as having CD4 counts >500 cells/μL ≤ 2 years after ART initiation; Immunologic non-responders (INR) as having CD4 counts <350 cells/ μL up to 2 years after ART initiation. Before and during ART, the frequency of total

(T) and integrated (I) HIV-DNA was measured in sorted blood naïve, central (CM), transitional (TM), and effector memory CD4 T-cells. T-cell levels, activation/proliferation states, expression of co-inhibitory receptors (Co-IRs) were analyzed by flow cytometry.

Median age of the cohort was 46; 90% were male and 82.8% were African-American. T and I HIV-DNA content in all CD4 T-cell subsets were significantly higher (P<0.01) prior to ART and on-ART in INR than IR. The increased HIV-DNA content in INR was associated with higher levels of T-cell proliferation and activation, both at pre- and on-ART (P<0.05). Expression of Co-IRs such as: PD-1 and TIGIT was significantly increased in memory CD4 T-cells of INR (P<0.05), with the frequency of these Co-IR-expressing T-cells correlating with levels of I HIV-DNA. HIV-DNA contents in IR were significantly reduced (P<0.01) on-ART as compared to pre-ART in all CD4 T-cell subsets. Remarkably, INR T and I HIV-DNA levels were significantly more stable in CM and TM CD4 T-cells between pre- and on-ART, and despite INR have been on-ART longer than IR.

When compared to IR, INR demonstrate higher levels of T-cell activation, Co-IRs expression, and viral burden in all memory CD4 T cell subsets, both prior to and on-ART. Furthermore, CM and TM CD4 T-cells harboring HIV-DNA persist longer during ART in INR. These data link levels of inflammation and CD4 T-cell infection prior to ART, particularly in long-lived CD4 T-cell subsets, with immune recovery and HIV persistence.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
Mirko Paiardini, PhD; R01AI110334 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Immune based interventions for HIV eradication

SPID#: 13113

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	

Prin. NPRC Core Sci.

Other Core and Affil.

PROJECT DESCRIPTION:
Although antiretroviral therapy (ART) suppresses HIV replication, immune dysfunctions and chronic inflammation critically contribute to non-AIDS-related morbidity and mortality in infected subjects. Furthermore, inflammation facilitates HIV persistence during ART. We previously demonstrated that addition of Interleukin (IL)-21, an immunomodulatory cytokine, reduces chronic inflammation and HIV persistence in ART-treated, SIV-infected rhesus macaques (RMs). In this study, sought to combine the anti-inflammatory functions of IL-21 with the antiviral properties of IFNα to reinvigorate antiviral responses. We hypothesize an impact on viral rebound following ART treatment interruption (ATI).

PROGRESS REPORT:

15 RMs were infected with SIV_{mac239} IV. RMs started a triple-formulation of TDF, FTC, and Dolutegravir (DTG) day 35 post-infection and continued for at least 12 months. Eight RMs received Macaquized (M)-IL-21-IgFc (100 μg/kg, SC, once weekly for four weeks) at initiation and mid-way thru ART. Additionally, this group received M-IFNα-IgFc (500,000 IU, SC, once weekly for five weeks) prior to ART-interruption. Upon ART-discontinuation, the eight IL-21-treated RMs received PEGylated-IFNα-2a (PEGASYS), 7 μg/kg, SC, once weekly for seven weeks; while the remaining seven RMs were ART-treated controls. Blood (PB), lymph nodes (LN), and colorectal (RB) biopsies were longitudinally collected to assess the effects of IL-21 and IFNα on inflammation, T cell subsets, and viral persistence.

ART fully suppressed plasma viremia (pVL) (<30 RNA copies/mL) in all RMs. During ART, IL-21 reduced levels of activated ($HLA\text{-}DR^{+}CD38^{+}$) and proliferating ($Ki\text{-}67^{+}$) T cells in PB, RB, and LN in comparison to ART-only controls ($P<0.01$). Levels of inflammation remained significantly lower also during and after addition of IFNα ($P<0.01$). Upon ART-interruption, IL-21/IFNα-treated RMs exhibited

delayed viral rebound with a median of 21 days as compared to 9 days in the controls ($P=0.0009$). Moreover, IL-21/IFNα-treated RMs maintained reduced viremia in comparison to controls up to 45 days after ATI ($P=0.0004$).

These data support the safety of a combined IL-21 and IFNα treatment for HIV infection. While IL-21-treatment effectively reduces inflammation, addition of IFNα prior- and after- ART-discontinuation resulted in a prolonged and more effective control of viral rebound. The synergy of such therapeutics may promote reinvigoration of host responses toward reduction of latent HIV reservoirs.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
Mirko Paiardini, PhD; R01 AI116379 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Targeting cytolytic cells to lymphoid sites of HIV persistence

SPID#: 13114

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Case Western Univeristy Microbiology Immunology	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:

Any strategy aimed at HIV eradication in chronic infection will need to address the persistence of virus in secondary lymphoid organs. Lymph nodes (LN) are rapidly infected in early infection, and maintain residual level of activation/inflammation during ART that may potentiate infection of susceptible cells to sustain the latent reservoir. Furthermore, cytolytic effector T cells are typically excluded from LN by their movement across a concentration gradient of the lysophospholipid sphingosine-1 phosphate (S1P). As a result, lymphoid tissues that constitute critical sites of HIV persistence are relatively protected from HIV-specific cytolytic cells. Based on these findings, we propose a novel approach to retain cytolytic cells in lymphoid tissues by administration of the S1P receptor agonist FTY720. We hypothesized that sustained exposure to cytolytic cells will promote a more inflammatory LN environment, will accelerate the stochastic bursts of SIV replication that play a role in sustaining HIV reservoirs, and will allow cytolytic cells to recognize and destroy virus expressing cells directly in lymphoid tissues. We will test this model in the well-established model of SIV infection of rhesus macaques (RMs) using the S1P receptor agonist FTY720, a molecule approved by the FDA for the treatment of multiple sclerosis that blocks the interaction of S1P with its receptors and results in significant circulating lymphopenia as a consequence of lymphocyte sequestration in LN. In the R21 phase of this proposal, we will assess the safety and activity of two different doses of FTY720 in retaining cytolytic cells in lymphoid tissues in ART-suppressed SIV-infected RMs. If successful, these studies will pave the way for the R33 phase, in which we will determine how FTY720 affects (i) antiviral cytotoxic responses and residual inflammation and (ii) HIV persistence in lymphoid tissues.

PROGRESS REPORT:

Ten RMs were infected with SIV_{mac239} and at d42 p.i. treated with ART (tenofovir, emtricitabine, and dolutegravir combined in a single daily injection). FTY720 (grp. 1: 18 µg/kg/day; grp. 2: 500 µg/kg/day) was administered daily for 28 consecutive days during the last 4 weeks of ART, when all animals showed undetectable plasma viremia (<30 copies/mL). T-cell quantification was performed by flow cytometry or multiplexed histocytometry. All animals completed FTY720 treatment without complication or toxicity, and plasma SIV levels remained undetectable. Both frequencies and absolute counts of CD4 and CD8 T-cells were remarkably lower during FTY720 treatment as compared to pre-FTY720 levels ($p<0.001$). This drastic

decrease was dose-dependent and includes circulating T-cells expressing molecules associated with cytolytic activity (perforin, granzyme, and T-bet; $p<0.001$ for all). Furthermore, histocytometry analysis confirmed a significant increase in T cells in LN, as well as increased levels of granzyme+ CD8 T cells in the follicles.

This study demonstrates an acceptable safety profile and a dose-dependent activity of FTY720 in promoting retention of cytolytic T-cells in LN sites of HIV persistence. These data provide rationale for testing effects of FTY720 on viral reservoirs in lymphoid tissues.

PUBLICATIONS:
None

FUNDING SOURCES:
Michael Lederman and Mirko Paiardini (MPI); R33 AI116171 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Dynamic modulation of expression of lentiviral restriction factors in primary CD4+ T cells following SIV infection

SPID#: 13077

UNIT/DIVISION: Microbiology and Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	
Prin. NPRC Core Sci.		M&I	
Other Core and Affil.		M&I	

PROJECT DESCRIPTION: Expression of 45 confirmed and putative HIV/SIV restriction factors was analyzed in CD4+ T cells from peripheral blood and jejunum in rhesus macaques, revealing distinct expression patterns in naïve and memory subsets. In both peripheral blood and jejunum, memory CD4+ T cells expressed higher levels of multiple restriction factors compared with naïve cells. However, relative to their expression in peripheral blood CD4+ T cells, jejunal CCR5+ CD4+ T cells exhibited significantly lower expression of multiple restriction factors, including APOBEC3G, MX2, and TRIM25, which may contribute to the exquisite susceptibility of these cells to SIV infection. In vitro stimulation with anti-CD3/CD28 antibodies or type I interferon resulted in upregulation of distinct subsets of multiple restriction factors. After infection of rhesus macaques with SIVmac239, expression of most confirmed and putative restriction factors substantially increased in all CD4+ T cell memory subsets at the peak of acute infection. Jejunal CCR5+ CD4+ T cells exhibited the highest levels of SIV RNA, corresponding to the lower restriction factor expression in this subset relative to peripheral blood prior to infection.

PROGRESS REPORT:
Nothing to report - new

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
internal

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: SINGLE CELL TRANSCRIPTIONAL PROFILING REVEALS A NOVEL POPULATION OF MUCOSAL TFH CELLS

SPID#: 13115

UNIT/DIVISION: M&I

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester		
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Despite extensive study, our understanding of the molecular events that determine the susceptibility of CD4+ T cells to SIV/HIV infection and the cellular events that follow lentiviral infection have been limited by our ability to track events that occur in single cells and analyze gene expression, including viral gene expression, on a single cell basis. New techniques that permit high-throughput analysis of gene expression in single cells can be used to deconvolute cell types in apparently homogenous populations of bulk cells.

PROGRESS REPORT:
We utilized acutely simian immunodeficiency virus (SIV)-infected rhesus macaques to isolate individual infected and uninfected CD4+ T cells from the intestinal mucosa, the primary site of viral replication in acute infection. Using high-throughput microfluidic quantitative real-time PCR of single cells, we measured expression of five viral transcripts used to define SIV-infected cells along with 91 cellular genes chosen for potential relevance in the viral replication cycle. Single cell analysis of over 300 single jejunal CD4+ T cells obtained 10 days after intravenous SIV infection revealed that approximately 20% of these cells were SIV-infected. Comparison of gene expression using multiple statistical methods identified PD-1 and CXCR5 as being the most significantly differentially expressed genes between infected and uninfected cells. The coexpression of PD-1 and CXCR5 on CD4+ T cells defines T follicular helper (Tfh) cells. However, Tfh have been classically associated with secondary lymphoid tissue. Flow cytometric analysis of jejunal samples from uninfected macaques identified a distinct population of PD-1+ CXCR5+ CD4+ T cells, with multiple phenotypic characteristics of classical Tfh cells, including expression of BCL-6 and IL-21. Transcriptional profiling of a panel of 70 Tfh-associated genes verified the similarity of this novel population to classical Tfh. PD-1+ CXCR5+ cells from jejunum contained an average of 3.4 SIV gag DNA copies/cell at the peak of acute infection. This level of infection over 10-times higher than that of bulk memory CD4+ T cells was observed despite low levels of cell surface expression of the SIV coreceptor CCR5. This study is the first single cell gene expression analysis of primate lentivirus-infected cells, and identified a novel and highly susceptible target cell population in vivo during acute infection.

PUBLICATIONS:
None

FUNDING SOURCES:
Internal

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Studies of Natural SIV-Infection of Sooty Mangabeys

SPID#: 556

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Understanding the reasons why SIV-infected sooty mangabeys (SMs) remain healthy despite high viremia is a key unanswered question in contemporary AIDS research, with important ramifications in terms of HIV pathogenesis, therapy, and vaccines. In recent studies, we have sorted stem-cell memory CD4+ T cells (CD4+ T_{SCM}), central memory CD4+ T cells (CD4+ TCM) and effector-memory CD4+ T cells (CD4+ TEM) from SIV-infected SMs and rhesus macaques (RMs), and that, while CD4+ TEM were similarly infected in both species, CD4+ T_{SCM} and CD4+ TCM of SMs show significantly (>1 log) fewer SIV-DNA copies *in vivo* than CD4+ TCM of RMs. Based on this result, we hypothesize that protection of CD4+ T_{SCM} and CD4+ TCM from virus infection is a key mechanisms by which SIV-infected SMs avoid CD4+ T cell depletion, chronic immune activation, and progression to AIDS. To test this hypothesis we will expand upon this previous work and propose a series of studies that will clarify the main features of *in vivo* and *in vitro* SIV infection in CD4+ TCM of both SMs and RMs, and elucidate the mechanisms by which CD4+ TCM of SMs are protected from SIV infection. In addition, our progress to date has helped us identify a number of directly related new lines of investigation to pursue under the overall umbrella of the hypotheses and research articulated in our "Studies of natural SIV infection of sooty mangabeys" grant proposal. We believe that these studies will advance significantly our understanding of how naturally SIV-infected SMs are resistant to AIDS despite high viremia. We envision that answering this question will provide clues to AIDS pathogenesis in humans that will have ultimately an impact on the prevention and treatment of HIV infection.

PROGRESS REPORT:

The observation that SIV-infected SMs harbor significantly less virus than SIV-infected RMs in specific subsets of memory CD4+ T cells (i.e., T_{CM} and T_{SCM}) may have implications for studies of HIV latency, reservoirs, and cure strategy, which are considered of the highest priority by the key stake-holders in contemporary HIV/AIDS research. To this end we recently completed a study in which SIV-infected SMs were treated with antiretroviral therapy (ART). We selected twelve chronically SIV-infected SMs, non-homozygous for CCR5-null alleles, and treated them for either 3, 6, 9 and 12 months with ART

regimen consisting of PMPA/Tenofovir, FTC/Emcitrabine, Raltegravir, and Darunavir. While the animals were on ART we monitored how suppression of virus replication affected the main virological and immunological features of this nonpathogenic infection. We observed that ART suppressed viremia to <60 copies/ml of plasma in 10/12 animals and induced a variable decrease in cell-associated SIV DNA in peripheral blood (average changes of 0.9-, 1.1-, 1.5-, and 3.7-fold for CD4+ transitional memory [T_{TM}], T_{CM}, T_{EM}, and T_{SCM}, respectively). ART-treated SIV-infected SMs showed (i) increased percentages of circulating CD4+ T_{CM}, (ii) increased levels of CD4+ T cells in the rectal mucosa, and (iii) significant declines in the frequencies of HLA-DR+CD8+ T cells in the blood and rectal mucosa. In addition, we observed that ART interruption resulted in rapid viral rebound in all SIV-infected SMs, indicating that the virus reservoir persists for at least a year under ART despite lower infection levels of CD4+ T_{CM} and T_{SCM} than those seen in SIV-infected macaques. Overall, these data indicate that ART induces specific immunological changes in SIV-infected SMs, thus suggesting that virus replication affects immune function even in the context of this clinically benign infection. Excluded by Requester

Excluded by Requester

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
NIAID R37 AI066998

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Antiviral role of CD8+T cells in ART-treated SIV-infected macaques

SPID#: 13078

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology Pediatrics	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The use of ART results in reduction of plasma viremia to below detectable levels in HIV-infected individuals but infection with HIV persists despite suppressive ART and treatment interruption results in viral rebound. In absence of ART, CD8+ T cells inhibit virus replication during SIV infection of rhesus macaques (RMs). However, the precise role of CD8+ lymphocytes in controlling virus replication during ART is unknown. Understanding the mechanisms controlling HIV/SIV reservoir dynamics under ART is critical to design effective strategies to reduce the size of these reservoirs and promote HIV/SIV remission.
In this proposal, we build upon our preliminary data indicating that CD8+ lymphocytes act in concert with ART to maintain virus suppression. We will answer three important questions regarding the mechanism(s) of CD8+ lymphocyte-mediated virus suppression. First, we will determine if the antiviral effect of CD8+ lymphocytes is present in SIV-infected ART-treated RMs with prolonged suppression of viremia (as an extension of our preliminary results demonstrating this effect in the setting of short-term virus suppression). In this study, we will perform CD8 depletion in SIV-infected RMs treated with ART for at least one year to moNonere closely mimic long-term ART-treated HIV-infected individuals with a stable virus reservoir. Second, we will determine if the observed antiviral effect of CD8+ lymphocytes under ART is mediated by CD8+ T cells vs. CD8+ NK cells. This critical experiment is made possible by a newly available monoclonal antibody (mAb) that targets cells expressing CD8□ (i.e., CD8□□+ T cells, but not CD8□+ NK cells) for depletion. Third, we will quantify the contribution of CD4+ T cell activation/proliferation to the increase in viremia that follows *in vivo* CD8 depletion. By using a neutralizing anti-IL-15 mAb together with CD8 depletion we can selectively block homeostatic CD4+ T cell activation and measure subsequent virologic outcomes.

PROGRESS REPORT:
This project was funded approximately eight months ago and since then we have made significant progress. Specifically, we completed all the relevant administrative procedures and genetic screening to identify and assign 30 healthy SIV-uninfected adult rhesus macaques (RMs) of Indian origin to the current study (Ais #1 and #2), with the assignment finalized in June 2016. Of note, animals carrying the MHC class-I alleles Mamu

B*08 (B008) and MamuB*17 were excluded from the current study due to their high propensity to become virus controllers. After the animal assignment and during the five-week baseline pre-infection period we have performed the proposed baseline blood and tissue collections as detailed in the original proposal, and analyzed the relevant data. As per the plan detailed in the original application, the animals were infected with the pathogenic SIV_{mac239} strain (i.v.; 3,000 TCID50) in September 2016 and longitudinal collections blood and tissues are currently being performed at several experimental time points post infection. All animals are routinely monitored for any health-related issues by the Yerkes Veterinarian and Animal Care services. We have started all animals at week eight post infection on a three-drug ART regimen that will be maintained for at least 12 months and includes Tenofovir (30 mg/kg/day s.c.), FTC/Emcitrabine (40 mg/kg/day s.c.), Dolutegravir (2.5 mg/kg/day s.c.). PMPA and FTC have been provided by GILEAD Sciences, Inc., as part of an ongoing collaboration with Excluded by Requester Dolutegravir is provided by ViiV as part of an ongoing collaboration with Excluded by Requester We are now in the process of achieving full suppression of SIV replication with ART before treatment with depletion antibodies. As such the experimental plan for this large in vivo experiment of CD8+ lymphocyte depletion in SIV-infected ART-treated RMs is moving forward quite successfully and in full agreement with the original plan.

PUBLICATIONS:
None

FUNDING SOURCES: Silvestri, G / NIAID R01 AI125064

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Targeting SIV Reserviors with Type I Interferons

SPID#: 13079

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:

Despite many major advances in AIDS research, a treatment that can cure the infection is still not available. Indeed, antiretroviral therapy (ART) must be taken for life, thus posing significant challenges in terms of costs and clinical safety, and interruption of therapy results in a rapid rebound of viremia. To this end, new approaches are required to eradicate the reservoirs of latently infected cells that persist during ART. The overarching Aim of this proposal is to explore the therapeutic potential of type I interferon (IFN-I), that activates a very potent natural antiviral molecular system, in reducing the reservoirs of virus-infected cells that persist under ART. In the R21 phase of this grant application we propose to use the existing, well-established nonhuman primate model of SIV_{mac} infection of rhesus macaques (RMs) to evaluate, in a pilot study, the potential impact of pegylated IFN-□2a (pIFN-□2a) on the overall size, anatomic location, and cellular distribution of the reservoirs of latently infected cells in ART-treated, SIV-infected RMs. We will use this very robust model to investigate directly *in vivo* and in multiple organs (i.e., blood, lymph nodes, spleen, mucosal tissues, etc) and cell types (i.e., memory CD4+ T-cell subsets and macrophages) whether and to what extent pIFN-□2a administration enhances the effect of ART on the virus reservoir. The results of the studies proposed in the R21 part of this application will pave the way for further experiments, to be conducted in the R33 phase of this proposal, in which we will test, in a larger cohort of SIV-infected RMs treated with long-term ART and exhibiting full suppression of virus replication, the effect of two consecutive cycles of pIFN-□2a treatment on (i) the size of the persisting reservoirs of latently infected cells, and (ii) the time of rebound of plasma viremia after ART interruption.

PROGRESS REPORT:

Two groups of six Indian origin rhesus macaques were intrarectally infected with $1x10^4$ TCID50 of SIV_{mac239}. At week 6 post infection, all SIV-infected RMs received a four-drug ART regimen. ART was continued for a total of 30 weeks (26 weeks before pIFN-α2a and 4 weeks with pIFN-α2a in the experimental group; 30 weeks of ART alone in the control group). Interferon treatment was administered at a weekly dose of 6μg/kg pIFNα2a. No animal developed AIDS-like symptoms and no major adverse effects were reported for ART and IFN treatment. All animals underwent selective necropsy at week 36 post infection.

To monitor the infection and evaluate ART regimen efficacy, plasma SIV_{mac239} RNA levels were measured by a quantitative TaqMan real-time RT-PCR assay. Full and consistent viral suppression was achieved in all animals after 24 weeks of ART treatment. Thus, IFN treatment was initiated in fully ART-suppressed RMs as

scheduled. Additionally, the $CD4^+$ T cell count in blood was measured throughout the study using flow cytometry immunophenotyping.

We assessed the level of residual viremia by using an ultrasensitive viral load assay with a detection limit of 1 copies/mL. Nonetheless, we did not detect any significant effect of IFN-treatment on residual viral load. Next, we evaluated whether pIFN-α2a administration has decreased the size of the virus reservoirs by quantification of total cell-associated SIV DNA in sorted $CD4^+$ T cells from blood and lymph nodes using quantitative SIV gag-specific real-time PCR in collaboration with the CFAR Virology Core. However, we observed no significant difference in total SIV DNA between IFN-treated and control animals.

Next, we will analyze interferon-stimulated gene (ISG) expression in $CD4^+$ T cells from PBMCs and lymph nodes by RNA-Seq analysis. Furthermore, we seek to quantify the inducible viral reservoir after IFN-treatment employing a viral outgrowth assay.

PUBLICATIONS:
None

FUNDING SOURCES: Silvestri, G / NIAID R21AI116200

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Collaboratory of AIDS Research for Eradication

SPID#: 13080

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	University of North Carolina at Chapel Hill Microbiology Immunology	

Prin. NPRC Core Sci.

Other Core and Affil. None

PROJECT DESCRIPTION:

The Scientific Research Support 2 (SRS 2): Primate Virology aims to support CARE by consolidating and focusing the preclinical evaluation of novel concepts and products. The SRS 2 will provide all the expertise, infrastructure, reagents, and personnel for the conduct of complex *in vivo* studies in RMs that will involve (i) experimental infection with SIV or SHIV; (ii) long-term treatment with ART; (iii) administration of specific anti-reservoir agents (i.e., LRAs and others); (iv) longitudinal monitoring of virus replication, virus reactivation, and overall reservoir size through validated, state-of-the-art assays; and (v) functional evaluation of the reservoir via analytical treatment interruption (ATI). The SRS 2 is based at the Yerkes National Primate Research Center (YNPRC), one of the seven NIH-funded primate research centers. This facility possesses all the necessary animal resources, infrastructure. and veterinarian and animal care expertise to fully meet the CARE goals. The SRS 2 is directed by Excluded by Requester (YNPRC, Emory University), who has >15 years experience in leading research projects involving complex *in vivo* interventions in SIV/SHIV-infected nonhuman primates. The SRS 2 will work in close collaboration with Excluded by Requester (University of North Carolina) for the overall coordination of the pre-clinical studies included in the CARE program, with Excluded by Requester (University of Pennsylvania) on the validation of novel, pathogenic clade-C envelope (Env) SHIVs for studies of latency and reservoirs in ART-treated RMs, and with Excluded by Requester (Duke University) for the coordination of the complex studies that will involve the combined use of LRAs and next-generation immune-based anti-reservoir approaches.

PROGRESS REPORT:

This project was funded approximately six months ago, and after the appropriate processing of the award the funds were made available to us in the late Fall of 2016. In this period since the project was awarded we have made initial progress in our proposed studies of LRA and DART administration in ART-treated SIV- or SHIV-infected RMs. Specifically, we completed all the relevant administrative procedures and genetic screening to request, identify and assign 14 healthy SIV-uninfected animals to the current study (10 for the LRA studies in ART-treated SIV-infected macaques, and four for the DART studies in ART-treated SIV-infected macaques), with the assignment finalized in January 2017. It should be noted that the animal assignment was delayed by

several weeks due to a temporary shortage of young Mamu-B*08-negative and MamuB*17-negative RMs at the Yerkes National Primate Research Center. After the assignment and during the five-week baseline pre-infection period we will perform the proposed baseline blood and tissue collections and analyze the relevant data. As originally proposed, the animals are slated to be infected with SIV_{mac239} (i.v.; 1,000 TCID50) and longitudinal collections blood and tissues will be collected at several experimental time points post infection. As detailed in the original proposal, we will start at week 8 post infection a treatment with a three-drug ART regimen that will be maintained for eight months and includes PMPA/Tenofovir (30 mg/kg/day s.c.), FTC/Emcitrabine (50 mg/kg/day s.c.), and Dolutegravir (2.5 mg/kg/day s.c.).

PUBLICATIONS:
None

FUNDING SOURCES:
NIAID U19AI096113

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Transcriptome resources for comparative primate models of lentivirus infection

SPID#: 13018

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Microbiology Immunology	
		Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The goal of this project is to generate whole transcriptome reference databases for several immune cell types at baseline and during the acute and chronic phases of HIV and SIV infection, with emphasis on the comparative models of pathogenic (i.e., humans and rhesus macaques (RMs)) and non-pathogenic (i.e., sooty mangabeys (SMs) and African green monkeys (AGMs)) infections. Specific Aim 1 is to generate baseline reference transcriptomes for several key immune cell subsets in healthy individuals belonging to four primate species (humans, RMs, SMs, and AGMs). Specific Aim 2 is to generate reference transcriptomes for the key immune cell subsets in the context of acute SIV infection in the pathogenic RM and the non-pathogenic AGM models. Specific Aim 3 is to generate reference transcriptomes for the key immune cell subsets in the context of chronic HIV and SIV infection in humans, RMs, SMs, and AGMs. Resource applications include: (i) improvements to gene models for already sequenced species (humans and RMs) and assistance for genome assem¬bly/annotation for new species (i.e., SMs and AGMs); (ii) development of tools (e.g., species-specific gene probes or microarrays) for AIDS-related systems biology research; (iii) investigation of the interaction between lentiviruses and the immune system during acute and chronic infection. The project was funded in September 2013 and the work conducted so far includes: (i) the optimization of the flow cytometric assays necessary to appropriately sort the immune cell subsets whose transcriptome is analyzed, (ii) the definition of the best strategies to conduct the microarray and next-generation sequencing analysis with related bioinformatics, and (iii) the first set of staining, sorting, and analyses relative to Aims 1 and 2.

PROGRESS REPORT:

In the last funding year of this project we made considerable progress – and have nearly completed the sorting of all samples as described in the original SOW. In 2015 we sorted 649 unique biological samples, collecting 2177 total tubes of sorted immune cells in RLT lysis buffer. To date, we have sorted 959 unique samples representing 5,108 samples. To obtain these samples, we infected 5 rhesus macaques with SIV and conducted a 28 day infection, sacrificing animals at Day 28 and collecting samples at pre-infection, Day 3, Day 7, Day 14 and Day 28. We identified 5 chronically SIV-infected rhesus macaques in a separately funded study of an experimental Lactobacillus vaccine and have obtained the sorts from these animals without any additional funds or needing any new recruitment of animals.We also obtained all subsets 2 chronically SIV infected sooty mangabeys, and recruited and

sorted samples from 2 ART-suppressed individuals and 2 Long-Term Non Progressor patients. In addition, work was performed at U. Pittsburgh as described in the original application. Although no animal work was budgeted for UPitt for Year 3 – we optimized further the sorting methods for CD4+ T cell subsets, macrophages, dendritic and NK cells from African green monkeys. In preparation of the Year 4 work – in which infections in 2 additional AGMs will be performed, 2 additional animals were requested and they are scheduled to arrive at the Pittsburgh facilities. As described in the original application, at the beginning of the fourth year of the project these animals will be ready to be inoculated with SIV and we will proceed with the sample collection and cell separation as described in the application. This material will be provided to our colleagues at the YNPRC for cell sorting.

PUBLICATIONS:
None

FUNDING SOURCES: Silvestri, G / NIH/OD/ORIP 1R24OD010445

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Monitoring SIV reservoirs with whole body immunoPET

SPID#: 13116

UNIT/DIVISION:

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	M&I	NIRC
Prin. NPRC Core Sci.		Pathology	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The project aims to optimize novel PET/CT imaging technologies for the mapping of virus replication in total body scans as well as immune determinants to interrogate host/pathogen interactions in real time at the macroscopic level. These optimized techniques will then be utilized to understand the viral dynamics during acute SIV infection via the IV, rectal and vaginal route and the dynamics of viral reservoirs in SIV infected monkeys that are subjected to extended ART followed by ART interruption.

PROGRESS REPORT:
During the past year, we have optimized the generation of smaller probes based on primatized monoclonal antibody fractionation and compared signal to noise ratios in our immunoPET/CT technology. Use of Fab and F(ab)2 version of antibody probe were found to considerably decrease background in liver, heart and spleen, allowing for better quantitation of signal. We also validated the results by combined administration of isotope and fluorescently labeled, generating PETimages as well as detection of signal microscopically following sacrifice. Finally we have optimized probes for he detection of CD4 T cells and SHIV infection in vivo.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:
R01 AI111907 (MPI: Villinger, Santangelo) 7/15/2014-6/30/2019 NIH/NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Synthetic DNA & Novel Env Vaccine for HIV

SPID#: 13081

UNIT/DIVISION: Microbiology Immunology

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Wistar Microbiology Immunology	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The broad goal of the Integrated Preclinical and Clinical AIDS Vaccine Development (IPCAVD) program "Synthetic DNA & Novel Env Vaccine for HIV" (U19 AI109646) is to produce a novel enhanced adaptive skin electroporation + gene adjuvanted DNA vaccine (E-DNA) as a prime to combine with a highly novel polyvalent A, B, C, A/E recombinant protein boost (PEB) as a vaccine to induce broad immunity to HIV. By using this combination of immunogens we hope to generate an improved spectrum of T and B anti-HIV immune responses compared to current HIV vaccine modalities. Currently, there is no HIV vaccine available that can drive a broad collection of functional antibody responses and potent Tfh as well as CD8 effector T cell responses. In the past few years we have reported exciting clinical results that a combination of adaptive EP + IL-12 cytokine gene adjuvant in normal healthy volunteers safely drives potent and long-lived CD4+ and CD8+ T cell responses. This program focuses on bringing forward a combined new EP delivered, enhanced DNA + gene adjuvant + adjuvanted polyvalent protein boost in a clinically manageable vaccine regime through development to present such a majorly improved clinical vaccine candidate to HVTN for examination in the clinic. The highly interrelated, translational focused Projects supported by this IPCAVD program include the DNA/adjuvant development with commensurate monitoring for cellular responses (Project 1), monitoring of humoral responses (Project 2), and product development including dermal EP development and GMP Envelope (Env) protein production (Project 3). Initial NHP experiments will be conducted as part of Projects 1 and 2, including two separate challenge experiments. These efforts will include screening of potential Env immunogens, prime-boost strategy using DNA prime with protein boost, novel adjuvant developments, and EP device advances, resulting in the final selection of a regimen for clinical evaluation.

PROGRESS REPORT:

The experimental design for the first NHP trial to be conducted as part of the IPCAVD U19AI109646 program was finalized as a four-arm, 40-macaque (i.e., 10 animals per arm) experiment that includes a 50-week immunization phase (three EP-DNA administrations followed by two Env protein boosts, all at a four-week interval) followed by a challenge phase in which the vaccinated rhesus macaques will be exposed weekly (for up to 15 weeks) to a low dose of SHIV intra-vaginally for up to a total of 15 challenges. We have first selected

and assigned to this project 40 adult female Mamu-B*08 and B*17 negative =rhesus macaques. We have then initiated the immunization procedure as planned, and at this time these animals have all received three immunizations by electroporation with various DNA plasmids including envelope, MEC, and IL-12 as well as the fourth and fifth immunizations consisting of a polyvalent protein boost adjuvented by monophosphoryl lipid A. Over the course of the study we collect blood for plasma and PBMC isolation as well as collecting tissues including bone marrow, and lymph node biopsies and fine needle aspirates for further immunological analyses. At selected time points we are also collecting fecal samples and vaginal secretions. All animals are slated for a low dose challenge (and relative follow up as detailed in the study design) that will take place 26 weeks following the last immunization. Following SHIV infection, the macaques will be monitored and samples will be collected for six months. At the end of the study all animals will be euthanized for necropsy to obtain extensive tissue samples that are not accessed during the study (spleen, mesenteric lymph nodes, brain, lung, liver, etc). All samples are sent to our collaborators at Duke and Wistar for further immunological analysis.

PUBLICATIONS:
None

FUNDING SOURCES:
NIAID U19 AI109646

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Emory Vaccine Center

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: VACCINE INDUCED IMMUNITY IN THE YOUNG AND AGED

SPID#: 13082

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Co-Investigator		EVC	
Prin. NPRC Core Sci.		-------	

Other Core and Affil.

PROJECT DESCRIPTION:
A major goal of Project 2 is to understand the molecular mechanisms of the integrated stress response. A fundamental feature of the integrated stress response is the formation of stress granules. Our previous work with the live attenuated yellow fever vaccine YF-17D demonstrates that this virus infects dendritic cells and stimulates the stress response kinase GCN2, which is necessary for antigen cross presentation and induction of antigen specific CD8+ T cell responses. In addition, YF-17D induces the formation of stress granules. During the past year we have focused our efforts in understanding the molecular mechanisms that regulate stress granule formation and in defining the molecular structures of stress granules. In particular, we have addressed the following questions:

- To determine whether other flaviviruses such as dengue or West Nile or the yellow fever Asibi strain are also capable of inducing stress granules.
- To determine if pattern recognition receptor (PRR) ligands could induce stress granule formation.
- To define the molecular mechanisms controlling the stress granule formation triggered by YF-17D and PRR ligand.
- To determine the protein components of the stress granules and their biological functions to YF-17D virus infection, and their impact in mediating the innate response to YF-17D.

PROGRESS REPORT:
Key outcomes: YF-17D infects both dendritic cells, non-immune epithelial cells and fibroblast cells, triggering PKR activation and stress granules formation. Importantly, this phenotype may contributed by the PRR ligands from YF-17D during the virus replication in the host cells. By using immunoprecipitation and proteomics assays, some novel stress granule candidates are identified. To knockdown of stress granule component or to block stress granule formation decrease YF-17D infection.

Rockefeller University Subcontract:
The entire YFV cDNA regions of the plasmids were sequenced. We found several nucleotide differences, relative to their respective sequence files as well as sequences available in Genbank, in both the 17D and Asibi parental cDNA constructs. For 17D, the nucleotides at these positions were compared to known

sequences of the vaccine strains (17DD, 17D-204 and 17D-213, as well as deep sequencing data from Beck, et al., 2014, JID 209, 334-344) and if not found in any of the vaccine strains, the nucleotide was "fixed" to reflect the correct nucleotide. Changes were made at nucleotide positions 4025 (A to G), 8563 (G to C), and 8566 (C to T). In the Asibi clone, the clone sequence was similarly compared and nucleotides that failed to reflect an Asibi-like identity were changed. Changes included 6013 (C to T), 6829 (T to C), and 8008 (C to T).

Key outcomes: Adventitious mutations have been corrected. New virus stocks derived from the corrected 17D and Asibi plasmids (designated pACNR-2015FLYF-17Da and pACNR-2015FLYF-Asibi) have been generated and titered. We are now poised to generate chimeric viruses on clean 17D and Asibi backbones.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: NK CELL-MEDIATED REGULATION OF T CELL IMMUNITY IN TB/HIV CO-INFECTION

SPID#: 13083

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:

One third of the world's population is infected with *Mycobacterium tuberculosis* (Mtb), and over 10 million are co-infected with human immunodeficiency virus (HIV). Latent Mtb infection (LTBI) represents immune containment, however HIV infection increases the risk of reactivation of LTBI from a 5-10% lifetime risk in HIV-uninfected individuals to a 10% annual risk in HIV-positive individuals. HIV-associated dysregulation of innate immunity and impairment of adaptive immunity by depletion of CD4 T helper cells likely contribute to loss of immune control of LTBI and progression to TB disease in HIV co-infected individuals. However, the parameters of immune control of LTBI that are perturbed in the setting of HIV co-infection have not been defined. The focus of this project is to examine how the innate immune response modulates Mtb-specific T cell immunity and determine how the regulatory pathways linking innate and adaptive immunity to Mtb are perturbed in the setting of HIV co-infection. We are (1) defining the phenotypic profiles, functional capacities, and NK cell receptor genotypes in persons with LTBI and HIV co-infection; (2) determining the relationship between NK cell profiles and the phenotype and function of Mtb-specific CD4 and CD8 T cell responses; and (3) defining the direct and indirect mechanisms whereby NK cells modulate Mtb-specific T cell immunity in LTBI, and how the mechanisms of cross-talk between NK cells and Mtb-specific T cells are dysregulated in the setting of HIV co-infection. Defining immune pathways involved in the generation, maintenance, and regulation of protective memory T cell responses to Mtb infection, and identifying the mechanisms whereby HIV infection impairs protective T cell immunity to Mtb, will be of vital importance to facilitate development of effective TB vaccines and targeted immunotherapeutic interventions and treatment of individuals co-infected with HIV and Mtb that are necessary to curb the TB epidemic worldwide.

PROGRESS REPORT:

During this reporting period, annual renewals for the study were obtained from the Emory University IRB, and the Kenya Medical Research Institute (KEMRI) Scientific and Ethics Unit. Standard operating procedures (SOPs), case report forms (CRFs) and databases have been developed for the study, and are currently in use. The Principal Investigator Excluded by Requester U.S.-based project supervisor(s) and coordinator(s) completed regular monitoring visits at the project site in Kenya to provide additional guidance and oversight on research-related activities, which was further supported by bi-monthly conference calls between the U.S. and Kenya-based

research teams. Enrollment has been completed for the HIV-negative Active TB, HIV-positive Active TB, HIV-negative LTBI, and HIV-negative Healthy Control cohorts. The HIV-positive LTBI and HIV-positive Healthy Control cohorts are continuing to enroll participants. The anticipated date of completion for study enrollment is June 2017. Emory study staff has conducted training for KEMRI/CDC-based staff in blood sample processing and immunology assay SOPs. Four shipments of biological specimens have been shipped from the KEMRI/CDC study site in Kisumu and received at the Emory Vaccine Center at Yerkes. Multiparameter flow cytometry antibody panels have been optimized for measurement of inhibitory receptor expression by Mtb-specific T cells. Preliminary experiments have been conducted to measure expression of PD-1, CTLA-4, and BTLA on Mtb-specific CD4 T cells in 12 HIV-negative subjects with LTBI and 17 HIV-positive subjects with LTBI. Data acquisition and analysis is ongoing.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ROLE OF ANTIGEN-SPECIFIC T CELL RESPONSES IN THE CONTROL OF TB

SPID#: 13084

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Co-PIs	Excluded by Requester	EVC	-------
		EVC	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Identifying immune correlates of control and protection to *Mycobacterium tuberculosis* (Mtb) infection is essential for designing vaccines for TB. The overall goals of our TBRU project are to identify antigen-specific T cell responses that are associated with distinct outcomes of Mtb infection: clearance, persistence, and progression to active disease. We currently lack the knowledge or tools to distinguish individuals who harbor persistent Mtb infection from those who may have resolved infection via immune-mediated clearance of bacteria. In Project 1 we are focusing on **"Identification of human Mtb-specific T cell signatures that are associated with resolved and persistent Mtb infection."** We are testing the hypothesis that distinct Mtb-specific memory T cell profiles are associated with bacterial clearance or persistence. This is supported by our data showing that distinct antigen-specific memory T cell phenotypes and functions are associated with LTBI, active TB disease and clinically resolved TB. We are using chemotherapy-mediated clearance to model immune-mediated clearance of Mtb, as the treatment regimen for LTBI should result in significant reduction or elimination of bacteria. We are enrolling individuals with LTBI in a low-exposure setting (Atlanta, GA) and systematically comparing their antigen-specific T cell responses before and after treatment. We are delineating the spectrum of antigens recognized by Mtb-specific memory T cells, characterizing their memory phenotypes, functional capacities and transcriptional profiles. Using statistical analyses, we are deriving Mtb-specific T cell signatures that represent bacterial clearance and persistence, and determining the prevalence of these signatures in treatment-naive individuals with LTBI in Kenya. We are longitudinally assessing the dynamics of Mtb-specific memory T cell responses and their homeostatic turnover in LTBI. We are also comparing clearance/persistence signatures with those associated with progression to TB. Overall, these studies will provide insights into protective immunity to TB and new tools to evaluate Mtb persistence or clearance in LTBI.

PROGRESS REPORT:

During this reporting period, the study protocol received annual renewal of approval by the Emory University IRB. Standard operating procedures (SOPs), case report forms (CRFs) and databases have developed for the study, and are currently in use. Monthly conference calls are in place to facilitate regular communication between all PI's of the projects and cores of this TBRU U19 project. Enrollment of participants with LTBI in Kenya has been completed for Project 1, with longitudinal follow-up ongoing. The first shipment of PBMCs from the TBRU Project 1 study participants in Kenya has been received and stored in liquid nitrogen at the Emory Vaccine Center at Yerkes. Enrollment of participants with LTBI from the DeKalb County Board of Health Refugee Clinic who accept treatment for LTBI is expected to be completed by April 2017. Longitudinal follow-up of these participants at 3-monthly intervals is ongoing. Enrollment of participants with LTBI who decline

treatment is expected to commence in February 2017, with a 2-year longitudinal follow-up period scheduled for completion in 2019. Blood samples are received from each participant at each time point, including EDTA blood for plasma isolation and storage; and sodium heparin blood for RSA, PBMC isolation, and plasma isolation and storage. Diluted whole blood response spectrum assays (RSA) have been conducted on all samples received to measure mycobacteria-specific T cell responses to a panel of 60 functionally diverse Mtb antigens. The RSA has been adapted for use with cryopreserved PBMCs. Data analysis is currently ongoing in collaboration with the TBRU Data Management Center.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: DETERMINANTS OF NEUTRALIZATION BREADTH IN EARLY HIV-1 INFECTION

SPID#: 0405

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
Antibodies that neutralize genetically diverse HIV-1 strains, known as broadly neutralizing antibodies (bnAbs) are rare and the mechanisms that expand the otherwise narrow neutralization capacity observed during early HIV-1 infection are currently undefined. The goals of this project are therefore to understand how viral and immune events that occur during early infection could be incorporated into HIV vaccination strategies that will elicit antibodies with neutralization breadth.

PROGRESS REPORT:
In the past year, we have demonstrated that more efficient glycosylation of the transmitted/founder virus envelope gp120 subunit correlated with subsequent development of neutralization breadth, as did extensive diversification in the gp120 V2, V4, and V5 regions, and contemporaneous viral escape. These findings suggest that variation in the efficiency of site-specific glycosylation influences neutralizing antibody elicitation and targeting, and could advance the design of immunogens. We also carried out an in-depth analysis of ~75 B cells and monoclonal antibodies each from two HIV-1 infected individuals selected for their distinct plasma neutralizing capacities. The results demonstrated that high B cell clonal diversity with low competition provided a 'relaxed' environment in which neutralizing antibodies against the CD4 binding site emerged. In contrast, biased heavy and light chain germline gene usage and pairing, with high somatic hypermutation in the antibody heavy chain variable domains and high affinity binding to antigen resulted in fierce competition that impeded development of neutralizing activity. These findings demonstrate a strong and previously unappreciated link between B cell diversity and the development of autologous neutralizing antibodies during early HIV-1 infection.

PUBLICATIONS:
Excluded by Requester

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Antibody Function and Viral Diversity Core

SPID#: 13118

UNIT/DIVISION: Emory Vaccine Ctr

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ✓ Yes No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	
Principal Investigator		EVC	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The Antibody Function and Viral Diversity Core will perform a thorough characterization of the antigen specific B cells, antibody effector functions, and antibody specificities elicited by the trimeric BG505 SOSIP-based HIV-1 envelope immunogens in rhesus macaques. We will also determine how vaccine elicited antibodies contribute to protection against an autologous SHIV challenge, and also assess viral determinants that mediate breakthrough of vaccine-mediated protection.

PROGRESS REPORT:
The funding for this consortium began on June 1, 2016. Since that time, we have successfully developed methods to sort antigen-specific memory B cells from immunized rhesus macaques for genetic characterization of germline genes and for recovery of monoclonal antibodies for functional characterization.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester PhD; funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Host Acute Models of Malaria to Study Experimental Resilience (THoR HAMMER)

SPID#: 13085

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Co-Principal Investigator		Dept. Pediatrics, Emory	
Co-Principal Investigator		Dept of Mathematics, UGA	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The Host Acute Models of Malaria to Study Experimental Resilience (HAMMER) project is a multi disciplinary, multi-institutional, multi-investigator project along with national and international collaborators to investigate the mechanisms behind "resilience" following malaria infection based on non-human primates and clinical human samples. The project covers a variety of diverse host-pathogen model systems and incorporates data generated by the six research cores (malaria, immune profiling, functional genomics, proteomics, lipidomics, and metabolomics) with the informatics, mathematical modeling, and computational analysis cores to evaluate key features associated with resilience as well as to develop interventions that could enhance resilience against malaria.

PROGRESS REPORT:
During the current period, we have completed the project's experimental and information technology infrastructure setup to accommodate high-frequency telemetry data capture and analysis. The telemetry system pioneered in E30 is now fully established and will enable our first data transfer to BTS in the next period. We performed our initial pilot experiment E30 with *M. mulatta* (rhesus) infected with *P. knowlesi* and the analyses of E30 data are in progress. Platforms and SOPs for targeted proteomics (SomaLogic) and metabolomics (Biocrates) of host plasma, host red blood cell (RBCs), scavenger cell-focused flow cytometry assays as well as for data production, validation, and release of data for E30 were developed. We established logistics and timeline for *M. mulatta* and *M. fascicularis* cohort infections (E06 and E07). The E07 experiment is currently in progress and E06 will be implemented until June 2017. Finally, we carried out extensive retrospective analyses on prior NHP experimental datasets and advanced plans to study metabolomics data retrospectively from *P. knowlesi* patients in Malaysia.

PUBLICATIONS:
None

GRANT NUMBER: # W911NF-16-C-0008

FUNDING SOURCES: Mary R. Galinski, PhD; funded by DARPA and NIAID

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TITLE: Systems Biology of Malaria as a Model For Host-Pathogen Interactions
Malaria Host Pathogen Interaction Center (MaHPIC)

SPID#: 12006
UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Co-PI:		EVC	
Prin. NPRC Core Sci.		-------	

Other Core and Affil.

PROJECT DESCRIPTION:
The Malaria Host Pathogen Interaction Center (MaHPIC) project is a large multidisciplinary, multi-institutional, multi-investigator project to study malaria systems biology based on both non-human primate infections and human clinical samples. The work is designed to integrate data generated by the six core research facilities (malaria, immune profiling, functional genomics, proteomics, lipidomics, and metabolomics) via the informatics, mathematical modeling, and computational analysis cores. The overarching hypothesis of this work is that by studying these model systems with these approaches, we will provide insights into the mechanisms and the indicators for human malarial disease.

PROGRESS REPORT:
During the current period, the MaHPIC team remained focused on the project's main overarching aims and biological questions with both NHP and human studies, generating, analyzing and integrating data, and developing and maintaining a critical set of multidisciplinary working group meetings and action plans, as well as advancing manuscript development, submissions and publications. We have completed a longitudinal *P. cynomolgi* experiment in *M. mulatta* (E23-24-25) and a *P. knowlesi* infection experiment in *M. mulatta* (E30) with real time telemetry data obtained from surgically implanted telemetry devices. E30 data continues to be generated, analyzed, and transferred as required via the project's Informatics Core and iRODs server for analysis by the team's modelers and experimentalists. We started a *P. knowlesi* infection of *M. fascicularis* experiment (E07) and continued synergistic activities with our collaborative project called THoR's HAMMER (Technologies for Host Resilience: Host Acute Models of Malaria to study Experimental Resilience), supported by DARPA. Among a few new genomes being developed, an updated genome for *P. knowlesi* was assembled using PacBio technologies and this is currently being annotated. We have also initiated a systems vaccinology trial and have continued to develop immunological and biological assays to carry out validation experiments. Data deposition with EuPathDB has begun. A special MaHPIC project page has been created in PlasmoDB. Data types without special open source archived locations will be available there for download. Finally, human plasma metabolomics analyses continued, with samples from Brazil, Thailand, Colombia, Malaysia, and Nigeria. Our progress has been detailed in major 6-month progress reports to NIAID officials, as required per this project's contract.

PUBLICATIONS:

Y:	Excluded by Requester
Excluded by Requester	

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Excluded by Requester

FUNDING SOURCES:

Excluded by Requester ; funded by NIAID and DoD/DARPA

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2016-17 Annual Progress Report SPID Form

TITLE: VIROLOGIC CORRELATES OF HETEROSEXUAL TRANSMISSION

SPID#: 0406

UNIT/DIVISION: Emory Vaccine Ctr

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ✓ Yes No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	
Co-Investigator		EVC	
Co-Investigator		EVC	
Co-Investigator		Projet San Francisco, Kigali, Rwanda	
Co-Investigator		ZEHRP, Zambia	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Heterosexual HIV-1 transmission is an inefficient process that occurs on average roughly once for every 100 unprotected sexual encounters. We have sought to understand why In approximately 85% of heterosexual epidemiologically linked couples located in a Zambian cohort where clade C virus prevails and in a Rwandan cohort where clade A virus predominates, that a single virus from the large swarm of variants present in the chronically infected donor establishes a new infection in the recipient, thus accounting for the so-called 'transmission bottleneck'. With the increasing use of antiretroviral drugs, we have also begun to examine the frequency and types of drug resistance which in theory might exaccerbate transmission rates within a population. Finally, we have examined why a subset of infected individuals contract a second heterologous virus from a different donor, a process known as superinfection (SI).

PROGRESS REPORT:
Our prior results showed that establishment of infection by a single transmitted founder (TF) virus is not due to enrichment of this variant within the donor's genital track nor because the TF envelope protein exhibits an enhanced binding to receptor protein on target cells. Recent analyses have shown that TF virions are more consensus like compared to nontransmitted (NT) virions. We next examined whether TFs might be better able to replicate in a new host despite an early interferon mediated innate immune response, but found no differences between TF and NT viruses in the presence of interferon alpha. In contrast, University of Pennsylvania colleagues showed evidence indicating an increased resistance to interferon alpha and beta cytokines for both clade B and clade C TF viruses. Interestingly, their results also showed reduced variability for in vitro replication rates compared to what we typically observe, perhaps owing to methodological differences.

In 2015, the World Health Organization suggested making antiretroviral therapy (ART) drugs available to all HIV infected subjects regardless of prevailing CD4 counts and to uninfected subjects at a high risk of infection. This is challenging in resource poor nations, and an increased use of ART could lead to drug resistance within a population. We have begun to assess the ability of individuals on ART to transmit virus to their partners as well as to determine the incidence of drug resistance in newly infected partners.

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Finally, SI might increase the genetic diversity within a viral population via recombination between heterologous viral stains. This could provide an advantage for viral evolution and make vaccine design more challenging. Our most recent survey results suggest that SI may not be as common as originally thought, perhaps owing to behavioral changes in within the cohort over time.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIAID

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TITLE: CTL AND HIV POLYMORPHISMS IN HETEROSEXUAL TRANSMISSION

SPID#: 0516

UNIT/DIVISION: Emory Vaccine Ctr

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ✓ Yes No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	
Co-Investigator		EVC	
Co-Investigator		EVC	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This collaborative project involving Emory and UAB scientists examines how the immune system in a newly infected individual exerts pressure on an incoming HIV-1 transmitted founder (TF) virus and its progeny, which then accounts for the development of mutations that allow virions to escape from immune surveillance and to propagate efficiently within the new host. In a prior analysis of 127 acutely infected Zambians, we demonstrated a dramatic and early impact of viral replicative capacity (vRC) on HIV-1 immunopathogenesis that is independent of viral load (VL). Individuals infected with high-RC viruses exhibited a distinct inflammatory cytokine profile as well as significantly elevated T-cell activation, proliferation, and CD8(+) T-cell exhaustion during the early months following infection. Moreover, the vRC of the transmitted virus was positively correlated with the magnitude of viral burden in naive and central memory CD4(+) T-cell populations, raising the possibility that transmitted viral phenotypes may influence the size of the initial latent viral reservoir. Taken together, these findings support an unprecedented role for the replicative fitness of the founder virus, independent of host protective genes and VL, in influencing multiple facets of HIV-1-related immunopathology, and that a greater focus on this parameter could provide novel insights with respect to developing clinical interventions. The main objectives of this grant are to: (1) Define and study the diverse proteomes in 80 TF viruses from the Rwandan cohort and in 120 TF viruses from the Zambian cohort; (2) To characterize early CD4 and CD8 responses that account for early viral control; and (3) To explore fine mapping of the human leukocyte antigen (HLA) and related sequence elements which might account for effective immune control by the host.

PROGRESS REPORT:
Two recently published papers by Carlson and Monaco each showed that a significant number of non-consensus polymorphisms are present in TF viruses, and hence these mutations must have arisen in the donor, the person who infected the donor, or perhaps someone earlier in this chain of viral transmissions. This is important because it shows that certain mutations providing an advantage to the virus might persist over time and become enriched within a viral population.

Numerous publications rely on temporal changes in viral load (VL) and CD4 counts as a reflection of the extent of pathogenesis. In a paper by Prentice et al, the authors evaluated CD8 counts over a period of up to 36

months following infection and found that factors associated with these CD8 counts had little overlap with other outcomes including VL, CD4 counts, and the CD4/CD8 ratio.

HIV transmission may occur as a result of the transmission of free or cell-associated virus. Excluded by Requester used mixed lymphocyte cultures and found that a more potent killing effect was seen when HLA B alleles differed between donor and recipient cells than when alleles were shared, suggesting that B allele sharing might prove detrimental in preventing cell associated viral transmissions.

The WHO has recommended the use of antiretroviral therapy (ART) drugs for all HIV infected and high risk uninfected subjects, but drug access can represent a significant obstacle, especially in resource poor nations. Moreover, as Excluded by Requester have observed, the level of drug resistance in ART naïve individuals can vary significantly.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: B-CELL BIOLOGY OF MUCOSAL IMMUNE PROTECTION FROM SIV CHALLENGE

SPID#: 0698

UNIT/DIVISION: Emory Vaccine Ctr

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ✓ Yes No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC M&I (Yerkes)	
		EVC	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The WHO has recommended the use of antiretroviral therapy (ART) drugs for those individuals infected by HIV-1 and to others who are at a high risk of infection. Unfortunately, provision of ART in resource poor nations is challenging, poor compliance often occurs when taking these medications, and drug resistance may develop over time which makes these pharmaceuticals less effective, requiring the use of a second line of medications that are often more expensive or difficuult to secure. For these reasons, an effective HIV vaccine may represent the best hope to eradicate the HIV epidemic. This consortium has developed and tested multiple combinations of vaccines and adjuvants in a Rhesus macaque animal model as means of learning about important mechanisms underlying innate and adaptive immune responses. It is hoped that information learned from these experiments will guide subsequent efforts to design and test vaccines exhibiting efficacy in countering the spread of HIV.

PROGRESS REPORT:
Our previous work has shown that antigens adjuvanted with specific ligands for toll-like receptor 4 (TLR4) and TLR7/8 encapsulated in poly (lactic-co-glycolic acid) (PLGA) based nanoparticles (NP), induced robust and durable immune responses in mice and macaques. We investigated the efficacy of these NP adjuvants in inducing protective immunity against simian immunodeficiency virus (SIV) as an early step toward developing an effective vaccine against the related HIV virus. Rhesus macaques (RMs) were immunized with NP containing TLR4 and TLR7/8 agonists mixed with soluble recombinant SIVmac239 derived envelope (Env) gp140 and Gag p55 (Protein), or with virus like particles (VLP) containing SIVmac239 Env and Gag. NP adjuvanted vaccines induced robust innate responses, a greater magnitude and persistence of antigen specific antibody responses, and enhanced plasmablast responses, compared to Alum adjuvanted vaccines. NP adjuvanted vaccines induced antigen specific, long-lived plasma cells (LLPCs), which persisted in the bone marrow for several months after vaccination. NP adjuvanted vaccines induced immune responses that were associated with enhanced protection against repeated low dose, intra-vaginal challenges with heterologous SIVsmE660, in animals that carried TRIM5α restrictive alleles. Protection induced by immunization with Protein + NP correlated with the pre-challenge titers of Env-specific IgG antibodies in serum and vaginal secretions.

However, no such correlate was apparent for immunization with VLP + NP or alum adjuvanted groups. Transcriptional profiling of PBMCs isolated within the first few hours to days after primary vaccination revealed that NP adjuvanted vaccines induced a molecular signature similar to the live attenuated yellow fever viral vaccine. This systems approach identified early blood transcriptional signatures that correlate with Env-specific antibody responses in vaginal secretions and protection against infection. These results demonstrate the adjuvanticity of NP adjuvant in inducing persistent and protective antibody responses against SIV in RM with implications for vaccine design against HIV.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: B and T Cell Biology of Protection from and Eradication of SIV/SHIV Infection

SPID#: 13065

UNIT/DIVISION: Emory Vaccine Ctr

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ✓ Yes No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	
Principal Investigator		M&I (Yerkes)	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

A major challenge in public health is to develop an effective way to combat the HIV-1 pandemic. One approach is to utilize antiretroviral therapy (ART) drugs to reduce circulating levels of virus. This has the dual advantage of preventing or delaying the onset of AIDS and reducing subsequent HIV transmission. Unfortunately, poor access to drugs in resource poor nations, poor compliance in taking medications on a regular schedule, and development of drug resistance all limit the overall effectiveness of this approach. An alternative might involve the development of an effective HIV vaccine, but this has been difficult in early clinical studies. This project extends efforts from a prior 5-year Emory-based U19 consortium that evaluated antigen and adjuvant combinations in a Rhesus macaque model as a means of preventing infection from a subsequent heterologous SIV vaginal challenge. This UM1 consortium differs from the prior U19 in that the two central foci are protection and eradication whereas the prior consortium focused exclusively on protection. Initial vaccinations will use a BG505 SOSIP to leverage available immunology reagents and repeated vaginal challenges will utilize a homologous SHIV. Efforts will focus on generating potent and persistant antibody and robust CD8 T cell responses elicited against infected cells. We will test the utility of using Rapamycin (mTOR inhibitor) to limit the abundance of CCR5 receptors on CD4+ target cells as a means of inhibiting viral entry during challenge. A promising vaccine regimen will be tested in Rhesus neonates to generate strong early anti-HIV responses before immune responses are circumvented by recognition of similar epitopes present in gastrointestinal flora. We will also test 'shock and kill' strategies for virus eradication by providing ART treated infected monkeys with the best available latency reactivating drugs coupled with optimal vaccine strategies in an effort to eliminate viral reservoirs.

PROGRESS REPORT:

The funding for this consortium began on June 1, 2016. Since that time consortium members have been developing plans to test new antigen and adjuvant combinations as described above. We have recruited monkeys to begin initial experimental trials, secured immunization reagents required for these studies, and planned blood and tissue collections to evaluate immune correlates of protection. As part of our initial trials, we will test the inclusion of viral vector expressed gag protein as a means of eliciting strong CD8 dependent cytotoxic lymphocyte mediated anti-viral responses. Since immunization strategies may enhance the expression of the CCR5 receptor on the surface of CD4+ target cells thereby countering any protective effects elicited by antigens and adjuvants, Rapamycin will also be evaluated in one experimental trial as a means to limit CCR5 expression and hopefully enhance protection. We are also in the planning phase of deciding how

best to test vaccination of neonates with the best combination of antigen and adjuvant. Our efforts are being guided in part from results generated by other large NHP studies (CHAVI, Gates, etc). We continue to share with NIH representatives on a monthly basis our proposed experimental plans and prior experimental findings. Recently smaller groups of investigators have begun to meet to discuss with greater focus issues related to developing potent neutralizing antibodies, how lymph node biopsies might be studied, coordination of scientific efforts, etc.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester nded by NIAID
funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Overcoming Maternal Antibody-Mediated Immunosuppression

SPID#: 12016
UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
Maternally derived antibodies are crucial for protecting infants during their first months of life. This is best exemplified in infants with agammaglobulinemia, who thrive during the first year of life, but succumb to repeated infections after the levels of circulating maternal antibodies wane. There is, however, one downside to maternal antibodies; they suppress vaccine-induced activation of the infant immune system. Because maternal antibodies suppress vaccine-induced activation of the infant immune system, any necessary and life-saving vaccines, such as measles, are given at delayed times, up to a year after birth. This leaves a wide window of time during which the infant is vulnerable to infection but unable to develop the antibody response necessary for its own protection.

PROGRESS REPORT:
Understanding how to activate the infant immune system in the presence of maternal antibodies is a critical area of research because it could lead to the development of more efficacious infant vaccines. Toward this end, we immunized cohorts of female mice, allowed them to proceed to memory phase and mated them to generate offspring pups that bear antigen-specific maternal antibodies. We also setup controls to yield pups without maternal antibodies. We are in the process of testing these pups with either soluble antigens or with adjuvants to see if maternal suppression can be overcome.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Dynamics and evolution of recall immune responses to influenza viruses-Yerkes Project 2

SPID#: 13087

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Affinity maturation – the progressive increase in antibody affinities – is a hallmark of humoral immunity. Somatic hypermutation generates a plethora of antibody mutants in antigen-specific B cells, including those with mutations in immunoglobulin frameworks. Survival of mutants is dependent on the functional preservation of the immunoglobulin framework as well as the increasingly fine specificity of the complementarity determining regions (CDRs) to antigen during selection.

PROGRESS REPORT:
Here we show that murine somatic mutations are introduced via gene conversion from other immunoglobulin gene segments from either the cis or trans allele. Similarly, analysis of two recent human immunoglobulin data sets reveals that a majority of mutations are traceable to other immunoglobulin gene segments. This suggests that diversity generated in a humoral response is templated and genetically restricted. Further, this suggests that gene conversion allows B lymphocytes to maintain the integrity of the framework while simultaneously allowing selection for rare CDR mutants with increased affinity.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Novel DC targeted adenovirus vector for malaria vaccine development

SPID#: 13088

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

We have developed a vaccine strategy that combines the flexibility of adenovirus vectors with the use of chimeric recombinant proteins tailored to deliver highly immunogenic multi-stage vaccine candidates using heterologous prime-boost immunization regimens. Several adenovirus vectors have been produced and tested to implement a vaccination regimen that can overcome the high prevalence of pre-existing immunity against the most commonly used Ad5 vector. DCs are a specialized subset of antigen-presenting cells (APCs) that express high levels of MHC class I and II proteins and are responsible for capturing, processing, and presenting antigens to naïve T cells, thereby activating the T cells. The central role of DCs in priming T cell responses provides a strong rationale for DC-targeted vaccination to enhance T cell responses. We are exploring in this project novel strategies for DC targeting to test if superior efficacy can be achieved.

PROGRESS REPORT:

Clinical trials of the first generation of vaccine vectors based on human Ad showed that a majority of adults possess significant titers of neutralizing antibodies to common human Ad serotypes such as Ad2 and Ad5, the most widely studied Ad serotypes. Neutralizing antibodies can reduce the potency of viral vector vaccines by inhibiting vector-mediated delivery of the encoded transgene. An approach towards administering Ad vectors in populations with pre-existing immunity (PEI) due to natural infections comprises the development of a series of vectors using virus serotypes to which previous exposure is unlikely. Several groups have developed vectors based on rare human serotypes, such as serotype 35 or nonhuman adenoviruses such as bovine, canine or ovine adenoviruses to which the human population is less exposed, including those of chimpanzee origin. Chimpanzee-derived Ad vectors have been shown to be highly immunogenic in animal models and recently in malaria vaccine trials. To address the issue of PEI, we have used SAd36, an E species Ad isolated from chimpanzees since the cross-neutralizing antibody titers against the species E Adenoviruses are low in humans. As with Ad5, the SAd36 vector contains an E1-deleted with a shuttle plasmid allowing transgene incorporation in place of the E1 region (kindly provided by Excluded by Requester University of Pennsylvania, Philadelphia, PA). Using this approach, we generated a novel SAd36 vector expressing a hybrid pre-erythrocytic/erythrocytic *P. vivax* chimeric antigen as a transgene. The recombinant vector has been tested in mice and immunogenicity, and efficacy assessments are ongoing.

PUBLICATIONS:

None

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Optimization of chimeric multi-stage immunogens for malaria vaccine development

SPID#: 13089

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Our group has developed effective malaria vaccines following a stepwise approach targeting different effector mechanisms for the induction of balanced immune responses. We have used a multi-stage malaria vaccine approach for the design of an effective vaccine since clinical trials have shown that if a single sporozoite can evade the immune response, it can lead to blood stage infection and clinical malaria, which is more likely to occur if only pre-erythrocytic stage antigens are targeted. Therefore, a multi-stage malaria vaccine able to target both hepatic and blood stage antigens is needed. Different cellular subsets are required to obtain protection in malaria as both T and B cells are needed to control the various parasite stages. From our observations, the best way to obtain a balanced immune response is the use of a heterologous recombinant adenovirus (Ad) vector prime – protein boost vaccination regimen as this immunization scheme elicits the optimal antibody and cellular immune responses.

PROGRESS REPORT:

Taking advantage of the molecular flexibility of the Ad vector platform, our group developed several malaria vaccine candidates and delivered them through different Ad vectors. First, we used a chimeric adenovirus serotype 5 in which its fiber knob was replaced with that of Ad3 since most of the pre-existing immunity is directed towards this region. We also have shown that a heterologous Ad prime-protein boost regimen including a *P. yoelii* protein vaccine based on selected epitopes from the circumsporozoite protein (CSP) and the merozoite surface protein-1 (MSP1), was more protective than a homologous protein regimen and induced sterilizing immunity in approximately 50% of the mice tested. The improved efficacy was related to the induction of protective effector memory CD8+ T cells. Modifications introduced in the Ad capsid can be used to modulate the immune responses induced by recombinant Ad vectors, as DCs mainly recognize the adenoviral capsid. In this regard, we developed a recombinant Ad5 vector that expresses a *Plasmodium* promiscuous T cell epitope derived from MSP1 within the hexon hypervariable region 2 (HVR2) region of the viral capsid, and a multi-stage *P. yoelii* experimental vaccine as a transgene. We hypothesized that the high copy number of this cognate T cell presented in the context of the hexon modification could improve the immunogenicity of the transgenic product. This capsid modification resulted in more robust antibody and cellular immune responses when compared to immunization regimen with a vector with the unmodified hexon. The immunogenicity differences resulted in a better protective efficacy.

PUBLICATIONS:

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Systems Biol Analysis of Innate, Adaptive Response to Vaccination-Zika Suppl

SPID#: 0649

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		EVC	
Other Core and Affil.		-------	
		None	

PROJECT DESCRIPTION:

In this project, my laboratory sought to better understand Zika virus (ZIKV) infection and host immune responses within human dendritic cells (DCs) and placental macrophages (Hofbauer cells; HCs).

PROGRESS REPORT:

In Aim 1, we focused on evaluating ZIKV replication in human monocyte-derived DCs, defined the molecular signatures through RNA-seq and performed extensive computational modeling. In Aim 2, we planned to focus on ZIKV infection of human HCs and on performing a similar RNA-seq/computational modeling set of studies. To this end, we recently published our findings evaluating ZIKV infection of human DCs (PLOS Pathogens) and HCs (Cell Host and Microbe). We are currently collecting samples to perform RNA-seq of ZIKV infection of human DCs and HCs over the next couple of months.

PUBLICATIONS:

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIAID, Private Source Private Source

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ROLE OF MUCOSAL ANTIGEN-PRESENTING CELLS IN REGULATING IMMUNE RESPONSE (MERIT)

SPID#: 13089

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:

The overall goal of this project, 'Understanding the Role of Mucosal Antigen-Presenting Cells in Regulating Immune Response,' is to understand how the innate immune system regulates adaptive immune responses, and to harness this understanding in designing vaccines. The subject of the research funded by the present grant during the current cycle focused on the central problem of how/ the immune system launches robust immunity against invading pathogens, while maintaining tolerance to self. This problem assumes a particular significance in the intestine because of the trillions of commensal microorganisms and food antigens that confront the intestinal immune system every day. Recent advances suggest that DCs and macrophages play a fundamental role in maintaining the balance between immunity and tolerance. The hypothesis of the application was that balance between immunity and tolerance in the intestine is a complex function of the subset of antigen-presenting cell (APC), the microbiota, and instructive signals from stromal elements. This hypothesis is being tested in the following specific aims: Aim 1; To determine whether distinct subsets of lamina propria DCs and macrophages differentially bias the class of innate and adaptive immune responses. Aim 2: To determine whether commensal bacterial flora regulate the functions of lamina propria DCs and macrophages and their ability to induce Thi 7 versus T regulatory responses. Aim 3 : To determine the innate responses of lamina propria DCs and macrophages to oral administration of adjuvants or vaccines, and the effects of such responses on the adaptive immune response.

PROGRESS REPORT:

To elucidate role of mTOR in DCs, we developed system to genetically ablate mTOR from APCs, using CD11c-Cre system. Despite significance as central metabolic regulator, we surprisingly found no global defects in mice lacking mTOR in DCs; we found minimal evidence of perturbation in DC frequency and function in both spleen and lymph node compartments; these mice revealed striking range of subset-specific phenotypes localizing anatomically to the lung.

Here, mTOR ablation led to specific defect in homeostatic accumulation of $CD103^{+}$ DCs, conferring profound defect in antiviral immunity following immunization with live attenuated influenza vaccine. Similarly, reduced frequencies of CD11c-expression lung alveolar macrophage fraction were observed, culminating in acquired pulmonary alveolar proteinosis, disease associated with impaired airway functions. Thus, although mTOR

appeared initially implicated as an obligate requirement for robust lung immunity via homeostatic maintenance of DC populations, we found no evidence for defect in lung CD11b$^+$ DCs in absence of mTOR ablation; this DC population was found at normal frequencies in the lung. To address if CD11b$^+$ DCs indeed represented an mTOR-independent DC population, we probed function by administering intranasal house dust mite (HDM) allergen - treatment that specifically activates the CD11b$^+$ lung DC subset to mount allergen-specific Th2-polarized adaptive immune responses.

We examined serum antibody concentrations, because readout is known to correlate with asthmatic severity in humans. To our surprise, mTOR DC-KO mice mounted robust humoral responses to HDM antigens, exceeding those of WT mice. Serum levels of both IgE and IgG1 were significantly enhanced in this strain, corresponding to elevated frequencies of germinal center B-cells and T-follicular helper responses, suggesting mTOR restrains inflammatory severity. T-cell responses were typified by profound lack of IL-4 production, the prototypical cytokine produced by Th2 cells. Instead, T-cells produced IL-17A cytokine, which recruited neutrophils into the lung environment, thus representing prototypical Th17 response.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester; funded by NIAID, Private Source Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: POLARIZING T CELL RESPONSES IN VIVO WITH DENDRITIC CELLS

SPID#: 13091

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
The major goal of this project is to determine the innate immune receptors and signaling pathways that program dendritic cells to acquire regulatory functions, and whether these represent targets for immune modulation in the context of autoimmune diseases.

PROGRESS REPORT:
We have made significant progress towards the accomplishment of the specific aims of this project. In particular, we have demonstrated in mice that GCN2 controls intestinal inflammation by suppressing inflammasome activation. Enhanced activation of GCN2 and the integrated stress response was observed in intestinal antigen presenting cells (APCs) and epithelial cells during amino acid starvation, or intestinal inflammation. Genetic deletion of Gcn2 (also known as Eif2ka4) in CD11c(+) APCs or intestinal epithelial cells resulted in enhanced intestinal inflammation and T helper 17 cell (TH17) responses, owing to enhanced inflammasome activation and interleukin (IL)-1β production. This was caused by reduced autophagy in Gcn2(-/-) intestinal APCs and epithelial cells, leading to increased reactive oxygen species (ROS), a potent activator of inflammasomes. Thus, conditional ablation of Atg5 or Atg7 in intestinal APCs resulted in enhanced ROS and TH17 responses. Furthermore, in vivo blockade of ROS and IL-1β resulted in inhibition of TH17 responses and reduced inflammation in Gcn2(-/-) mice. Importantly, acute amino acid starvation suppressed intestinal inflammation via a mechanism dependent on GCN2. These results reveal a mechanism that couples amino acid sensing with control of intestinal inflammation via GCN2.

Publication:
Excluded by Requester

FUNDING SOURCES:
Excluded by Requester funded by NIAID Private Source, Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: HIPC: SYSTEM BIOLOGICAL ANALYSES OF INNATE AND ADAPTIVE RESPONSES TO VACCINATION

SPID#: 13092

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:

Systems vaccinology approaches are defining molecular signatures that can predict vaccine induced immune responses in humans. These studies have mostly used healthy adults and two important vaccine target populations, children and the elderly, have not been examined in detail. In this proposal we extend the systems vaccinology approach to these two target populations at the extremes of age; infants (12-15 months old) and the elderly over 70 years. Herpes zoster (shingles), which is caused by VZV, affects several million people/year globally and is a significant public health concern for the elderly. Zostavax(r), the currently licensed live VZV vaccine against zoster, has limited efficacy n subjects >70yrs old. An investigational recombinant glycoprotein E subunit vaccine (gE vaccine) has shown promising results in phase I trials but no comparative studies have been done with these two vaccines. In this program, two closely knit and synergistic projects will assess innate and adaptive responses to vaccination with Zostavax(r) versus the gE vaccine.. VZV also causes chickenpox in children and the live Varivax(r) vaccine is highly effective in preventing chickenpox yet there is a paucity of knowledge about the nature of innate and adaptive immunity to vaccination in the pediatric population. In Aim 2, Project 1 will conduct a systems analysis of innate responses induced by Varivax(r) in infants and children, and define signature that predict adaptive immunity (Project 2). These studies in Aims 1 and 2 should provide new insights into understanding the immune response to the same vaccine at the two extremes of age. Finally, in Aim 3, both projects will use systems vaccinology approaches to probe the immune response of transplant recipients to vaccination against pneumococcal diseases. Our proposed studies with this immunocompromised population, at high risk against invasive pneumococcal disease, could provide new guidelines for pneumococcal vaccination in transplant recipients.

PROGRESS REPORT:

Applied systems approaches were applied to study immune responses in young, elderly, and diabetic subjects vaccinated with the seasonal influenza vaccine across five consecutive seasons. Signatures of innate immunity and plasmablasts correlated with and predicted influenza antibody titers at 1 month after vaccination with >80% accuracy across multiple seasons but were not associated with the longevity of the response. Baseline signatures of lymphocyte and monocyte inflammation were positively and negatively correlated, respectively, with antibody responses at 1 month. Finally, integrative analysis of microRNAs and transcriptomic profiling revealed potential regulators of

vaccine immunity. These results identify shared vaccine-induced signatures across multiple seasons and in diverse populations and might help guide the development of next-generation vaccines that provide persistent immunity against influenza.

PUBLICATIONS:
Submitted separately.

FUNDING SOURCES:
Excluded by Requester funded by NIAID, Private Source, Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: CHAVI-ID: Focus 2: Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery

SPID#: 13093

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
A major focus as part of the CHAVI-ID consortium in the Pulendran lab at the Yerkes National Primate Research Center within Emory University and the Emory Vaccine Center involves evaluating the immunogenicity of BG505 SOSIP trimers in non-human primates (NHPs).

Objective: *Determine if BG505 HIV-1 SOSIP trimers in the presence of PLGA/TLR ligand and Iscomatrix formulations can induce robust magnitude, quality, persistence, and/or breadth of HIV-1 Env specific humoral responses in NHPs.*

PROGRESS REPORT:

- Vaccinations completed; now investigating presence of SOSIP-specific B cells in high frequencies in draining lymph nodes.
- Collected PAX gene tubes, stored RNA from PBMCs, which allows probe of differences in innate responses induced by Iscomatrix and NP adjuvants using systems biological approaches.
- No significant differences in antibody responses observed in animals vaccinated with Iscomatrix and PLGA (MPL+R848) adjuvants. BG505 gp120 monomer specific responses observed at higher levels in comparison with trimer responses.
- 3/6 animals immunized with BG505 Env and Iscomatrix had Tier 2 virus neutralizing activity at this time point. Observed Tier 2 neutralizing activity in 2/6 animals vaccinated with PLGA (MPL+R848) adjuvant. Response rates consistent with previously published NHP studies with BG505 and Iscomatrix adjuvant (Sanders et al, 2015). However, in contrast to tier 2 neutralizing activity, PLGA (MPL+R848) adjuvant induced significantly higher heterologous, Clade B Tier 1 A virus neutralizing activity.
- Quantified numbers of SOSIP Env-specific plasma cells in bone marrow using GNL modified ELISPOT assays five weeks after first cocktail immunization with SOSIP clades A, B, C. Appreciable numbers of SOSIP-specific plasma cells observed in bone marrow. Of note, animals in study at this time point received only one vaccination with Clades B and C immunogens and yet plasma cell frequencies compare with responses against the Clade A immunogen used five times.
- Observed significantly higher production of IL-4 in animals immunized only with Iscomatrix adjuvant at week 67 suggesting that Iscomatrix adjuvant stimulates a mixed Th1/Th2 response in NHPs. In contrast, PLGA (MPL+R848) was capable of only inducing Th1 response. Higher frequencies of IL-4

producing CD4+ t cells were observed in response to Env immunogens of all Clades A, B, C used in vaccine.

- Preliminary analysis indicates it's possible to identify SOSIP-specific B cells in NHP peripheral blood using biotinylated Env probe with minimal non-specific staining.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID, Priva te Source Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Modulation of Innate Immune Defenses by Mucobacterium Tuberculosis

SPID#: 0663

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
The original aims focused on delineating the role of a predicted hydrolase (Hip1/Rv2224c) in Mtb pathogenesis and the host immune response to M. tuberculosis.

PROGRESS REPORT:
Our studies have led to several important contributions to the field. We defined host innate immune pathways modulated by Hip1 in macrophages and dendritic cells and characterized the immune response to the *hip1* mutant in mice. We defined Hip1 enzymatic activity using synthetic substrates, performed molecular and biochemical studies to characterize Hip1 protease activity and identified a key physiological substrate, Mtb GroEL2. Our studies identified a novel mechanism of immune evasion in which Hip1-mediated cleavage of GroEL2 dampens macrophage and DC responses to Mtb infection by modulating TLR2 activation. This fine-tuned immunomodulatory strategy allows Mtb to rapidly respond to changing immune environments and shape immune responses to its advantage. Our studies also show that Mtb interactions with innate immune cells impact development of Mtb-specific T cell immunity and illustrate that absence of immune evasion factors such as Hip1 can enhance protective immunity and provide new host targets for improving vaccines for TB. 2 manuscripts have been submitted that reflect the work conducted in 2016 and are under review.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ROLE OF OXIDO-STRESS IN REGULATING HIV-TB COINFECTION

SPID#: 13015

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.			

PROJECT DESCRIPTION:
The goal of this project is to examine how oxidative stress induced by HIV affects TB disease progression.

PROGRESS REPORT:
Pilot experiments are ongoing at Yerkes (Excluded by Requester) in collaboration with Excluded by Requester. HIV-transgenic mice have been transferred to the Yerkes vivarium and groups of mice have been infected with M. tuberculosis. At various time points after infection, we are measuring oxidative stress and bacterial burdens in the lungs of mice to study the effect of HIV proteins on tuberculosis disease progression. We found that Mtb infection causes oxidative stress in HIV transgenic mice and this manuscipt is under preparation.

PUBLICATIONS:
None

FUNDING SOURCES:
Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Perturbation of antigen-specific T cell responses in latent TB/SIV co-infection

SPID#: 13094

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

This goal of this project is to investigate how co-infection with HIV impairs the functional capacities of *Mtb*-specific CD4 and CD8 T cells to drive reactivation of LTBI and study how antiretroviral therapy (ART) restores these functions. Mechanistic studies require precisely determining the timing and sequence of *Mtb* and HIV infections, experimental verification of bacterial and viral loads and detailed study of immune responses at the site of infection by longitudinal sampling of broncheoalveolar lavage (BAL) and lung tissue, studies that are difficult to conduct in humans. The rhesus macaque NHP model of low-dose aerosol *Mtb* infection overcomes these limitations and recapitulates the spectrum of human lung pathological lesions, including LTBI and its reactivation to ATB by Simian Immunodeficiency Virus (SIV). In this highly collaborative dual-PI R01 application with Excluded by Requester at Tulane Primate Center, we are using state-of-the-art immunological approaches to delineate the mechanisms underlying how SIV perturbs *Mtb*-specific CD4 and CD8 T cell functions, as well as to provide critical new tools for pre-clinical studies in NHPs.

Aim 1. Define the nature of *Mtb*-specific CD4 and CD8 T cell responses associated with immune control of *Mtb* infection in the lungs, BAL and peripheral blood of Indian rhesus macaques with LTBI.

Aim 2. Test the hypothesis that co-infection with SIVmac239 progressively impairs *Mtb*-specific CD4 and CD8 T cell functions, leading to reactivation of LTBI.

Aim 3. Examine the effect of antiretroviral therapy on reconstitution of *Mtb*-specific CD4 and CD8 T cell responses in *Mtb*/SIV co-infected NHP.

PROGRESS REPORT:

In collaboration with Excluded by Requester at Tulane Primate Center, we have infected 6 NHP with Mtb that have achieved latent TB infection and were then co-infected with SIV. Blood, bronchial alveolar lavage (BAL) and lung specimens have been collected and flow cytometry conducted on whole blood and BAL at various timepoints. Experiments are in progress to evaluate the antigen-specific T cell responses proposed in Aim1 and Aim 2.

PUBLICATIONS:

None

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Genetics screen to probe the RLR signaling pathway in CD8+ T cells

SPID#: 13095

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

The major milestones of this proposal are to: 1) Generate an RLR shRNAmir mini-library, 2) Perform an RNAi screen in WNV-specific CD8+ T cells, 3) Identify RLR associated genes for CD8+ T cell responses to WNV infection, and 4) Perform validation studies of candidate genes.

PROGRESS REPORT:

In this reporting period, we received the RIG-I like receptor (RLR) shRNAmir mini-library (Aim 1.1) from the Crotty laboratory. This library consists of 219 shRNAmir constructs that directly target molecules within the RLR signaling pathway. We also received a number of negative control constructs that target irrelevant genes. We characterized the WNV NS4b transgenic mice and have defined expansion, migration to the CNS, effector functions and memory formation in the spleen and brain following WNV infection. We have also optimized the transduction of these cells with the retrovirus constructs. We plan to begin our screen later this month and have results over the next 2-3 months.

PUBLICATIONS:
None

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Identifying host genetic determinants that regulate dendritic cell activation

SPID#: 13096

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Our project is focused on understanding how genetic diversity influences innate immune signaling in response to virus infection and vaccination. We hypothesized that host genetic variation impacts innate immune sensing and antiviral responses within dendritic cells (DCs).

PROGRESS REPORT:

In Aim 1, we proposed to investigate the impact of genetic diversity on innate immune sensing. To this end, we have been able to screen multiple CC lines and identify hyper and hypo responding CC lines. In one study of 20 cc lines, we evaluated IFN-beta transcription following RIG-I agonist treatment and, at 6 hours post-transfection, we observed approximately a 64-fold difference in IFN-beta transcription between the extreme tails of the CC lines. By 24 hours post-transfection, this difference grew to over 1000 fold. We also evaluated DC activation at 24 hours post-RIG-I agonist transfection. DC activation is measured by the cell surface upregulation of key co-stimulatory molecules. In our study, we focused on the upregulation of CD86 and CD40. Similar to the findings with IFN-beta transcription, we observed major differences in CD86 and CD40 expression following RIG-I agonist transfection. Several lines appeared to upregulate CD86 and CD40 similar to that of C57BL/6 mice, whereas other lines showed minimal expression, comparable to that of MAVSko cells. In addition, we found a few lines which showed discordance between CD86 and CD40 expression, suggesting that expression of these molecules are influenced by separate factors downstream of RIG-I signaling activation. These findings firmly demonstrate that RIG-I signaling in DCs is influenced by host genetics. We have also performed a similar analysis with West Nile virus infection. We have been able to demonstrate feasibility of this experiment, and the initial findings are showing strong promise that our screens using these mouse lines will provide novel insight to RIG-I signaling activation and virus infection.

PUBLICATIONS:

Excluded by Requester

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Excluded by Requester

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: VTEU14-0094:Phase I Trial Systems Biology Approach to 'Omics' Response

SPID#: 13097

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Co-Investigator		EVC	
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Vaccine Trial Evaluation Unit Phase I Trial to utilize systems biology approaches to examine the safety, immunogenicity and 'Omics' response to MVA-BN®-Filo and Ad26.ZEBOV vaccines in healthy volunteers

PROGRESS REPORT:

We have performed all the necessary training for executing this clinical trial in my laboratory. This trial has not yet commenced. Meanwhile, we have been working to optimize blood collection procedures, developing standard operating procedures, and performed several pilot studies to ensure smooth collection of samples during the clinical trial.

PUBLICATIONS:
None

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Systems analysis of the innate response to WNV infection at single-cell resolution

SPID#: 13098

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

A critical parameter in the development of a single cell assay for evaluating the host response to virus infection from a bulk cell population is to accurately discriminate infected from bystander cells.

PROGRESS REPORT:

In Aim 1, we proposed to optimize conditions for detecting viral RNA and: 1) determine the sensitivity of stand-specific detection of viral RNA by high-throughput qRT-PCR; and 2) evaluate the reproducibility and reliability for detecting virally infected cells using the Fluidigm C1 single cell platform. Thus far, we have been able to generate and optimize virus-specific primers for detection of WNV and determine sensitivity of our primers to detect WNV RNA (in vitro transcribed standard and cellular RNA). In Aim 2, we proposed to use the Fluidigm platform to measure gene expression within WNV-infected and bystander cells at single cell resolution. Specifically, we proposed to: 1) prioritize a list of genes to be evaluated at the single cell level; 2) perform primer qualification to ensure sensitivity and linearity of the Taqman primer-probes; and 3) perform gene expression analysis at a single cell level from a bulk population of WNV-infected DCs. For this specific aim, we have identified a gene list of approximately 100 genes that we would like to evaluate at the single cell level. We performed primer linearity and sensitivity tests and the outcome of this analysis was promising. We performed our first Fluidigm C1 run with mock-infected and WNV-infected BM-DCs and we are still analyzing the datasets.

PUBLICATIONS:

None

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Regulation of T cell immunity by the cytosolic RIG-I like receptors

SPID#: 13099

NIT/DIVISION:

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Our studies are focused on understanding how canonical and non-canonical innate immune signaling promotes immunity during virus infection. Specifically, our studies have been focused on understanding: 1) how the pattern recognition receptor RIG-I signaling pathway drives dendritic cell antiviral responses, activation, and priming T cells; and 2) how the RIG-I signaling pathway works in T cells to promote activation, proliferation and effector functions during virus infection. These studies are being completed using West Nile virus (WNV) as a model system. WNV continues to be the leading cause of mosquito-borne encephalitis in the United States and there are currently no antivirals or vaccines to combat or protect against infection. Thus, there continues to be a pressing need to understand the immune factors that control WNV infection. Our studies are unique and will likely reveal new avenues for therapeutic intervention to enhance protective T cell responses during virus infection.

PROGRESS REPORT:

Overall, we have made significant progress with our studies. We are currently preparing three manuscripts describing our work associated with this grant. In one study, we utilized a systems biology approach to reveal that In Preparation We are In Preparation In another study, we have dissected the mechanisms underlying negative regulation by the RLR LGP2 and found that In Preparation In Preparation In Preparation In Preparation Thirdly, we have been Unpublished Unpublished This mouse has not been published before and would provide a tremendous reagent to allow a more efficient and specific tool to dissect the RIG-I signaling pathway in T cells.

PUBLICATIONS:

None

FUNDING SOURCES:

Suthar, Mehul, NIAID 1R56AI110516-01

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: RIG-I-like receptor regulation of T cell immunity against flavivirus infection

SPID#: 13100

UNIT/DIVISION: EVC

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This is a subcontract with the University of Washington on an NIH-funded U19 (see below).
The overall objective of Project 4 (Suthar) is to understand the crosstalk between innate immune sensing and the regulation of protective T cell immune responses following flavivirus infection. Our studies are divided into three specific aims:

Aim 1. To determine the role of RLR signaling and function in regulating T cell priming

Aim 2. To define the T-cell intrinsic function of MAVS and LGP2 in regulating effector and memory T cell responses

Aim 3. To determine how MAVS and LGP2 function to regulate memory T cell recall responses.

PROGRESS REPORT:
This past funding year, our research efforts have continued to focus on the studies described within Aims 1 and 2. Our major focus has continued to study the host response to WNV infection of human primary DCs. Furthermore, we expanded our studies to include analysis of Zika virus (ZIKV) infection of primary immune cells, including placental macrophages and human DCs. These studies resulted in two publications (Cell Host Microbe and PLOS Pathogens). Additionally, we published findings related to dengue virus cross-reactive antibodies to ZIKV (PNAS). This finding has significant implications as these cross-reactive antibodies may confer neutralization or worse, provide a mechanism by which ZIKV cross the placental barrier to infect the developing fetus. Lastly, we have been characterizing WNV NS4B CD8+ T cell transgenic mice (WNV-I) for use in our studies to understand the cell-intrinsic functions of the RLRs in T cells.

PUBLICATIONS:
None

FUNDING SOURCES: Suthar, Mehul / U19AI083019-06 (Excluded by Requeste University of Washington)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Private Source

SPID#: 13101

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Bacterial pathogens are a major cause of morbidity and mortality worldwide, and antibiotic-resistant bacteria threaten to send us back to the pre-antibiotic era. In order to cause disease, bacterial pathogens must rapidly adapt to the host environment and counteract immune defenses so they can survive and replicate. We have identified a novel regulatory system that is induced during infection of host cells by the intracellular pathogen *Francisella novicida*. The CRISPR (Clustered Regularly Interspaced Palindromic Repeats)-CAS (CRISPR-associated) system is a recently described bacterial defense against invading foreign DNA derived from bacteriophages or plasmids. It has been unclear if these systems have additional functions in bacterial physiology. We demonstrate a novel RNAi-like function of this system in targeting an endogenous mRNA, regulating the expression of a bacterial lipoprotein (BLP). We now propose to further elucidate critical mechanistic details of how Cas9 mediates degradation of endogenous mRNA. In addition, we will study the conditions in which the Cas9 regulatory system is induced during infection, and test its role in the virulence of the antibiotic-resistant pathogens *Staphylococcus aureus* and *Enterococcus faecalis*. This work will lead to a deeper understanding of host-pathogen interactions, and will also be applied for research and translational purposes. We will determine whether we can "program" this system to target the degradation of any endogenous bacterial mRNA, thus creating a bacterial RNAi-like knockdown system with numerous research and biotechnological applications. We will also further determine the potential of Cas9 system mutants to serve as attenuated vaccine strains, potentially providing a novel means by which to combat pathogenic bacteria including antibiotic-resistant strains.

PROGRESS REPORT:

In the past year, we have explored the contribution of Cas9-mediated BLP repression to a very basic aspect of bacterial physiology, membrane integrity. We reasoned that the ability to regulate BLP levels might be critical to bacterial membrane structure, and indeed revealed that Cas9 plays an important role in enhancing membrane integrity as measured by resistance to uptake of propidium iodide. Furthermore, we observed that Cas9-dependent BLP repression is essential for resistance to the membrane-targeting antibiotic polymyxin B, as well as resistance to other antibiotics including kanamycin and streptomycin (likely because these latter antibiotics can access the bacterial cytosol more easily). This is the first description of a role for Cas9 in the

basic physiological process of controlling membrane integrity and the first demonstration of its role in promoting antibiotic resistance, a severe and growing public health problem.

PUBLICATIONS:

List submitted separately.

FUNDING SOURCES:

Excluded by Requester funded by NIAID, Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: CRISPR/CAS systems in bacterial gene regulation and virulence

SPID#: 13102

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

CRISPR-Cas systems have recently been described to mediate bacterial defense against invading foreign nucleic acid derived from bacteriophages or plasmids, which they target for degradation. These systems have not previously been shown to target mRNA or control endogenous gene expression. We demonstrate that the CRISPR-Cas protein Cas9 targets an endogenous mRNA, revealing a novel bacterial RNA silencing machinery and genetic regulatory paradigm. Since Cas9 targeting of a BLP mRNA in *F. novicida* is the only currently known example of CRISPR-Cas-mediated endogenous gene regulation, we will employ this model to answer fundamental questions about the mechanism of action of this system, as well as the parameters controlling its induction. This will lead to the elucidation of basic foundational principles governing Cas9 and CRISPR-Cas biology. The proposed research will have a sustained and powerful impact on our understanding of Cas9, CRISPR-Cas systems, RNA silencing, genetic regulatory mechanisms, bacterial virulence, and innate immune evasion, and lay the framework for a much broader knowledge of how diverse bacterial pathogens cause disease.

PROGRESS REPORT:

Our most significant advance over the last year has been our elucidation that the Cas9 complex is involved in enhancing envelope integrity through the regulation of BLP (published in *PNAS*, reference below). The *cas9* mutant (and other mutant strains lacking components of this complex; tracrRNA and scaRNA) exhibited greatly increased sensitivity to the membrane-damaging antibiotic polymyxin B as compared to wild-type bacteria, as well as sensitivity to several other antibiotics and membrane-damaging agents. Interestingly, expression of CRISPR-Cas components can be induced by bacterial envelope stress, disruptions in envelope protein localization and the presence of bacteriophage. Taken together, this suggests that CRISPR-Cas systems are induced in response to membrane stressors, and their regulatory activity can subsequently result in the enhancement of envelope integrity to promote resistance to such stressors. It is therefore tempting to speculate that the CRISPR-Cas response to envelope stress serves two distinct purposes: 1) the activation of its canonical function as the adaptive, foreign nucleic acid restriction system and, 2) the regulation of envelope structure and content to enhance the integrity of the bacterial envelope and combat membrane stress, which represents a previously unappreciated role in bacterial physiology and a significant shift in the understanding of these systems.

PUBLICATIONS:

List submitted separately.

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES:

Excluded by Requester funded by NIAID, Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: ArmR: a novel drug target and mediator of antibiotic resistance

SPID#: 13103

UNIT/DIVISION: EVC

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	EVC	-------
Prin. NPRC Core Sci.		-------	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
Drug resistant Gram-negative bacterial pathogens are an increasing cause of hospital-acquired infections, mortality, and a huge burden on healthcare costs. Acinetobacter baumannii is a major cause of such infections and strains have recently emerged which are resistant even to the last line of defense drugs, polymyxin B and colistin (polymyxin E), which target and disrupt the lipid A portion of lipopolysaccharide (LPS) in the outer membrane.

PROGRESS REPORT:
Understanding the mechanism of this resistance at the molecular level would facilitate the development of novel therapeutics aimed at reversing resistance, in much the same way that beta-lactamase inhibitors can counteract penicillin resistance. To this end, we have recently identified a novel protein that we have named ArmR (or Armor - Antimicrobial Resistance by Modification of lipid A surface chaRge) that is widely conserved and which we show is required for resistance to polymyxins in A. baumannii as well as other Gram-negative bacteria. ArmR is required for a lipid A modification that leads to the increase of surface charge on the bacterial membrane, acting to repel the positively charged polymyxins as well as positively charged host-derived antimicrobial peptides. We hypothesize that inhibition of ArmR would reverse the resistance to polymyxins, preserving their utility in the clinic, and also sensitize the bacteria to innate host defenses.

In the first year of the R33 portion of this project we have successfully optimized the high-throughput screen (HTS) to begin identifying compounds with inhibitory activity. We have completed a significant portion of the HTS, identifying several compounds with such inhibitory activity. We have also completed a portion of the virtual screening, identifying several inhibitory compounds with mild activity. We are now completing both the HTS and virtual screening, and beginning to try and optimize the compounds that represent lead hits thus far.

PUBLICATIONS:
List submitted separately

FUNDING SOURCES:

Excluded by Requester funded by NIAID

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Division of Animal Resources

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Accuracy of Veterinary and Human Glucometers in NHP Species

SPID#: 13104

UNIT/DIVISION: Animal Resources

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Vet Med / Animal Resources	
Prin. NPRC Core Sci.			
Other Core and Affil.	None		

PROJECT DESCRIPTION:

There are several indications in nonhuman primate (NHP) medicine and research for the use of hand-held, point-of-care glucometers. Veterinary specific glucometers were recently developed for companion animals, but it is currently unknown whether human or veterinary glucometers are more appropriate for use in NHPs. Glucometers measure glucose in whole blood, but perform a calculation to estimate and report the plasma glucose level. The distribution of glucose between plasma and red blood cells varies species to species. Based on these differences, veterinary glucometers utilize the same technology as human glucometers, but apply a species-specific algorithm to estimate plasma glucose. Human studies have shown that several other factors can affect glucometer measurement including hematocrit (HCT), glycemic state and collection site. The primary aims of this study were: 1) to compare the accuracy of 2 veterinary and 2 human glucometers in 2 NHP species with naturally different HCT ranges (rhesus macaques and sooty mangabeys); 2) to determine the accuracy of 2 human glucometers during hypoglycemia and hyperglycemia; and 3) to compare glucometer performance between capillary and venous sampling sites.

PROGRESS REPORT:

This study is completed and results have been analyzed.

PUBLICATIONS:

None

FUNDING SOURCES: Excluded by Requester departmental funding

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Use of automated feeders to control obesity in socially-housed macaques

SPID#: 13105

UNIT/DIVISION: Animal Resources

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 54%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Animal Resources	
Prin. NPRC Core Sci		DCN	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
This project seeks to evaluate the feasibility and potential benefits of a novel automated, computer-controlled feeding system for veterinary and colony management purposes. Using rhesus macaques (*Macaca mulatta*) in large breeding troops at Yerkes National Primate Research Center (NPRC) Field Station, the current proposal has three primary goals: 1) to compare food wastage associated with automated feeders to traditional bin feeders; 2) to determine whether automated feeders increase food competition in social groups fed *ad libitum* monkey chow; and 3) to determine if automated feeder enabled caloric restriction is a feasible method to reduce adiposity and improve metabolic health of overweight adult female macaques without inducing food competition in a complex social environment.

PROGRESS REPORT:
As of 2/9/17, aims 1, 2, and 3 have been completed. For aim 1 and 2, food wastage and behavioral observations were collected from two compounds housing approximately 150 animals each and fed from either a standard bin system or automated feeders. For aim 3, sixteen obese female macaques were fed *ad libitum* a standard monkey chow diet while another cohort of obese female rhesus macaques were calorie restricted up to 40% of their baseline values. Blood was collected to measure metabolic parameters and focal behavior observations were done to determine difference in food competition between the two feeding conditions (calorie restricted and unrestricted). Data analysis for aim 1 and 3 has been completed. For aim 2, data analysis is still on-going, but will be completed by May 2017. It is anticipated that this project will yield 2 manuscripts.

This project employs significant Yerkes resources, including colony management staff, animal care staff, veterinary staff, and rhesus macaques.

PUBLICATIONS:
None

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

FUNDING SOURCES:

Excluded by Requester funded by Private Source

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Maternal stress and obesity, milk immunobiology, infant growth

SPID#: 13106

UNIT/DIVISION: Animal Resources

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Animal Resources	
Prin. NPRC Core Sci.		DCN	
Other Core and Affil.		None	

PROJECT DESCRIPTION:

Evidence from human and animal studies show that chronic stress exposure and obesity synergize to elevate circulating stress and pro-inflammatory signals. What is less clear and particularly important for nursing mothers, however, is whether these signals translate to milk and affect infant development. Human milk contains many hormonal and immunological signals including cytokines, adipokines, immunoglobulins (Ig), and growth factors that mediate infant health and development; however, it is not known whether and to what extent maternal stress and obesity may alter these and produce adverse growth trajectories for infants. To disentangle prepartum maternal stress from postpartum stress, fourty-three newborns were either cross-fostered to mothers of the same or different ranks or raised by their biological mothers. In addition, half of the mother-infant dyads will be maintained on a low calorie diet through lactation while the other half will be switched to a rich dietary condition. *Aim 1* tests the hypothesis that chronic social stress and adiposity will synergize to increase stress and inflammatory signals in milk. This aim will accomplished by measuring cortisol, cytokine and adipokine markers in milk and serum from lactating rhesus monkeys of different social rank (dominant vs. subordinate) and postpartum diet exposure (high calorie vs. low calorie). *Aim 2* tests the hypothesis that chronic social stress and adiposity will interact to decrease immune defense components in milk. Milk levels of sIgA in lactating dams will be evaluated in parallel with stress and inflammatory markers studied in Aim 1. Finally, *Aim 3* determines the contribution of milk signals studied in aims 1 and 2 to infant growth and health trajectories. Specifically, Aim 3 tests the hypothesis that pro-inflammatory cytokines and adipokines significantly predict infant growth in addition to milk energy in a rich dietary environment.

PROGRESS REPORT:

During Year 1 of this R21 (April 2014-March 2015), we recruited 14 mother-infant pairs into the study. We collected milk, blood, feces, body composition and growth measures on these subjects at 48-72hrs, 2 weeks, 6 weeks, 12 weeks, and 24 weeks of age as described in the original proposal. During Year 2 (April 2015-March 2016), we recruited 20 mother-infant pairs and collected milk, blood, feces, body composition, and growth measures as previously described. During Year 3 (April 2016-Present), we completed the enrollment and data collection on the third (and final) cohort of mother-infant pairs (n=10) through 24 weeks post-partum. A no cost extension was requested from the NICHD for Year 3. Because the final mother-infant pair completed their 24

week assessment in January 2017, final assays for hormonal and immunological markers are currently underway. It is anticipated that this project will yield at least 3 manuscripts.

This project employed significant Yerkes resources, including rhesus macaques and procedure rooms.

PUBLICATIONS:
None

FUNDING SOURCES:
Kelly Ethun, DVM, PhD; funded by NIH/NICHD (R21 HD 079969)

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Automated Feeders, Clinical Monitoring, Breeding Rhesus Macaques

SPID#: 13107

UNIT/DIVISION: Animal Resources

TYPE (indicate): Management (Management/Research/Pilot)

Percent P51 $: 28%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester		Vet Med / Animal Resources
Prin. NPRC Core Sci.			
Other Core and Affil.	None		

PROJECT DESCRIPTION:
This project seeks to determine whether feeding data generated by computer-controlled automated feeding stations can be used to enhance the clinical monitoring of rhesus macaques living in large outdoor breeding groups. As animals obtain food pellets, the computer-controlled system records grams obtained in real-time by detecting RFID microchips implanted subcutaneously in each hand of individual animals. The primary outcomes of this study include: 1) quantification of daily caloric intake according to sex, gender, and reproductive stage; 2) the association of various clinical conditions (e.g. trauma, diarrhea, retained placentas) with a significant reduction in caloric intake; 3) association of select breeding and social behaviors with changes in caloric intake.

PROGRESS REPORT:
As of 2/9/17, feeding data has been collected from 3 large breeding groups of rhesus macaques for 24 consecutive months. Data analysis is currently underway. It is anticipated that data analysis and manuscript preparation will be completed over the next 12 months.

PUBLICATIONS:
None

FUNDING SOURCES:
Ethun, K. / NIH P51 OD011132

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Chronic Stress, anti-tetanus immunogenicity, female Rhesus Macagues

SPID#: 13108

UNIT/DIVISION: Veterinary Medicine, Animal Resources

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Vet Med / Animal Resources	
Prin. NPRC Core Sci.			
Other Core and Affil.		None	

PROJECT DESCRIPTION:

This project seeks to evaluate how chronic stress may negatively affect anti-tetanus immunity among breeding female rhesus macaques (*Macaca mulatta*) and their offspring. Using rhesus macaques in large breeding troops at Yerkes National Primate Research Center (NPRC) Field Station, the aim of the current proposal is to determine whether and to what extent social subordination impairs the durability and prenatal transfer of anti-tetanus immunity in breeding female rhesus macaques.

PROGRESS REPORT:

As of 2/9/17, sample collection is complete and data analysis is underway. Blood and hair samples were collected during the Fall 2015 and 2016 surveys from 60 breeding aged female rhesus macaques at either an average of 10 years or 5 years post-initial tetanus toxoid vaccination, including dams from the upper and lower half of their social hierarchy. The infants of the aforementioned dams also had blood collected at this time. Blood was collected from dams and infants prior to administration of a tetanus booster and primary immunization, respectively. Anti-tetanus antibody levels were measured by ELISA. Hair cortisol content was measured by ELISA following methanol-extraction. Data analysis and manuscript preparation will be completed in the next 4-6 months.

PUBLICATIONS:

None

FUNDING SOURCES:

Excluded by Requester funded by departmental funding

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: Influence and Evaluation of Dietary Properties on Chewing Patterns in Primates

SPID#: 13109

UNIT/DIVISION: Animal Resources

TYPE (indicate): Research

Percent P51 $: 0%

AIDS RELATED?: ☐ Yes ☒ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	D	University of Notre Dame
Prin. NPRC Core Sci.		Animal Resources	
Other Core and Affil.		None	

PROJECT DESCRIPTION: Our current understanding of the functional relationship between diet and primate mandibular form is poorly known due to the lack of experimental control with regard to food type, bolus size and inter-individual variation in analyses of feeding behavior. Prior behavioral studies of chewing patterns in mammals have typically lumped together data on food items of different material properties which has been incomplete for all the individuals sampled to characterize a given species profile. As food properties may influence chewing duration, chewing cycle number and/or chewing frequency, it is important to understand the role of such influences prior to comparing chewing patterns across taxa. We look to fill a significant gap in our understanding of the role of food material properties on chewing patterns that can be integrated with existing physiological information on jaw-loading patterns and bone formation for primate and non-primate mammals. By first comparing chewing patterns for each food type within an individual, the proposed study will provide much greater control on the role of food properties and inter-individual variation on intra- and inter-specific chewing patterns. With this in mind, we wish to observe as many anthropoid and strepsirrhine primate species as possible, particularly those adults that vary in body size, dietary preference and phylogenetic diversity. We aspire to capture chewing data as it relates to a wide array of material properties that map onto diets in the wild. These data include tallying time for a specific mass for each of five food groups that span a range of stiffness and toughness values, as well as capturing video data of jaw movement for each food that can be used to construct a chewing profile for each individual and, eventually, species that relates food properties to chewing duration, chewing cycles and chewing frequency.

PROGRESS REPORT:
In September 2016 personnel from Excluded by Requester at the University of Notre Dame came to Yerkes for a week-long visit. All animal work at Yerkes was completed by September 16, 2016.

PUBLICATIONS:
None

FUNDING SOURCES: Matthew Ravosa, Ph. D, National Science Foundation, Grant # 1555168

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

Clinical Pathology

Yerkes National Primate Research Center
2016-17 Annual Progress Report SPID Form

TITLE: DEVELOMENT OF RECTAL ENEMA AS MICROBICIDE

SPID#: 13117

UNIT/DIVISION:

TYPE (indicate): Research (Management/Research/Pilot)

Percent P51 $: 0%

AIDS RELATED?: ☒ Yes ☐ No

INVESTIGATORS:

	Name	Dept	Non-host Affiliation (if applicable)
Principal Investigator	Excluded by Requester	Clinical Pharmacology	Johns Hopkins University
Prin. NPRC Core Sci.		Pathology	
Other Core and Affil.		None	

PROJECT DESCRIPTION:
The overall objective of this project is to optimize the Tenovir (TFV) enema formulation in animal models to inform clinical development. Various TFV enema formulations were tested to optimize TFV enema characteristics (tonicity, ion composition, drug) in rhesus macaques for tissue and cellular bioavailability. Since enemas are routinely used by MSMs, a unique rectal enema formulation as microbicide was created to deliver ART to mucosal tissue to prevent SIV/SHIV infection.

PROGRESS REPORT:
During the current reporting period, a significant progress in the studies was acheived in understanding pharmacokinetics and efficacy of iso- (IOsm) and hypo-osmolar formulations (HOsm) of TFV enemas in a macaque model. Markedly higher plasma TFV concentrations were seen after administration of the HOsm high dose enema compared to other formulations tested at all-time points. This formulation also showed higher TFV concentrations and TFV diphosphate (TFV-DP) concentrations in colorectal tissues collected at 1 and 24 hr compared to other formulations. The data from the macaque model supports the clinical development of the effective TFV enema formulation.

PUBLICATIONS:
None.

FUNDING SOURCES:
U19 AI113127-01 (MPI: Hendrix) 09/01/14 – 04/30/2019 NIH/NIAID
Development of rectal enema as microbicide

List of Publications (2016 – 2017)

Excluded by Requester

Excluded by Requester

B.2 (B2 Accomplishment_overall.pdf)

Excluded by Requester

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B.2 (B2 Accomplishment_overall.pdf)

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BOOK CHAPTERS

Excluded by Requester

B.4. Training and Professional Development Opportunities

Scientific

The Center is actively involved in training and continuing education activities. Students and Postdoctoral Fellows are an integral part of the scientific fabric of Yerkes and participate in all elements of the research mission. In the last year, 137 undergraduate and 107 graduate students received training and experience in Yerkes laboratories. During this same period, the Center employed 43 Postdoctoral Fellows. Yerkes currently is the focal point for a substantial portion of the Neuroscience Graduate Program at Emory. The Director of the NIH training grant that supports students in the Graduate Neuroscience Program and many members of the Neuroscience Program Executive committee, all reside at Yerkes. Additionally, almost 30% of graduate students in the Neuroscience and Immunology programs are carrying out their dissertation research in Yerkes laboratories, including several MD/PhD students. Essentially all of our Divisions have NRSA or NSF-supported students and we have worked with each Division in facilitating the process for trainees' applications to NIH/NSF or private foundations for financial support. The Yerkes Center is the administrative home for the NIH Training grant (T32GM08605-Training in Systems and Integrative Biology-Neuroscience) that supports trainees in the Emory Neuroscience Graduate Program. The Yerkes Center is also the administrator of the NIH-funded UDALL Center of Excellence for Parkinson's disease at Emory University and the home for three of the core scientists participating in this Center. In addition to research activities, the Parkinson's disease Center is very active in education and community outreach for trainees and the public. It also provides pilot grants to young investigators interested in developing new areas of research for Parkinson's disease.

The Division of Animal Resources (DAR) at Yerkes and at Emory's School of Medicine (SOM) continue their joint effort in supporting the Emory Laboratory Animal Medicine Residency Training Program. Since 2009, one of Yerkes veterinary faculty members is the Training Program Assistant Director. In addition, Yerkes veterinarians have taken responsibility as course directors for classes within the Residency Training program. Yerkes also supports two residency positions per year. Our goal is to train and retain laboratory animal veterinarians who will grow with Yerkes, and help develop programs of research around their own specialties. All veterinary faculty continue to be actively involved in the Emory Laboratory Animal Medicine Program and remain closely partnered with the Division of Animal Resources at the School of Medicine. In 2007, an NCRR R25 training grant enabled Yerkes to include an additional third year of specialized NHP training for three residents (one each year – funding to support years two and three of the training). In 2009, an administrative supplement to the R25 provided support for a fourth resident to enter the program. The three-year YNPRC NHP Residency Program builds upon our successful Emory/YNPRC two-year program and provides extensive nonhuman primate clinical and resource management experience for the residents. We have successfully recruited four trainees, all of them having completed the program between June 2009, and June 2011. In addition, all have obtained their ACLAM Board Certification, the gold standard to measure success of a Laboratory Medicine Training program. One of those trainees is now a full time veterinarian at Yerkes. In light of the success of this specialized Training Program, YNPRC decided to continue to support a third year Fellowship in Nonhuman Primate Medicine and Management. We have already recruited five trainees for the Fellowship Program. The first one completed her training in June 2013 and obtained her ACLAM Board certification in July 2013. She is now a full time clinical veterinarian at Yerkes. The second trainee finished her fellowship training in July 2014 and successfully took her ACLAM Board exam in June 2015. The third fellow completed his training in June 2015 and is expected to sit for Board in 2017. One trainee completed her program and obtained her ACLAM Board in July 2016. One fellow is currently in training and is expected to sit for his Board exam in 2018.

YNPRC has continued to provide opportunities for veterinary internships and externships. These opportunities introduce veterinary students to the field of lab animal medicine and have sometimes led to students applying for lab animal residency positions as offered by the School of Medicine/YNPRC. Two of our current residents have been through our externship program. In 2016, five externs and one intern came to Yerkes for a period of time that can vary between three to ten weeks. Students from veterinary technical schools also have participated in externships and have sometimes been motivated to apply for available technical positions at Yerkes where they could put to good use their newfound knowledge of nonhuman primates. We did hire one of the veterinary technician externs in 2014. The various students work closely

with veterinary faculty,
residents and technicians to gain a working knowledge and appreciation of the specialty of nonhuman primate
medicine.

The Yerkes Center is closely linked with several components of the Emory University Clinical Translational Science Award (CTSA); (here called the Atlanta Clinical and Translational Science Institute – ACTSI – that includes Morehouse School of Medicine and the Georgia Institute of Technology). The key functional areas of the ACTSI with which the Yerkes Center is involved are brain imaging and education.

Yerkes has collaborated with the Institute on Neuroscience (ION) at Georgia State University to continue to enable high school students and middle and high school teachers to participate in scientific research. Success with this program has led to a five-year NIH grant to continue the ION program. Four high school students worked in Yerkes Neuroscience laboratories through this program last year.

In addition, the Center regularly hosts scientific seminars and sponsors frequent talks (Lunch and Learn, Frontiers in Neuroscience) by faculty for the staff to promote understanding of the scientific mission.

Employee Training

As noted in the Core Service Units section, prior to beginning employment, all personnel are given a packet that provides information on the Yerkes Center, general information on primate research, the nonhuman primate behavioral management program, laboratory animal zoonoses information, personnel policies, Center security information, standards and procedures for working safely at the Center, training information, and biosafety issues (e.g., B-virus information). Supervisors are responsible for training employees in procedures that specifically relate to their areas of responsibility. Individuals with practical experience are appointed to train new employees/students within their units. All new employees (investigators, animal care personnel, research technicians, etc.) and students/volunteers receive an approximately 1 hour orientation that includes a slideshow related to organization of the Yerkes Center, procedures for handling incidents and potential exposures, and general guidelines for working safely in laboratory and animal research settings. All new employees complete online training on the Emory Learning Management System or on Emory's Blackboard site, including a "Yerkes Orientation" module in addition to other modules as are relevant to the employee's job responsibilities. All personnel who will have animal contact are required to complete Animal User Orientations that cover nonhuman primate and/or rodent biology and behavior, U.S. regulations and guidelines for laboratory animals, IACUC policies, identifying and reporting sick animals and reporting animal welfare concerns. Animal Research personnel are required to complete applicable AALAS Learning Library online training modules and be added to an existing IACUC protocol prior to working with animals. A hands-on instructional tour of the nonhuman primate and/or rodent research facility is required for research personnel to gain access to these areas. General information memoranda are circulated providing any new information or reminding personnel of existing standards when necessary.

Training classes are provided as part of Yerkes continuing education efforts. Animal care technician training needs and programs are assessed and enhanced by supervisors and managers on an ongoing basis and may be influenced by research designs as well as changes in husbandry and care. Animal care technicians receive initial general training upon hire and orientation. Over time, experienced care staff also receive additional specialized training focused on specific topics such as husbandry and care of nursery animals, automated feeder training, behavioral management certification training, forklift training, as well as cross training within other Animal Resources units such as the veterinary staff, research resources staff and colony management staff. These training sessions, as well information disseminated during staff meetings, presentations or review classes, are based on materials and resources that are part of the American Association for Laboratory Animal Science certification program. Although all Animal Care Technicians are encouraged to work toward certification by AALAS, the AALAS certification examination is not mandatory. Regular staff meetings are conducted at which time there is generally a review of some aspects of husbandry and care that relate to certification. Manuals for the Assistant Laboratory Animal Technician, Laboratory Animal Technician and the Laboratory Animal Technologist are made available to Yerkes technicians without charge for use in the in-house training program or for self-study. Additionally, the Emory

University IACUC Office subscribes to the AALAS Learning Library for online, individualized training. The Yerkes Center pays the fee for the certification examination at each level. A salary increase is provided to individuals who achieve certification. Twenty seven percent (27%) of the Main Station animal care unit and forty three percent (43%) of the Field Station animal care unit are currently AALAS certified at some level. Opportunities for additional training are also available when Animal Care Technicians attend National AALAS, SEAALAS and AALAS District IV meetings in 2015. Supervisors and Managers have been attending Webinars sponsored by NABR, OLAW, AALAS, USDA and AAALAC. Additionally Continuing Education sessions are available for Veterinary Technicians through the Gwinnett Veterinary Medical Association monthly meetings as well as a series of lectures (scheduled 6-8 times a year) organized by the School of Medicine's DAR.

The Training Coordinator for the Yerkes Division of Animal Resources coordinates the training requirements for personnel who work with research animals. After completing the Animal User Orientations, trainings offered to animal users at Yerkes include 1) a didactic presentation on aseptic surgery technique (mandatory for anyone conducting surgery); 2) rodent biomethodology including restraint (required for anyone new to working with rodents), blood collection techniques and injection procedures; 3) humane rodent euthanasia methods; 4) weaning training (a review of the IACUC weaning policy for mice and rats; 5) restraint training (a 2-part series on preparing nonhuman primate for studies involving physical restraint, specifically chair restraint; 6) behavioral management of nonhuman primates; and 7) a facility refresher for all research staff working with animals. Instructional manuals for identifying sick rodents are developed and distributed to animal research and animal care personnel. The Training Coordinator is a member of the IACUC Subcommittee on Training and Continuing Education, which develops the policy on rate, frequency and types of training and continuing education requirements for animal users at Emory University and Yerkes.

In addition to the initial orientation which includes information on zoonoses (including B-Virus), biosafety, personal protective equipment, and Center policies on safety, the Yerkes Environmental Health and Safety Office conducts and/or facilitates annual training programs for all personnel. These annual training programs include but are not limited to: (1) B-virus training for all staff who work with nonhuman primates or nonhuman primate blood or tissues; (2) annual updates on the use of personal protective equipment (PPE) to include a review of current requirements, demonstration on how to use PPE, and information on the storage, limitations of and decontamination and disposal of PPE; (3) information on hazards communications and the chemical hygiene plan, including how to work with hazardous chemicals, how to respond to a spill, labeling and storage requirements, disposal procedures and Safety Data Sheets (SDS); (4) biosafety reviews which include a review of biosafety level 1-4, blood borne pathogens standards, biological safety cabinets, emergency procedures, disposal practices, and a review of zoonoses; (5) radiation safety which includes discussion of the characteristics of radiation, safe use and storage, disposal, and employee monitoring; (6) ergonomics training for employees in animal care, research, or any other position that involves strenuous or repetitive physical activity; and (7) fire safety training which includes fire prevention strategies, evacuation plans, emergency procedures, and training for the use of fire extinguishers; (8) respirator program which includes annual fit testing, training, and medical surveillance; and (9) training for facilities management personnel that address general safety and industrial hygiene topics such as asbestos awareness, lockout/tagout, and confined spaces.

Type of trainee	**Number of trainees**
Postdoctoral Fellow	43
Graduate Student	107
Undergraduate Student	137
Veterinary Residents	3
Veterinary Externs/Interns	6
Pathology Extern	1
High School Student (ION Program Students)	4
Total	**301**

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?

No

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

Category	Explanation
Other	Working with Emory University Woodruff Health Sciences Center (WHSC) staff as well as central Communications and Marketing staff, Yerkes NPRC includes Yerkes news on the WHSC website and in its Lab Land blog, available at http://whsc.emory.edu/home/, as well as the University's news site, http://whsc.emory.edu/home/news/index.html;
Other	The nprcresearch.org site represents all seven NPRCs and provides NIH-funded investigators with information about NPRC research resources, including the expertise our researchers provide, the capabilities our centers offer outside investigators, and the animals available for inclusion in NIH-funded research studies. This website captures news releases posted on the Yerkes NPRC website. These releases are highlighted on the nprcresearch.org's Home page, and full release information is available at http://nprcresearch.org/primate/news.php.
Other	One of the ways the Yerkes National Primate Research Center digitally distributes information about our scientific advancements is by posting news releases on the Yerkes website – our Home page, www.yerkes.emory.edu, as well as our News page, http://www.yerkes.emory.edu/about/news/index.html;

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

Category	Explanation
Other	Please see section G: Special Reporting Requirements section for additional information requested in the P51 RPPR instructions.

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	LEWIN, JONATHAN S	MD	PD/PI	EFFORT				Admin Core-5961 (Office of the Director)		NA
	N	Excluded by Requester		Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Project-5995 (Pilot Projects)		NA
	N			Technician					Other-5975 (Research Services)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5970 (Veterinary Medicine)		NA
	N			Technician					Other-5975 (Research Services)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5970 (Veterinary Medicine)		NA
	N			Technician					Core-5982 (Genomics Core)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5970 (Veterinary Medicine)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5971 (Animal Care)		NA
	N			Technician					Other-5970 (Veterinary Medicine)		NA
	N			Technician					Other-5977		NA

eRA Commons User Name		Excluded by Requester			EFFORT				
							(Division of Pathology)		
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5973 (Behavioral Management)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Core-5980 (Imaging Core)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Core-5980 (Imaging Core)		NA
	N			Technician			Other-5973 (Behavioral Management)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care), Other-5972 (Colony Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA

eRA Commons User Name	N	Excluded by Requester		Technician	EFFORT		Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5973 (Behavioral Management)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5975 (Research Services)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5973 (Behavioral Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA

eRA Commons User Name	N	Excluded by Requester		Technician	EFFORT		Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5975 (Research Services)		NA
	N			Technician			Other-5976 (Env. Health and Safety)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Core-5981 (Virology Core)		NA
	N			Staff scientist (Doctoral level)			Core-5980 (Imaging Core)		NA
	N			Technician			Core-5978 (Biomarkers Core)		NA
	N			Technician			Project-5995 (Pilot Projects)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Core-5982 (Genomics Core)		NA

eRA Commons User Name	N	Excluded by Requester		Technician	EFFORT		Other-5971 (Animal Care)		NA
	N			Technician			Other-5973 (Behavioral Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care), Other-5972 (Colony Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Staff scientist (Doctoral level)			Core-5980 (Imaging Core)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA

eRA Commons User Name	N	Excluded by Requester		Technician	EFFORT		Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Core-5981 (Virology Core)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Core-5980 (Imaging Core)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5972 (Colony Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Project-5995 (Pilot Projects)		NA
	N			Technician			Other-5973 (Behavioral Management)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA

eRA Commons User Name	N	Excluded by Requester		Technician	EFFORT		Other-5975 (Research Services)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5975 (Research Services)		NA
	N			Technician			Other-5970 (Veterinary Medicine)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N			Technician			Other-5971 (Animal Care), Other-5976 (Env. Health and Safety)		NA
	N			Technician			Other-5977 (Division of Pathology)		NA
	N			Technician			Other-5971 (Animal Care)		NA
	N		PHD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position			Project-5995 (Pilot Projects)		NA
	N			Supervisor			Other-5970 (Veterinary Medicine)		NA

eRA Commons User Name		Excluded by Requester			EFFORT					
	N			Manager				Other-5971 (Animal Care)		NA
	N			Facilities/Shop Staff				Admin Core-5967 (Facilities Management)		NA
	N			Facilities/Shop Staff				Admin Core-5967 (Facilities Management)		NA
	Y			Veterinarian				Other-5970 (Veterinary Medicine)		NA
	N			Facilities/Shop Staff				Admin Core-5967 (Facilities Management)		NA
	Y			Asst Dir, Animal Resources				Other-5969 (Asc. Dir. for Animal Resources), Other-5970 (Veterinary Medicine)		NA
	N			Supervisor				Other-5977 (Division of Pathology)		NA
	N			Supervisor				Other-5977 (Division of Pathology)		NA
	N			Manager				Other-5975 (Research Services)		NA
	N			Supervisor				Other-5971 (Animal Care)		NA
	N			Facilities/Shop Staff				Admin Core-5967 (Facilities Management)		NA
	N			Manager				Other-5971 (Animal Care)		NA
	N			EHS Professional				Other-5976 (Env. Health and Safety)		NA
	N			Facilities/Shop Staff				Admin Core-5967 (Facilities Management)		NA
	N			Research Proj Coordinator				Other-5975 (Research Services)		NA
	N			Facilities/Shop Staff				Admin Core-5967 (Facilities Management)		NA
	N			Supervisor				Admin Core-5967 (Facilities Management)		NA

eRA Commons User Name		Excluded by Requester			EFFORT				
	N			Records Support			Other-5974 (Animal Records)		NA
	N			Records Support			Other-5974 (Animal Records)		NA
	Y			Veterinarian			Other-5970 (Veterinary Medicine)		NA
	Y			Veterinarian			Other-5970 (Veterinary Medicine)		NA
	N			Supervisor			Other-5971 (Animal Care)		NA
	N			Facilities/Shop Staff			Admin Core-5967 (Facilities Management)		NA
	N			Facilities/Shop Staff			Admin Core-5967 (Facilities Management)		NA
	N			Supervisor			Other-5974 (Animal Records)		NA
	N			Facilities/Shop Staff			Admin Core-5967 (Facilities Management)		NA
	N			Supervisor			Other-5971 (Animal Care)		NA
	Y			Veterinarian			Core-5980 (Imaging Core), Other-5970 (Veterinary Medicine)		NA
	Y			Veterinarian			Other-5970 (Veterinary Medicine)		NA
	N			Supervisor			Core-5978 (Biomarkers Core)		NA
	N			Facilities/Shop Staff			Admin Core-5967 (Facilities Management)		NA
	N			Facilities/Shop Staff			Admin Core-5967 (Facilities Management)		NA
	N			Facilities/Shop Staff			Admin Core-5967 (Facilities Management), Other-5971 (Animal Care)		NA
	N			Manager			Other-5971		NA

eRA Commons User Name	Excluded by Requester			EFFORT			
						(Animal Care)	
	N		Admin Support			Core-5980 (Imaging Core)	NA
	N		Training Coordinator			Other-5969 (Asc. Dir. for Animal Resources)	NA
	N		Manager			Core-5979 (Comparative AIDS Core), Other-5972 (Colony Management)	NA
	N		Supervisor			Other-5971 (Animal Care)	NA
	N		Manager			Other-5971 (Animal Care)	NA
	N		Facilities/Shop Staff			Admin Core-5967 (Facilities Management)	NA
	Y		Veterinarian			Other-5970 (Veterinary Medicine)	NA
	N		Supervisor			Other-5977 (Division of Pathology)	NA
	N		m			Other-5976 (Env. Health and Safety)	NA
	N		Manager			Core-5982 (Genomics Core)	NA
	N		Manager			Other-5973 (Behavioral Management)	NA
	Y		Pathologist			Other-5977 (Division of Pathology)	NA
	N		Records Support			Other-5974 (Animal Records)	NA
	N		Supervisor			Other-5972 (Colony Management)	NA
	N		Supervisor			Other-5971 (Animal Care)	NA
	N		Manager			Other-5971 (Animal Care)	NA
	N		Supervisor			Other-5975 (Research	NA

eRA Commons User Name		Excluded by Requester			EFFORT				
								Services)	
	N			Supervisor			Other-5971 (Animal Care)		NA
	Y			Veterinarian			Other-5970 (Veterinary Medicine)		NA
	Y			Veterinarian			Core-5979 (Comparative AIDS Core), Other-5970 (Veterinary Medicine)		NA
	N			Bioinformatics Specialist			Core-5982 (Genomics Core)		NA
	N			Asst Dir, EHSO			Other-5976 (Env. Health and Safety)		NA
	N			Supervisor			Other-5973 (Behavioral Management)		NA
	N			Records Support			Other-5974 (Animal Records)		NA
	N			Animal Surgery Specialist			Other-5970 (Veterinary Medicine)		NA
	Y			Veterinarian			Other-5970 (Veterinary Medicine)		NA
	Y			Pathologist			Other-5977 (Division of Pathology)		NA
	Y		PHD,PHD,MS,BS,MS,BS	Behavioral Mgt Head			Other-5973 (Behavioral Management)		NA
	Y		BA,VMD	Asc Dir, Animal Resources/Interim AD, Pathology			Core-5979 (Comparative AIDS Core), Other-5969 (Asc. Dir. for Animal Resources), Other-5970 (Veterinary Medicine), Other-5977 (Division of Pathology)		NA
	N		BA,MS,PHD	Affliate Scientist			Project-5995 (Pilot Projects)		NA
	Y		MD	Division			Core-5979		NA

eRA Commons User Name		Excluded by Requester			EFFORT				
				Director				(Comparative AIDS Core), Other-5990 (M&I)		
	Y		BS,DVM,PHD	Veterinarian				Other-5970 (Veterinary Medicine)		NA
	Y		PHD	Asc Dir, Scientific Pgms				Admin Core-5962 (Asc. Dir. for Scientific Programs), Core-5980 (Imaging Core), Other-5994 (NND)		NA
	N		PHD,BA,MA	Affliate Scientist				Project-5995 (Pilot Projects)		NA
	Y		MD,BS	Center Director				Admin Core-5961 (Office of the Director)		NA
	Y			Colony Director				Other-5972 (Colony Management)		NA
	Y		PHD,DVM,MS	Pathologist				Other-5977 (Division of Pathology)		NA
	Y		PHD,BS	Core Director				Core-5978 (Biomarkers Core), Core-5981 (Virology Core)		NA
	Y			Core Asst Director				Core-5980 (Imaging Core)		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?

Yes

Excluded by Requester is no longer a core scientist for Yerkes NPRC. As a result, he is no longer part of the key personnel for this award.

D.2.b New Senior/Key Personnel

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

Yes

File uploaded: D2b New Key Personnel.pdf

D.2.c Changes in Other Support

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

Yes

File uploaded: D2d Other Support.pdf

D.2.d New Other Significant Contributors

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

No

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

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

NA

D.2.b New Senior/Key Personnel

The following individuals are new key personnel for this award:

Excluded by Requester joined Yerkes as a veterinary pathologist in August 2016. He will be key personnel in the Division of Pathology component.

Excluded by Requester became Core Scientist in the division of Developmental and Cognitive Neuroscience in January 2017. She will be key personnel in the DCN component.

Please see the following pages for their biosketches as well as other support information.

OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

Excluded by Requester

Excluded by Requester

D.2.b (D2b New Key Personnel.pdf)

Excluded by Requester

OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Excluded by Requester

Other Support

Excluded by Requester

D.2.b (D2b New Key Personnel.pdf)

Excluded by Requester

OTHER SUPPORT

Excluded by Requester

Excluded by Requester

Excluded by Requester

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D.2.c (D2d Other Support.pdf)

None

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Excluded by Requester

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?

Type of improvement	Source of support
FS G-11 roof replacement	ORIP P51 I/M funds
MET Room generator	ORIP P51 I/M funds
RMY replacement server	ORIP P51 I/M funds
SurgiVet monitor	ORIP P51 I/M funds
CO2 Incubator	ORIP P51 I/M funds
Necropsy table	ORIP P51 I/M funds
Animal Transport Van	ORIP P51 I/M funds
MS van	ORIP P51 I/M funds
Propane suppression system	ORIP P51 I/M funds
Behavioral Research/Colony Management observation tower renovation	Program income
Main Station new slide gate installation	Program income
FS M4 Roof replacement	Institutional funds
FS G11 Roof replacement	Institutional funds
MS Siemens building automation system (VRC AHU)	Institutional funds

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

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

NOTHING TO REPORT

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

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS

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

File(s) uploaded:
G Special Reporting Requirements.pdf

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

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

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

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

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

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

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

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

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: Emory University, Yerkes National Primate Research Center	066469933	GA-005	Specific Animal Location
Emory University, Yerkes National Primate Research Center Field Station	066469933	GA-007	Specific Animal Location

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?

Proprietary Info

Anticipated Amount	Source(s)
	Primate Use Fees, Per Diem, Services

G.12 F&A COSTS

Not Applicable

Yerkes NPRC
Information Requested in P51 RPPR Instructions

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

Census Date: 2/8/2017

Genus/Species	Breeding Colony[2]				Animals Not in Breeding Colony[3]				Total Colony Census
	M	F	U[4]	Total	M	F	U[4]	Total	
Macaca mulatta (SPF)	416	1,008	105	**1,529**	68	9		**77**	**1,606**
Macaca mulatta (Non-SPF)					111	203		**314**	**314**
Macaca fascicularis					1			**1**	**1**
Macaca nemestrina									**0**
Cercocebus torquatus atys	28	66	8	**102**	43	26		**69**	**171**
Saimiri					18			**18**	**18**
Total	**444**	**1,074**	**113**	**1,631**	**241**	**238**	**0**	**479**	**2,110**

[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 YNPRC, but not supported by the P51 grant[1].

Census Date: 2/8/2017

Genus/Species	Breeding Colony[2]				Animals Not in Breeding Colony[3]				Total Colony Census
	M	F	U[4]	Total	M	F	U[4]	Total	
Macaca mulatta (SPF)	27	122		**149**	6	11		**17**	**166**
Macaca mulatta (Non-SPF)					300	319		**619**	**619**
Macaca fascicularis					6	2		**8**	**8**
Macaca nemestrina					5			**5**	**5**
Cercocebus torquatus atys									**0**
Saimiri					1	2		**3**	**3**
Total	**27**	**122**	**0**	**149**	**318**	**334**	**0**	**652**	**801**

[1]This entry includes 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 YNPRC, irrespective of source of support.

Census Date: 2/8/2017

Genus/Species	Total Number of Animals
Macaca mulatta (SPF)	**1,772**
Macaca mulatta (Non-SPF)	**933**
Macaca fascicularis	**9**
Cercocebus torquatus atys	**5**
Saimiri	**21**
Total	**2,911**

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

Dates covered by the report: 4/1/2016 – 1/31/2017

Sample type	Number of samples distributed
Tissues	261
Organs	7
Whole	11
Total	**279**

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

Project Type	Number of Projects
Management	12
Research	113
Pilot	4
Total	**129**

4. Percentage of AIDS-related P51 grant dollars

Approximately 53 % of our P51 grant dollars is AIDS-related

5. Information regarding the number of investigators by type

Type of Investigator	Number
Core Scientist	15
Affiliate Scientist	42
Visiting Scientist	1
Collaborators	83
Total	**141**

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.

169 articles in peer-reviewed journals and 5 book chapters are attributed to the P51 during the reporting period. These are based on articles that directly cite the P51 grant, and articles arising from research that utilized any Yerkes Resources. Please see section B.2 for the Overall component for a listing of these publications.

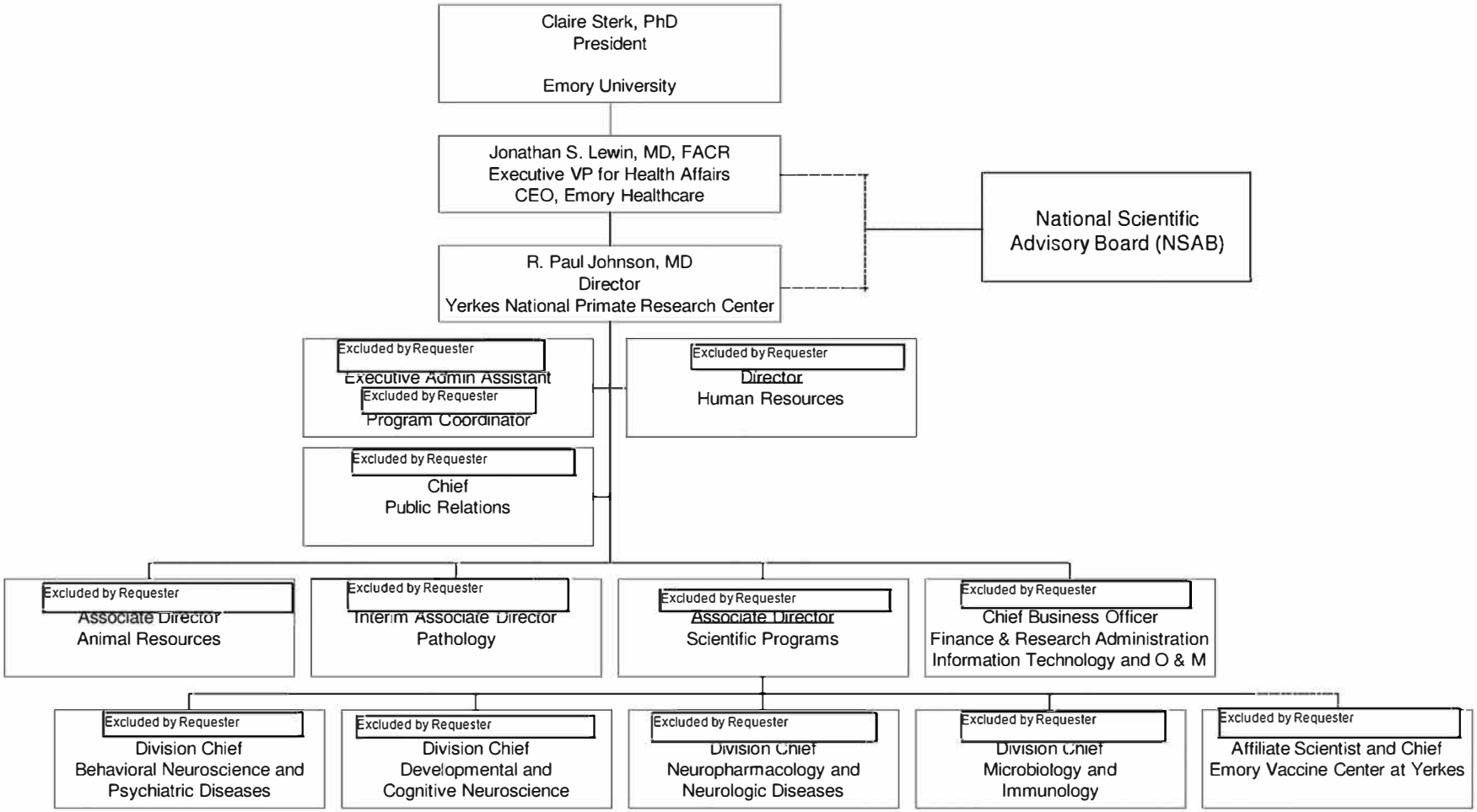
7. The number of individuals trained during the reporting period by type.

This information is provided in section B.4 in the Overall component.

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

See Next Page

Yerkes National Primate Research Center
Organizational Chart



9. Individual projects performed during the reporting period.

This information is provided in section B.2 in the Overall component.

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).

The Yerkes National Primate Research Center informs scientists about our role as a resource to researchers by publishing in peer-reviewed scientific journals, making presentations to the scientific community at local, national and international scientific meetings, manning an exhibit booth on behalf of all NPRCs at the annual Society for Neuroscience meeting and providing information to the nprcresearch.org website.

The center is also proactive in informing the general public about our role to discover causes, preventions, treatments and cures to improve human health and lives worldwide. We distribute news releases to media, maintain the Yerkes.emory.edu website, give presentations at community meetings and to elementary, junior high and high school students, and offer tours of our center.

In 2016, the Yerkes Research Center took the lead working with a public relations agency on behalf of all NPRCs to develop a brand foundation we can use in our public outreach. We are currently finalizing plans for the nationwide roll out.

11. Financial Support for the Resource.
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
$7,950,707	Proprietary Info	Proprietary Info	
Includes Year 56 supplement	Estimated program income as the current budget period is still ongoing	Includes F&A cost recovery, internal funds, etc	

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.

The Yerkes Research Center is interested in feedback from our faculty, staff and students as well as other customers we serve. Yerkes NPRC regularly solicits feedback from these individuals. One example is that we ask those who attend our Field Station Open Houses to complete a short exit survey. To date, all responses have rated the tour experience at the highest level.

As another example, every resolved IT Help (Service Now) request automatically generates an email notice to the customer with a request to complete a satisfaction survey. Research Administration Service staff (pre- and post-awards grants manager) has links to both pre-award and post-award satisfaction surveys on his/her e-mail signature to make these surveys easily accessible to their customers. The Imaging Core holds meetings

annually with all users to receive feedback on their ability to serve user needs as well as gauge user interest in future opportunities that may require technical development.

One of the most significant feedback efforts we've had this project period is the Employee Engagement Survey. It was conducted in June 2016 in collaboration with the Learning and Organizational Development Office at Emory. It was distributed to all of our faculty, staff, postdoctoral fellows and paid students. We had a response rate of 42% which is quite high for these types of employee surveys, and overall results showed high levels of satisfaction among the respondents. We are currently working on prioritizing action items to address areas of improvements that came out from the results of the survey. Some actions have already been taken, such as the return to an internal newsletter and Fantastic Service Behaviors Training course for all Business Office staff including Research Administration Service members.

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.

The following information is also reported in section E.3. of the Overall component.

Type of Improvement	Source of support
FS G-11 roof replacement	ORIP P51 I/M funds
MET Room generator	ORIP P51 I/M funds
RMY replacement server	ORIP P51 I/M funds
SurgiVet monitor	ORIP P51 I/M funds
CO2 Incubator	ORIP P51 I/M funds
Necropsy table	ORIP P51 I/M funds
Animal Transport Van	ORIP P51 I/M funds
MS van	ORIP P51 I/M funds
Propane suppression system	ORIP P51 I/M funds
Behavioral Research/Colony Management observation tower renovation	NIH Program income
Main Station new slide gate installation	NIH Program income
FS M4 Roof replacement	Institutional funds
FS G11 Roof replacement	Institutional funds
MS Siemens building automation system (VRC AHU)	Institutional funds

Excluded by Requester

From: Excluded by Requester
Sent: Tuesday, February 28, 2017 4:50 PM
To: Excluded by Requester
Subject: FW: IACUC Annual Renewal Approval "YER-2003042-022518GA" Excluded by approval letter

Excluded by Requester

Please let me know if you need anything else.

Best,
Excluded by Requester

EMORY UNIVERSITY
Institutional Animal Care and Use Committee
1599 Clifton Road, 5th Floor, Room 5.207 1599-001-1AU Atlanta, Georgia 30322-4250
Phone: 404-712-0734 Fax: 404-727-8452
Email: IACUC@emory.edu
Web Site: www.iacuc.emory.edu

Principal Investigator: Excluded by Requester

Your IACUC protocol #2003042 "Maintenance of the Yerkes Primate Center Animal Colony" has been reviewed and approved by the IACUC. It has now been assigned the IACUC protocol number "YER-2003042-022518GA" and was approved on "2/25/2015" and will expire on "2/25/2018". Protocols containing species covered by the Animal Welfare Act (AWA) or funded by the DoD require an annual review for the protocol to remain valid. The IACUC office will initiate annual reviews for Act species and DoD protocols, no action will be required on the part of the PI. There is no requirement for annual review of non-Act species animals, and none will be conducted.

NOTE: If your approval is for !
an amendment, the protocol number and expiration date have not changed.

Amendment Approval for:

Protocol funding:
Restricted Funding Sources:

Species:
NHP: Rhesus Macaque (ACT)

Protocol Review Requirements:

The USDA requires annual renewal of research projects using animals and PHS policy requires a de novo review of your protocol every three years before animal use approval can be extended. Both must be reviewed and approved by the IACUC prior to the anniversary or expiration date of this study. Emory's Animal Welfare Assurance Number is A3180-01.

IACUC Protocol Dissemination Policy:
Please note that all individuals listed on the approved protocol must have access to the protocol and any subsequent modifications. It is expected that all protocol associates will be familiar with the protocol and will have an up-to-date version of the protocol available to them at all times. It is the responsibility of the PI to!
ensure that all individuals on the protocol have access to, a!
nd are f
amiliar with the protocol. PDF versions of the protocol can be generated from the approved protocol in Elements by accessing the reports icon and then selecting "Protocol Detail Report".

If there are additions or changes to this protocol, you must submit an amendment form in Elements.

You can access this approved protocol on your dashboard under "My Protocols".

If you have any questions, please call the IACUC office at 404-712-0734.

Sincerely,
Larry Iten, DVM
Director, Emory IACUC

Composite Application Budget Summary

Categories	Budget Period
Salary, Wages and Fringe Benefits	4,735,605
Equipment	600,000
Travel	39,556
Participant/Trainee Support Costs	0
Other Direct Costs (excluding Consortium)	2,080,427
Consortium Costs	0
Direct Costs	7,455,588
Indirect Costs	3,085,014
Total Direct and Indirect Costs	10,540,602

Component Budget Summary

Components	Categories	Budget Period
5968-001 (Admin Core)	Salary, Wages and Fringe Benefits	0
	Equipment	600,000
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	600,000
	Indirect Costs	0
TOTALS	Total Direct and Indirect Costs	600,000
5967-002 (Admin Core)	Salary, Wages and Fringe Benefits	121,250
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	121,250
	Indirect Costs	54,563
TOTALS	Total Direct and Indirect Costs	175,813
5966-003 (Admin Core)	Salary, Wages and Fringe Benefits	8,534
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	8,534
	Indirect Costs	3,840
TOTALS	Total Direct and Indirect Costs	12,374
5965-004 (Admin Core)	Salary, Wages and Fringe Benefits	15,982
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	4,000
	Consortium Costs	0
	Direct Costs	19,982
	Indirect Costs	8,992
TOTALS	Total Direct and Indirect Costs	28,974
5964-005 (Admin Core)	Salary, Wages and Fringe Benefits	5,863
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	5,863
	Indirect Costs	2,638
TOTALS	Total Direct and Indirect Costs	8,501

5963-006 (Admin Core)	Salary, Wages and Fringe Benefits	19,376
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	21,376
	Indirect Costs	9,619
TOTALS	Total Direct and Indirect Costs	30,995
5962-007 (Admin Core)	Salary, Wages and Fringe Benefits	15,376
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	17,376
	Indirect Costs	7,819
TOTALS	Total Direct and Indirect Costs	25,195
5961-008 (Admin Core)	Salary, Wages and Fringe Benefits	119,654
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	4,000
	Consortium Costs	0

	Direct Costs	125,654
	Indirect Costs	56,544
TOTALS	Total Direct and Indirect Costs	182,198
5978-001 (Core)	Salary, Wages and Fringe Benefits	22,653
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	21,000
	Consortium Costs	0
	Direct Costs	43,653
	Indirect Costs	19,644
TOTALS	Total Direct and Indirect Costs	63,297
5982-002 (Core)	Salary, Wages and Fringe Benefits	63,427
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	21,000
	Consortium Costs	0
	Direct Costs	84,427
	Indirect Costs	37,992
TOTALS	Total Direct and Indirect Costs	122,419
5981-003 (Core)	Salary, Wages and Fringe Benefits	16,290
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	6,000
	Consortium Costs	0
	Direct Costs	22,290
	Indirect Costs	10,031
TOTALS	Total Direct and Indirect Costs	32,321
5980-004 (Core)	Salary, Wages and Fringe Benefits	101,808
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	14,000
	Consortium Costs	0
	Direct Costs	115,808
	Indirect Costs	52,113
TOTALS	Total Direct and Indirect Costs	167,921
5979-005 (Core)	Salary, Wages and Fringe Benefits	31,675
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	468,325
	Consortium Costs	0
	Direct Costs	500,000
	Indirect Costs	225,000
TOTALS	Total Direct and Indirect Costs	725,000

5977-001 (Other)	Salary, Wages and Fringe Benefits	532,862
	Equipment	0
	Travel	5,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	103,000
	Consortium Costs	0
	Direct Costs	640,862
	Indirect Costs	288,388
TOTALS	Total Direct and Indirect Costs	929,250
5976-002 (Other)	Salary, Wages and Fringe Benefits	121,410
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	150,000
	Consortium Costs	0
	Direct Costs	273,410
	Indirect Costs	123,035
TOTALS	Total Direct and Indirect Costs	396,445
5975-003 (Other)	Salary, Wages and Fringe Benefits	109,641
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	20,000
	Consortium Costs	0

	Direct Costs	131,641
	Indirect Costs	59,238
TOTALS	Total Direct and Indirect Costs	190,879
5974-004 (Other)	Salary, Wages and Fringe Benefits	27,582
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	29,582
	Indirect Costs	13,312
TOTALS	Total Direct and Indirect Costs	42,894
5973-005 (Other)	Salary, Wages and Fringe Benefits	305,039
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	50,000
	Consortium Costs	0
	Direct Costs	357,039
	Indirect Costs	160,668
TOTALS	Total Direct and Indirect Costs	517,707
5972-006 (Other)	Salary, Wages and Fringe Benefits	314,433
	Equipment	0
	Travel	2,000

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	388,683
	Consortium Costs	0
	Direct Costs	705,116
	Indirect Costs	317,302
TOTALS	Total Direct and Indirect Costs	1,022,418
5971-007 (Other)	Salary, Wages and Fringe Benefits	1,836,870
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	473,019
	Consortium Costs	0
	Direct Costs	2,311,889
	Indirect Costs	1,040,350
TOTALS	Total Direct and Indirect Costs	3,352,239
5970-008 (Other)	Salary, Wages and Fringe Benefits	749,300
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	142,000
	Consortium Costs	0
	Direct Costs	893,300
	Indirect Costs	401,985
TOTALS	Total Direct and Indirect Costs	1,295,285

5990-009 (Other)	Salary, Wages and Fringe Benefits	45,107
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	45,107
	Indirect Costs	20,298
TOTALS	Total Direct and Indirect Costs	65,405
5969-010 (Other)	Salary, Wages and Fringe Benefits	43,193
	Equipment	0
	Travel	2,000
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	45,193
	Indirect Costs	20,337
TOTALS	Total Direct and Indirect Costs	65,530
5997-011 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	7,542
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0

	Direct Costs	7,542
	Indirect Costs	3,394
TOTALS	Total Direct and Indirect Costs	10,936
5996-012 (Other)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	5,014
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	5,400
	Consortium Costs	0
	Direct Costs	10,414
	Indirect Costs	4,686
TOTALS	Total Direct and Indirect Costs	15,100
5994-013 (Other)	Salary, Wages and Fringe Benefits	47,105
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	47,105
	Indirect Costs	21,197
TOTALS	Total Direct and Indirect Costs	68,302
5984-014 (Other)	Salary, Wages and Fringe Benefits	46,076
	Equipment	0
	Travel	0

	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	46,076
	Indirect Costs	20,734
TOTALS	Total Direct and Indirect Costs	66,810
5983-015 (Other)	Salary, Wages and Fringe Benefits	15,099
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	0
	Consortium Costs	0
	Direct Costs	15,099
	Indirect Costs	6,795
TOTALS	Total Direct and Indirect Costs	21,894
5995-001 (Project)	Salary, Wages and Fringe Benefits	0
	Equipment	0
	Travel	0
	Participant/Trainee Support Costs	0
	Other Direct Costs (excluding Consortium)	210,000
	Consortium Costs	0
	Direct Costs	210,000
	Indirect Costs	94,500
TOTALS	Total Direct and Indirect Costs	304,500

TOTALS		**10,540,602**

Categories Budget Summary

Categories	Components	Budget Period
R&R Budget - Senior/Key Person Funds Requested	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	11,541
	5962-007 (Admin Core)	11,541
	5961-008 (Admin Core)	115,410
	5978-001 (Core)	4,212
	5982-002 (Core)	6,102
	5981-003 (Core)	4,212
	5980-004 (Core)	34,229
	5979-005 (Core)	27,183
	5977-001 (Other)	94,937
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	32,643
	5972-006 (Other)	22,829
	5971-007 (Other)	0
	5970-008 (Other)	340,113

	5990-009 (Other)	40,538
	5969-010 (Other)	20,437
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	44,065
	5984-014 (Other)	41,567
	5983-015 (Other)	11,541
	5995-001 (Project)	0
TOTALS		863,100
R&R Budget - Other Personnel Funds Requested	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	121,250
	5966-003 (Admin Core)	8,534
	5965-004 (Admin Core)	15,982
	5964-005 (Admin Core)	5,863
	5963-006 (Admin Core)	7,835
	5962-007 (Admin Core)	3,835
	5961-008 (Admin Core)	4,244
	5978-001 (Core)	18,441
	5982-002 (Core)	57,325
	5981-003 (Core)	12,078
	5980-004 (Core)	67,579
	5979-005 (Core)	4,492
	5977-001 (Other)	437,925
	5976-002 (Other)	121,410

	5975-003 (Other)	109,641
	5974-004 (Other)	27,582
	5973-005 (Other)	272,396
	5972-006 (Other)	291,604
	5971-007 (Other)	1,836,870
	5970-008 (Other)	409,187
	5990-009 (Other)	4,569
	5969-010 (Other)	22,756
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	3,040
	5984-014 (Other)	4,509
	5983-015 (Other)	3,558
	5995-001 (Project)	0
TOTALS		3,872,505
R&R Budget - Section A & B. Total Salary, Wages and Fringe Benefits (A+B)	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	121,250
	5966-003 (Admin Core)	8,534
	5965-004 (Admin Core)	15,982
	5964-005 (Admin Core)	5,863
	5963-006 (Admin Core)	19,376
	5962-007 (Admin Core)	15,376
	5961-008 (Admin Core)	119,654
	5978-001 (Core)	22,653

	5982-002 (Core)	63,427
	5981-003 (Core)	16,290
	5980-004 (Core)	101,808
	5979-005 (Core)	31,675
	5977-001 (Other)	532,862
	5976-002 (Other)	121,410
	5975-003 (Other)	109,641
	5974-004 (Other)	27,582
	5973-005 (Other)	305,039
	5972-006 (Other)	314,433
	5971-007 (Other)	1,836,870
	5970-008 (Other)	749,300
	5990-009 (Other)	45,107
	5969-010 (Other)	43,193
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	47,105
	5984-014 (Other)	46,076
	5983-015 (Other)	15,099
	5995-001 (Project)	0
TOTALS		4,735,605
R&R Budget - Section C. Total Equipment	5968-001 (Admin Core)	600,000
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0

	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0

	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		600,000
R&R Budget - Domestic Travel	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	2,000
	5962-007 (Admin Core)	2,000
	5961-008 (Admin Core)	2,000
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	5,000
	5976-002 (Other)	2,000
	5975-003 (Other)	2,000
	5974-004 (Other)	2,000
	5973-005 (Other)	2,000
	5972-006 (Other)	2,000
	5971-007 (Other)	2,000
	5970-008 (Other)	2,000

	5990-009 (Other)	0
	5969-010 (Other)	2,000
	5997-011 (Other)	7,542
	5996-012 (Other)	5,014
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		39,556
R&R Budget - Foreign Travel	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0

	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Section D. Total Travel	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	2,000
	5962-007 (Admin Core)	2,000
	5961-008 (Admin Core)	2,000
	5978-001 (Core)	0

	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	5,000
	5976-002 (Other)	2,000
	5975-003 (Other)	2,000
	5974-004 (Other)	2,000
	5973-005 (Other)	2,000
	5972-006 (Other)	2,000
	5971-007 (Other)	2,000
	5970-008 (Other)	2,000
	5990-009 (Other)	0
	5969-010 (Other)	2,000
	5997-011 (Other)	7,542
	5996-012 (Other)	5,014
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		39,556
R&R Budget - Tuition/Fees/Health Insurance	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0

	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0

	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Stipends	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0

	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Trainee Travel	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0

	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Subsistence	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0

	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Other Participants/Trainee Support Costs	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0

	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0

	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Section E. Total Participants/Trainee Support Costs	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0

	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Materials and Supplies	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	20,000
	5982-002 (Core)	20,000
	5981-003 (Core)	5,000
	5980-004 (Core)	11,000
	5979-005 (Core)	40,000
	5977-001 (Other)	60,000
	5976-002 (Other)	150,000

	5975-003 (Other)	20,000
	5974-004 (Other)	0
	5973-005 (Other)	30,000
	5972-006 (Other)	22,000
	5971-007 (Other)	300,000
	5970-008 (Other)	53,000
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	300
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		731,300
R&R Budget - Publication Costs	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0

	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Consultant Services	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0

	5965-004 (Admin Core)	4,000
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	4,000
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0

	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		8,000
R&R Budget - ADP/Computer Services	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0

	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Subawards/Consortium/Contractual Costs	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0

	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Equipment or Facility Rental User Fees	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0

	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Alterations and Renovations	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0

	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	0
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	0
	5972-006 (Other)	0
	5971-007 (Other)	0
	5970-008 (Other)	0
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0

	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		0
R&R Budget - Other Direct Cost 1	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	1,000
	5982-002 (Core)	1,000
	5981-003 (Core)	1,000
	5980-004 (Core)	3,000
	5979-005 (Core)	382,892
	5977-001 (Other)	20,000
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	10,000
	5972-006 (Other)	363,683
	5971-007 (Other)	50,000
	5970-008 (Other)	67,000

	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	5,100
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	210,000
TOTALS		1,114,675
R&R Budget - Other Direct Cost 2	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0
	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	45,433
	5977-001 (Other)	20,000
	5976-002 (Other)	0

	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	5,000
	5972-006 (Other)	1,000
	5971-007 (Other)	86,000
	5970-008 (Other)	20,000
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		177,433
R&R Budget - Other Direct Cost 3	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0
	5965-004 (Admin Core)	0
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	0
	5978-001 (Core)	0

	5982-002 (Core)	0
	5981-003 (Core)	0
	5980-004 (Core)	0
	5979-005 (Core)	0
	5977-001 (Other)	3,000
	5976-002 (Other)	0
	5975-003 (Other)	0
	5974-004 (Other)	0
	5973-005 (Other)	5,000
	5972-006 (Other)	2,000
	5971-007 (Other)	37,019
	5970-008 (Other)	2,000
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	0
	5994-013 (Other)	0
	5984-014 (Other)	0
	5983-015 (Other)	0
	5995-001 (Project)	0
TOTALS		49,019
R&R Budget - Section F. Total Other Direct Cost	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	0
	5966-003 (Admin Core)	0

	5965-004 (Admin Core)	4,000
	5964-005 (Admin Core)	0
	5963-006 (Admin Core)	0
	5962-007 (Admin Core)	0
	5961-008 (Admin Core)	4,000
	5978-001 (Core)	21,000
	5982-002 (Core)	21,000
	5981-003 (Core)	6,000
	5980-004 (Core)	14,000
	5979-005 (Core)	468,325
	5977-001 (Other)	103,000
	5976-002 (Other)	150,000
	5975-003 (Other)	20,000
	5974-004 (Other)	0
	5973-005 (Other)	50,000
	5972-006 (Other)	388,683
	5971-007 (Other)	473,019
	5970-008 (Other)	142,000
	5990-009 (Other)	0
	5969-010 (Other)	0
	5997-011 (Other)	0
	5996-012 (Other)	5,400
	5994-013 (Other)	0
	5984-014 (Other)	0

	5983-015 (Other)	0
	5995-001 (Project)	210,000
TOTALS		2,080,427
R&R Budget - Section G. Total Direct Cost (A thru F)	5968-001 (Admin Core)	600,000
	5967-002 (Admin Core)	121,250
	5966-003 (Admin Core)	8,534
	5965-004 (Admin Core)	19,982
	5964-005 (Admin Core)	5,863
	5963-006 (Admin Core)	21,376
	5962-007 (Admin Core)	17,376
	5961-008 (Admin Core)	125,654
	5978-001 (Core)	43,653
	5982-002 (Core)	84,427
	5981-003 (Core)	22,290
	5980-004 (Core)	115,808
	5979-005 (Core)	500,000
	5977-001 (Other)	640,862
	5976-002 (Other)	273,410
	5975-003 (Other)	131,641
	5974-004 (Other)	29,582
	5973-005 (Other)	357,039
	5972-006 (Other)	705,116
	5971-007 (Other)	2,311,889
	5970-008 (Other)	893,300

	5990-009 (Other)	45,107
	5969-010 (Other)	45,193
	5997-011 (Other)	7,542
	5996-012 (Other)	10,414
	5994-013 (Other)	47,105
	5984-014 (Other)	46,076
	5983-015 (Other)	15,099
	5995-001 (Project)	210,000
TOTALS		7,455,588
R&R Budget - Section H. Indirect Costs	5968-001 (Admin Core)	0
	5967-002 (Admin Core)	54,563
	5966-003 (Admin Core)	3,840
	5965-004 (Admin Core)	8,992
	5964-005 (Admin Core)	2,638
	5963-006 (Admin Core)	9,619
	5962-007 (Admin Core)	7,819
	5961-008 (Admin Core)	56,544
	5978-001 (Core)	19,644
	5982-002 (Core)	37,992
	5981-003 (Core)	10,031
	5980-004 (Core)	52,113
	5979-005 (Core)	225.000
	5977-001 (Other)	288,388
	5976-002 (Other)	123,035

	5975-003 (Other)	59,238
	5974-004 (Other)	13,312
	5973-005 (Other)	160,668
	5972-006 (Other)	317,302
	5971-007 (Other)	1,040,350
	5970-008 (Other)	401,985
	5990-009 (Other)	20,298
	5969-010 (Other)	20,337
	5997-011 (Other)	3,394
	5996-012 (Other)	4,686
	5994-013 (Other)	21,197
	5984-014 (Other)	20,734
	5983-015 (Other)	6,795
	5995-001 (Project)	94,500
TOTALS		3,085,014
R&R Budget - Section I. Total Direct and Indirect Costs (G +H)	5968-001 (Admin Core)	600,000
	5967-002 (Admin Core)	175,813
	5966-003 (Admin Core)	12,374
	5965-004 (Admin Core)	28,974
	5964-005 (Admin Core)	8,501
	5963-006 (Admin Core)	30,995
	5962-007 (Admin Core)	25,195
	5961-008 (Admin Core)	182,198
	5978-001 (Core)	63,297

	5982-002 (Core)	122,419
	5981-003 (Core)	32,321
	5980-004 (Core)	167,921
	5979-005 (Core)	725,000
	5977-001 (Other)	929,250
	5976-002 (Other)	396,445
	5975-003 (Other)	190,879
	5974-004 (Other)	42,894
	5973-005 (Other)	517,707
	5972-006 (Other)	1,022,418
	5971-007 (Other)	3,352,239
	5970-008 (Other)	1,295,285
	5990-009 (Other)	65,405
	5969-010 (Other)	65,530
	5997-011 (Other)	10,936
	5996-012 (Other)	15,100
	5994-013 (Other)	68,302
	5984-014 (Other)	66,810
	5983-015 (Other)	21,894
	5995-001 (Project)	304,500
TOTALS		10,540,602

A. COMPONENT COVER PAGE

Project Title: Office of the Director

Component Project Lead Information:

JOHNSON, R. PAUL

B. COMPONENT ACCOMPLISHMENTS

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

The Yerkes Director's Office serves to establish key strategic objectives and to coordinate the overall management of the Center. The guideposts for our management of the Center include the strategic objectives of the NIH, as well as the outcomes of strategic planning exercises within the Emory University Woodruff Health Sciences Center (WHSC) and within Yerkes. Strategic planning is conducted in close collaboration with the Associate Director for Scientific Programs (ADSP), and is a unified process that reflects not only our structured internal planning efforts but also the integration of these internal strategic plans with those of our affiliates, including the other NPRCs, Office of Research Infrastructure Programs (ORIP) and the WHSC. The Director also works closely with the ADSP on recruitment, retention and promotion of faculty. In collaboration with the Chief Business Officer (CBO), the Director works to ensure effective fiscal and administrative oversight of funds used for both sponsored research activities and operations of the Center in compliance with University and Federal guidelines. The Director also works closely with the CBO and other members of the Yerkes leadership team to identify new sources of support for the Center. Finally, the Director works in concert with the Chief of Public Affairs to communicate the results of key scientific studies, not only to our scientific colleagues but also, to our Center employees and the public at large. The Director will also ensure the coordination and communication of plans with appropriate counterparts in WHSC, as well as in the ORIP and with other NPRCs.

The Specific Aims are:

1. To establish scientific and strategic priorities for the Yerkes Center and to orchestrate efforts to achieve these goals within the Center, WHSC, and nationwide;

2. To work collaboratively with the ADSP to recruit outstanding scientists, retain our faculty, and support their promotion in rank at Emory University;

3. To work in concert with the Yerkes CBO and other members of the Yerkes leadership team to ensure equitable and strategic allocation of financial resources and to identify new sources of support for the Center;

4. To provide effective communication regarding Center activities and priorities to the Yerkes community, WHSC and the national biomedical research and lay communities.

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_5961_Director.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

Strategic Planning

Strategic planning at Yerkes plays a central role in the establishment of short-term and long-term goals to advance nonhuman primate translational research. Strategic planning is conducted in close collaboration with the ADSP, and is a cohesive process that reflects not only the structured internal planning efforts but also the integration of these internal strategic plans with those of our affiliates, including the other NPRCs, ORIP and the WHSC. Working with the ADSP, as well as the Scientific Division Chiefs, the CBO, the other Associate Directors, and the Yerkes faculty, the Director will help identify short-term and long-term goals that will guide the recruitment of new faculty, allocation of resources, and the future directions of the Center's Core services. Of particular interest are efforts to leverage advances in genomics to advance our scientific programs and the opportunities to create greater synergy between our neuroscience and microbiology/immunology communities. These strategic goals will be reevaluated on at least an annual basis, and aligned with the strategic objectives of the WHSC and University, as well as ORIP and the NIH.

Faculty Recruitment

The Center Director will continue to work closely with the ADSP in coordinating faculty recruitment and promotion activities. Structured

faculty recruitments will be based on specific needs in focused research areas and will be initiated in close cooperation with the Science Divisions. These recruitment efforts will also be coordinated with other units of the University, typically departments within the School of Medicine, based on research program relevance. Retention efforts will occur as both proactive and reactive steps to retain our most productive faculty but will be guided by the overarching objectives of the strategic planning process to ensure that there is an alignment of resource commitments to overall strategic goals.

Specific areas of faculty recruitment in the upcoming funding period include: 1. Associate Director for Pathology, 2. Genetic/Genomics, 3. Imaging Center Director, and 4. Faculty positions for the ERASE AIDS initiative, which is focused on nonhuman primate models of HIV cure research.

B.2. Accomplishments—Director's Office

A robust, integrated and effective leadership team is essential for the short-term and long-term success of the Yerkes National Primate Research Center (NPRC) and its ability to achieve its operating and strategic goals. The Center Director provides overall leadership for the Center, establishing scientific and administrative priorities that are guided by the Center's strategic plans. The Director is ultimately responsible for the oversight of all activities at the Center, including establishment of scientific priorities, strategic planning, coordination of new faculty recruits, financial management and business planning, human resources and public communications. In order to efficiently and effectively manage these diverse responsibilities, the Director of the Yerkes Center works closely with the Associate Director for Scientific Programs (ADSP), the Chief Business Officer (CBO), the Associate Director for Animal Resources, the Associate Director for Pathology, the four Chiefs of the Scientific Divisions, the Director of Human Resources and the Chief of Public Affairs.

The Specific Aims of the Director's Office, which are unchanged, are:

1. To establish scientific and strategic priorities for the Yerkes Center and to orchestrate efforts to achieve these goals within the Center, WHSC, and nationwide;

2. To work collaboratively with the ADSP to recruit outstanding scientists, retain our faculty, and support their promotion in rank at Emory University.

3. To work in concert with the Yerkes CBO and other members of the Yerkes leadership team to ensure equitable and strategic allocation of financial resources and to identify new sources of support for the Center;

4. To provide effective communication regarding Center activities and priorities to the Yerkes community, WHSC and the national biomedical research and lay communities.

The Yerkes Director's Office has demonstrated significant progress in meeting each of our key objectives during the reporting period (5/1/16 to 4/30/17), and in particular, has made key progress in strategic planning and in faculty recruitment. Specific progress in each of these areas includes:

Strategic Planning:

The Center Director has worked closely with the Associate Director for Scientific Programs, Excluded by Requester Excluded by Requester to organize a series of strategic planning sessions for the three scientific divisions focused on neuroscience-related research. Separately, we organized a similar strategic planning session for the Division of Microbiology and Immunology and the Emory Vaccine Center. Subsequent planning included all four Science Divisions and the Emory Vaccine Center, and focused specifically to integrate these research programs into novel areas of investigation, including programs aimed at better understanding and treating CNS dysfunction and cognitive impairment associated with infectious diseases.

Faculty recruitment:

After a three year search, Excluded by Requester was named the inaugural Rollins Chair in Stroke and Imaging Research at Yerkes. Excluded by a physician scientist and board-certified vascular neurologist, has made numerous contributions to understanding how the brain responds to stroke and other injuries, and has a long history of research funding from the National Institutes of Health (NIH) and private foundations. He has published more than 90 scientific articles, book chapters and textbooks, and is the recipient of two patents. Excluded by is a tenured professor of neurology at Emory University and director of the Atlanta Veterans Affairs Medical Center Stroke Team.

In addition, the Yerkes Center recruited Excluded by Requester to serve as a staff pathologist. Excluded by Requester obtained his DVM from Mississippi State and his PhD from the University of Guelph, Ontario.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5961

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	Dr	Robert	Paul	Johnson		Project Lead	Institutional Base Salary	EFFORT			92,550.00	22,860.00	115,410.00
2.	Dr	Jonathan		Lewin		PI					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** **115,410.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			3,403.00	841.00	4,244.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**4,244.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**119,654.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	4,000.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**4,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**125,654.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	125,654.00	56,544.00
		Total Indirect Costs	**56,544.00**

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)	**182,198.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Asc. Dir. for Scientific Programs

Component Project Lead Information:

JOHNSON, R. PAUL

B. COMPONENT ACCOMPLISHMENTS

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

The Associate Director for Scientific Programs (ADSP) provides assistance to the Director in all aspects of scientific programs of the Center, including formulating short-term and long-range goals and strategic planning, establishing specific objectives and implementing steps for promoting the scientific programs and resource enhancements of the Center. The ADSP serves as Acting Director during the Director's absence. The responsibilities of the office are accomplished in conjunction with the Director, Science Division Chiefs, Science Core Directors and with affiliate and collaborating scientists, to identify needs and establish priorities. Specifically, the ADSP promotes the further development and expansion of the Center's core, affiliate and collaborative research programs, and assists the Director in guiding the Center's research and management activities while participating in the development and implementation of a strategic research plan. Additionally, the ADSP works closely with the Director by participating in the Consortium of NPRCs and through promoting the NPRC mission to key individuals in NIH and elsewhere in government. The ADSP will continue to serve in a number of leadership roles, including Chief of the Division of Neuropharmacology and Neurologic Diseases and Director of the Imaging Center. Specific activities encompassed by this new leadership position include taking a lead role in the organization of the 2015 P51 Base Grant application, organizing strategic planning for research programs, serving as Chair of the Yerkes Space Committee, coordinating faculty recruitment and promotion activities, enhancing the mentoring programs for junior scientists, exploring new collaborative research opportunities, providing oversight of the Science Cores, as well as taking on other activities as needed that will support scientific research at Yerkes. [Excluded by Re...] has appropriate scientific expertise and leadership experience to meet the challenges of these multiple roles at the Center and will be a significant asset to the Center Director.

The Specific Aims are:

1.To enhance the scientific programs of the Center through the development and application of innovative technologies and collaborative efforts among Center scientists and outside investigators at the national and international level;

2.To provide leadership and oversight in strategic planning, promotion of scientific programs, and expansion of the Center infrastructure, including the evaluation of research programs for mission relevance and scientific merit to ensure that required state-of-the-art resources are available;

3.To coordinate faculty recruitment and promotion and to enhance mentoring activities for junior scientists.

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_5962_ADSP.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The continued success of the Center in future years will depend largely on the ability to strengthen its scientific programs and its leadership position within Emory University, and at the national and international levels. Genetics and genomics have become essential in many aspects of biomedical research. Genomic analysis of nonhuman primates will take on a growing significance due to the dependency of researchers in multiple fields to incorporate genomic information into primate models of human disease. The Yerkes Center is especially well positioned, with its outstanding programs in molecular biology and immunology, infectious diseases, and neuroscience, to take a leadership role in this regard by initiating a large-scale program that will involve genome sequencing in its primate colonies. Future efforts also will emphasize the importance of developing complex, multi-dimensional phenotyping information related to normal and abnormal behavior and physiology that is highly relevant to human disease and pathology. Moreover, the Yerkes Center has the expertise and initiative to move techniques that allow for genetic manipulation of targeted circuits (optogenetics, DREADDs) from the rodent to the nonhuman primate. This is a very important initiative, since it will allow for more mechanistic studies linking brain circuits to function and pathology. Finally, successful recruitment and retention of research faculty are essential to the mission of the Center. Yerkes has initiated a new national search for a permanent Associate Director of the Division of Pathology. These recruitments will provide opportunities to develop important new research collaborations both within Emory University and at other biomedical research institutions. Lastly, successful faculty retention requires strong mentoring of junior faculty. The Yerkes Mentoring Program with well-defined roles for mentors and mentees will continue to develop in order to ensure proper faculty development at every

level.

B.2. Accomplishments—Associate Director for Scientific Programs

The Associate Director for Scientific Programs (ADSP), Excluded by Requester works closely with the Center Director in all aspects of scientific programs of the Center, including formulating short-term and long-range goals and strategic planning, establishing specific objectives, and promoting the scientific programs and resource enhancements of the Center. The ADSP and the Center Director organized a series of strategic planning sessions for the three Science Divisions focused on neuroscience-related research. Separately, we organized a similar strategic planning session for the Division of Microbiology and Immunology, and the Emory Vaccine Center. Subsequent planning included all four Science Divisions and the Emory Vaccine Center, and focused specifically to integrate these research programs into novel areas of investigation, including programs aimed at better understanding and treating CNS dysfunction and cognitive impairment associated with infectious diseases. Moreover, the ADSP has been very active in working with the research scientists at the Yerkes Field Station in order to enhance the unique research opportunities provided by our large groups of socially-housed rhesus monkeys. The Yerkes Imaging Center plays a significant role in support of these research programs. The ADSP works closely with the Center Director in coordinating faculty recruitment and promotion activities. The ADSP serves as Chair of the Faculty Promotion Committee comprised of the Chiefs of the four Science Divisions, the Associate Director of Animal Resources, and the Associate Director of Pathology. We recently appointed the first endowed chair at the Yerkes Center in the area of stroke imaging. Lastly, the ADSP provides oversight of the Yerkes Center Mentoring Program. Based on the value of mentoring with regard to ensuring the success of junior faculty members and enhancing the quality of the professional and personal lives of junior faculty, Research Associates and Assistant Professors are expected to have at least one mentor. There are two different avenues for mentor selection within the Center. Junior faculty members choose their own mentor(s) based on similar scientific or professional interests and/or someone who has shown particular interest in their professional growth and success; or junior faculty members who do not select a mentor are assigned a mentor based on similar scientific or professional interests and the needs and goals the mentee has established for their career path. A key goal of the mentoring relationship is to support the career development and the career independence of the junior person.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5962

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	Dr	Robert	Paul	Johnson		Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.	Excluded by Requester					Asc Dir, Scientific Pgms					9,255.00	2,286.00	11,541.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **11,541.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			3,075.00	760.00	3,835.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**3,835.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**15,376.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**17,376.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	17,376.00	7,819.00
		Total Indirect Costs	**7,819.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**25,195.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Business Services

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Business Services Office (also referred to as Business and Finance) is responsible for an array of services required for the day-to-day operations of the Center. It is responsible for budgeting and financial management, to assist in grant proposal preparation, for financial review of grant proposals, post-award administration of grants, procurement of goods and services, billing and recharge recovery, shipping, bi-weekly payroll, labor distribution, effort certification and other research compliance issues, and reception of visitors to the Center. The business functions are centrally organized and provided to all laboratories and service units at Yerkes. Because so much of the activity is grant-driven, the staff must focus on compliance issues as well as service aspects. The Business Services Office is responsible for all of the above activities relating to the Yerkes P51 Base Grant as well as for the other approximately $64M in sponsored research funding at Yerkes. This office must safeguard the resources of the Yerkes Center. Business Services is responsible for the financial management and accounting of the Emory-designated Unrestricted Operating Budget (UOB) funds, designated funds, endowment funds, all discretionary funds used by faculty and staff, and for the financial and compliance activities relating to extramural support for investigators. The Chief Business Officer, who reports to the Yerkes Director, Chief University Financial Officer, and the Chief University Budget Officer, heads this office.
The Specific Aims are:

1.To continue to provide comprehensive and effective financial management and oversight of all funds used in support of both the operations and sponsored research associated with the Yerkes Center including, most importantly, the management of the P51 award;

2.To provide high level customer service to our cohort of faculty, staff, and students in each Division within Yerkes by outlining and adhering to established internal policies as well as university-level policies and providing operational support on all activities;

3.To continue to provide financial oversight, rate setting, and cost recovery for our numerous service center activities at Yerkes;

4.To represent Yerkes on university-level committees and initiatives to ensure that the needs and interests of Yerkes are taken into consideration when policies and strategic plans are developed.

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_5963_BusSvs.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

Continue to provide comprehensive and effective financial management and oversight of all funds used in support of both the operations and sponsored research associated with the Yerkes Center including, most importantly, the management of the P51 award.

Business Services will work with faculty, leadership and central offices such as Emory's Office of Sponsored Research (OSP) and Finance: Grants and Contracts (FGC) to provide information and acquire training and updates to more effectively manage the P51 as well as our numerous other externally-funded grants.

Provide high level customer service to our cohort of faculty, staff, and students in each Division within Yerkes by outlining and adhering to established internal policies as well as university-level policies and providing operational support on all activities. As noted in our Accomplishments, our staff recently received an excellent training session on service behaviors. Other training sessions will be held as opportunities arise.

Continue to provide financial oversight, rate setting, and cost recovery for our numerous service center activities at Yerkes. The CBO and the Director of Business and Finance will continue to work with the leaders of Animal Resources, Pathology, and the Service Cores to conduct regular, comprehensive reviews of expenses and recharge recovery. These reviews will include annual rate setting analyses and projections. New rates will be posted on the Yerkes website and will be disseminated to faculty at the regular faculty meetings and by email using the faculty listserv. The financial performance of Service Cores and units providing experimental clinical services will receive financial reports on a regular basis and these will include annualized projections for the fiscal year.

Represent Yerkes on university-level committees and initiatives to ensure that the needs and interests of Yerkes are taken into consideration when policies and strategic plans are developed.

B.2. Accomplishments—Business Services

The Business Services Office, primarily through its Research Administration Services component, managed $79,097,405 in sponsored research funding in FY16, an increase of nearly 19% over the prior year without any increase in FTE levels. This was accomplished, in part, by a careful review of workload distribution and reassigning portfolios between existing staff.

In February, a four-hour Fantastic Service Behaviors Training was held for all of the staff in the Business Services Office including all of the pre- and post-award managers. This was in response to feedback received from the comprehensive Employee Engagement Survey conducted at Yerkes.

A security guard was added to the front desk reception for screening visitors and vendors to enhance security. Video monitors were installed at that location to add real-time access to all surveillance cameras at the Main Station.

The Chief Business Officer continued to serve as the Co-Chair of Emory's Compass Upgrade Steering Committee which oversaw the multi-year planning and launch process for the upgrade of the university's financial operating system. The successful launch occurred on November 14, 2016. Several members of the Business Services unit served as subject matter experts during User Acceptance Testing processes.

Updated the internal reimbursement request review process to adapt to Emory University's financial system upgrade

Worked with recharge units to update their rates for FY17. Service units recovered recharge funding at about the same level as for FY15. Indirect cost recovery was up by roughly 2% over the prior fiscal year. FY17 trends are favorable to FY16.

The CBO, Director of Business and Finance, and the RAS Director continue to serve on university-level committees and initiatives

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **11,541.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Business/Finance Director	0.6			6,283.00	1,552.00	7,835.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**7,835.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**19,376.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**21,376.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	21,376.00	9,619.00
		Total Indirect Costs	**9,619.00**

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)	**30,995.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Human Resources

Component Project Lead Information:

JOHNSON, R. PAUL

B. COMPONENT ACCOMPLISHMENTS

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

The Yerkes Human Resources (HR) Office is comprised of three employees, each responsible for working with various components within Emory's Central Human Resources. Policies and procedures related to benefits, compensation, recruitment, learning and development, and employee relations, are administered through Yerkes Human Resources. In addition, this office interacts with Emory's International Student and Scholar Services unit at Emory with visa related matters as well as providing orientation and information to new faculty, staff and students at the Center. The Human Resources office works in conjunction with the Office of General Counsel on the student and scholar liability agreements for unpaid individuals who participate in research at the Center. We also work together with the Office of Equity and Inclusion on equal opportunity, disability and compliance services. Working with our internal committees, the well-established Yerkes Staff Council and the Wellness Committee (established two years ago), the HR office sponsors several special events throughout the year for our staff employees. These activities are designed to create a balance between their job duties and the opportunity to interact with other departments on a social level. With a greater focus on health and well-being and positive lifestyle changes, the establishment of our Wellness Committee has been met with great enthusiasm by all Center employees. The members of this committee work with the wellness component of the campus Faculty Staff Assistance Program (FSAP) to provide our employees with programs that include healthy changes in their diets, nutrition and daily exercise routines so that living healthier becomes a lifestyle change.

The Specific Aims are:

1.To continue to work efficiently and effectively with all of our employees to provide the best service in all aspects of human resources;

2.To build upon our already established, collaborative efforts with Central Human Resources and other departments within Emory and work together to provide enhanced support in the services we provide to our overseas scholars in both legal and equal opportunity initiatives;

3.To work with an outside contractor to continue the English as a Second Language Program at Yerkes. For our international employees who lack the necessary grasp of the English language, this program offers them the opportunity to advance and function productively with their peers and other departments within the institution.

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_5964_HR.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

Ties with the Office of Equity and Inclusion will continue to be strengthened, with collaboration on programs such as Unconscious Bias training for faculty and staff, and encouragement for completion of online programs that address issues such as Bullying in the Workplace, Diversity: Skills for Collab oration, Intersections: Anti-Harassment (Supervisor) and, Intersections: Preventing Discrimination and Harassment (employee).

The English as a Second Language Program continues but with changes that will be beneficial in the long run, such as changing from an 8-week to a 16-week block session; pretests and final tests during each session, and more recently, consideration of a test that would require a score of 80% or higher providing an option to those who score high to opt out of the program.

This office is working with the C&D Committee at Yerkes to draft a Mentor Program plant that will make mentorship opportunities available to employees at Yerkes to assist with career development.

B.2. Accomplishments—Human Resources

The Yerkes Human Resources Office currently staffed with three employees, continues to be the onsite resource office for all Human Resources functions, i.e. recruitment and employment, payroll and compensation, benefits, learning and development, employee relations. In addition, relative to the HR functions, the Human Resources Office interacts with other departments with Emory University– International Student and Scholar Services (for visas and visa related matters), Office of General Counsel (for student and other personnel liability agreements), the Office of Equity and Inclusion for compliance and diversity issues and with the Faculty Staff Assistance Program for wellness and other matters.

Internally, with assistance and input from committee members, the HR office works on Community and Diversity issues. The Yerkes Staff and Wellness Council (combined from what was formerly two separate committees) continue to work with the HR Office to provide social and wellness events and programs through the year, in conjunction with Emory's Wellness Office and its Faculty Staff Assistance Program.

During the past year, the Human Resources Office has continued to endeavor to provide the level of service to all faculty, staff and students as has been done in the past.

In addition to the regular duties and responsibilities, this office worked with Central Human Resources last year on the proposed FLSA changes that were to be implemented closer to the end of 2016. That initiative involved additional time and effort in facilitating the process at the Center, reviewing information regarding eligibility of titles and positions that would be affected by the proposed regulatory changes, etc. The entire process is now on hold pending final decisions subsequent to the injunction issued by a Federal judge in November 2016.

Also of significance is the Engagement Survey that was conducted in June 2016 in collaboration with the Learning and Organizational Development Office at Emory. Team effort with the C&D Committee and the Director's office is ongoing to prioritize and address results of that survey.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5964

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			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						
1	HR Division Director	0.6			4,702.00	1,161.00	5,863.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**5,863.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**5,863.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**5,863.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	5,863.00	2,638.00
		Total Indirect Costs	**2,638.00**

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)	**8,501.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Information Technology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Yerkes Information Technology Department (YITD) promotes a user-centric environment that enables researchers, students, and staff to be more effective in their roles as they work to accomplish the Center's mission in alignment with that of Woodruff Health Sciences Center and the NIH. YITD's primary mission is to apply IT-related principles and practices to assist programs that produce healthcare and industry leaders whose research results in the innovation of human and animal health. The department has spent the last five years improving its enterprise level service offerings, operational capacity, and a framework to best meet that mission. We continue to enhance our capabilities by creating efficiency in the routine core services and freeing up the staff to support the growing interests of our researchers. The IT department has worked over the last four years to address several core operational issues that had critical impact to the Center in areas of administration and research. We are now able to better focus on process improvement and new technologies that will have beneficial impact to specific research programs and administrative workflow. We are working with ONPRC and WaNPRC on models to distribute animal data through federated resources and shared repositories of reporting tools. A partnership is underway with Library Information Technology Services (LITS) to consider expanding data sharing capabilities between universities for LIMS-related services. This is being done in an effort to provide greater clarity on functional requirements, scheduling of deliverables, and consistency in product improvements and changes. The Animal Research Management System (ARMS) and the Electronic Animal Search (EAS) web service were the first application development projects to introduce this methodology. As other Center services are evaluated for enhanced functionality, this model will be implemented. In an effort to facilitate and accelerate the creation of new research services, an evaluation will take place to determine a common set of data elements that can be readily provided to secondary systems. This data offering will also reduce the possibility of error when creating a combined data view for a subject from the secondary system.
The Specific Aims are:
1.To increase YITD staff presence in divisional areas to implement strategic planning processes in an effort to accurately understand the needs and translate them into sustainable IT solutions;

2.To investigate and encourage scalable technologies in informatics and animal resources that will optimize the research endeavors beyond the Center to Emory University and the NPRCs;

3.To implement application development with an Software Development Life Cycle (SDLC) model;

4.To perform an assessment of current research data sources around the Center combined with the data in ARMS for the possibility of a data warehouse.

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_5965_IT.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

1.YITD will work with the Division Chiefs in their areas of specialization to create a job shadow event. The IT staff will participate with lab personnel during daily activities to experience procedures and challenges faced by the lab staff with respect to IT services. These events will also contribute to a holistic view of the Center's research labs for the IT staff, and reveal areas of overlapping IT service needs and gaps. YITD will suggest strategic IT initiatives to the Senior Administration from their findings.
2.The YITD Systems Group will work with their counterparts at WaNRPC to review the ARMS data reporting structure in Business Objects to determine if improvements can be made at both Centers to reports, data retrieval speed, and the possibility of using Oracle Business Intelligence in conjunction with Business Objects based on the same ARMS database schema.
3.RAAC/EAS will be reviewed by YITD and SMEs for continued enhancement in functionality and possible updating of the core Drupal codebase from v6 to v8 using an SDLC model.
4.The database architect in YITD has begun work in the last week to brainstorm with his colleagues and review notes taken over the last year to plan mockups for the data model of the data warehouse based off the ARMS core clinical data. This project is still significantly impacted by the loss of three YITD FTEs over 2016. One desktop position was filled 01/2017. An operations candidate is expected in 03/2017, and the most critical vacant position for the project of the Sr. IT Manager is still open.

B.2. Accomplishments—Information Technology

1. Over the last year, the Yerkes IT Department (YITD) Systems Group conducted quarterly meetings for creating and prioritizing the strategy on the future requirements and development in the Animal Research Management System (ARMS). These meetings included leaders from the divisional areas in Animal Resources, Finance, Grants, and Senior Administration. The Systems Group also started another quarterly meeting specific to the Field Station SMEs in ARMS. These meetings discuss the mission differences between Field Station and Main Center on the strategy applied to the requirements and development in ARMS.

2. YITD has assisted the research efforts of two PI's in establishing LabKey instances to record Zika data and offer those curated data to the Zika LabKey instance at WNPRC for open use to the global community interested in incorporating the information in their studies. One PI's instance has been created and can share the data, and the second PI is in discussions as to how best to offer the service.

3. The Research Animal Allocation Committee application Electronic Animal Search (RAAC/EAS) has been through five of the six stages of SDLC over the last year. A new version of the application will be deployed in the next few weeks. The SME in RAAC/EAS have responded well to this approach of improving the application and have already begun talks to prepare for the next cycle.

4. A preliminary discussion is underway to determine a proper data model for exporting ARMS clinical data and importing lab research data to expand the NHP phenotypes. YITD lost the Sr. IT Manager who acted as PM on this effort, and a candidate search is still underway to find the appropriate hire for this critical role in developing the model.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5965

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			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	IT Director/Sr. Mgr	1.2			12,816.00	3,166.00	15,982.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**15,982.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**15,982.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	4,000.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**4,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**19,982.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	19,982.00	8,992.00
		Total Indirect Costs	**8,992.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**28,974.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Public Affairs

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Yerkes Public Affairs (PA) Office directs the Yerkes Research Center's Public Affairs Unit as well as its Outreach and Community Engagement activities. For the purpose of this P51 Base Grant submission, there will be two related components: this Public Affairs section under the Administration component and a separate Outreach component.

The Yerkes PA Office is responsible for the increasing recognition of Yerkes as a premier research center dedicated to conducting essential basic science and translational research to advance scientific understanding and to improve human health and wellbeing. To achieve this mission, PA works proactively in the multiple, complementary areas of Public Relations and Outreach. Specific activities that fall under Public Affairs are:

•Media Relations
•Issues Management
•Emergency Preparedness (in collaboration with Facilities Management)
•Special Projects as strategically determined and/or requested by the Center Director

For Media Relations, PA develops key messages and documents with background information, promotes published studies and awards via news releases and research video clips, coordinates media interviews and on-site filming, serves as an information resource and trains researchers to speak with media. In the area of Issues Management, PA proactively monitors diverse media sources for issues of concern, such as animal rights, frames these in perspective, develops strategic messages and serves as a spokesperson. To emergency preparedness issues relevant to Public Affairs, PA again monitors public media for issues of concern, works with Emory's Office of Critical Event Preparedness and Response, and serves as a Risk Management Process Owner for the University's Risk Management team for the animal rights risk. Other responsibilities that fall to the PA unit include managing the Center's National Scientific Advisory Board and coordinating fund-raising initiatives.

The Specific Aims are:

1.To maintain a proactive approach to public relations;

2.To continue distributing news releases about published studies, connecting the research whenever possible to improvements in human health and facilitating interviews between researchers and media;

3.To continue monitoring issues of concern and determine how we can strategically share information that presents accurate and balanced information with key audiences.

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_5966_PA.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

During the next year, the Yerkes National Primate Research Center PA Office will continue to be proactive in its public relations, including promoting our research successes via media relations, managing issues, monitoring animal rights and taking on special projects as requested by the Director.

For one such project, Yerkes PA will continue to lead the national public relations efforts on behalf of the seven NPRCs, which will include launching a new public website and conducting a national media relations campaign.

To enhance the information available on the Yerkes website as well as to contribute to an Americans for Medical Progress campaign to share current research photos with the public, Yerkes PA will work with Emory's videographer to produce new video footage (B-roll) of our facilities and animals.

As always, PA staff will also monitoring animal rights activities. With the new branding, we will work with the PR agency to place stories that present a balanced view of research with animals and will look to reach new audiences with our messages.

B.2. Accomplishments—Public Affairs

The Yerkes Public Affairs (PA) Office is responsible for increasing recognition of Yerkes as one of the seven National Primate Research Centers fighting disease and improving human health by making breakthrough discoveries possible. To achieve this, the PA office works in the areas of Media Relations; Issues Management; Emergency Preparedness (in collaboration with Yerkes Facilities Management); and Special Projects as strategically determined by the Center Director. PA staff also works in the area of Outreach and Community Engagement, which is reported in another section within this progress report.

One of the strategic PA projects this year was to lead the collaborative branding effort on behalf of all seven NPRCs. This included providing background information, coordinating a brand excavation session, managing two core review groups (branding and logo), guiding the PR agency in its strategic and tactical activities, and managing the contract, billings and payments. The resulting NPRC vision is “People across generations and the world living longer, healthier lives,” and our new essence is “Discovering Causes, Preventions, Treatments and Cures.”

In addition, PA staff distributed 19 news releases, continued to proactively monitor animal rights activities and other related issues, and coordinated the center’s 2016 National Scientific Advisory Board meeting.

B.6. Plans—Public Affairs (Text entry)

During the next year, the Yerkes National Primate Research Center PA Office will continue to be proactive in its public relations, including promoting our research successes via media relations, managing issues, monitoring animal rights and taking on special projects as requested by the Director.

For one such project, Yerkes PA will continue to lead the national public relations efforts on behalf of the seven NPRCs, which will include launching a new public website and conducting a national media relations campaign.

To enhance the information available on the Yerkes website as well as to contribute to an Americans for Medical Progress campaign to share current research photos with the public, Yerkes PA will work with Emory's videographer to produce new video footage (B-roll) of our facilities and animals.

As always, PA staff will also monitoring animal rights activities. With the new branding, we will work with the PR agency to place stories that present a balanced view of research with animals and will look to reach new audiences with our messages.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5966

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary		EFFORT		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						
1	Sr. Communications Director	0.6			6,844.00	1,690.00	8,534.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**8,534.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**8,534.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**8,534.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	8,534.00	3,840.00
		Total Indirect Costs	**3,840.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**12,374.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Facilities Management

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Facilities Management is responsible for providing and maintaining a safe and efficient physical environment that supports scientific discovery, humane animal care, and productive administrative services. Along with providing operations and maintenance of buildings and grounds, the facilities unit is responsible for security, as well as operating a Main Station shuttle service, daily transportation to/from the Field Station, package delivery and distribution, project management for new construction and major repairs and renovations, and fabrication shop operations. Ongoing and past efforts to improve the physical environment and services provided by Facilities Management have focused on emergency preparedness, lifecycle replacement of the physical plant, and improving finishes and systems in animal housing rooms.

While making improvements in these areas will remain part of the efforts of Facilities Management, specific aims for the next five-year period will include improving customer service, reducing energy consumption and continuing to improve security. Facilities work requests and preventive maintenance tasks are managed by a work order management system implemented by Emory University. Yerkes began using the Emory system in 2013 when a 14-year old work order management system was retired. When fully implemented, the system will contain features that will improve service delivery to our customers. Energy conservation is a second focus of facilities for the next budget period. Past progress in our efforts to consume less energy includes light fixture replacements and installation of high efficiency building equipment when end-of-life replacements occur. In addition to continuing those efforts, focus will include water and natural gas conservation and increased efforts to reduce electricity consumption. Continuing to improve security is the third focus of facilities for the next budget period. Installation of a new high security fence at the Field Station and employing contract security personnel at the Main Station are two recent, significant accomplishments related to security. Increasing the number and quality of video cameras and continuing to raise awareness of security issues among employees are two areas of security enhancement that will be addressed during the next budget period.

The specific aims are:

1.To continually improve service delivery by maximizing the work order and preventive maintenance systems;

2.To research and implement strategies that reduce energy consumption;

3.To sustain ongoing efforts to improve security.

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_5967_FacMgt.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

Plans for the next budget year include continuing efforts to improve security by replacing analog cameras with higher resolution cameras and adding more cameras to exterior locations, continuing efforts to reduce energy consumption by updating existing lighting fixtures, improve emergency preparedness by researching and implementing solutions for emergency water service, and improving service delivery by continuing to leverage the many features of the automated work order system.

B.2. Accomplishments—Facilities Management

Facilities Management provides comprehensive facilities services in support of the Center's central mission of scientific discovery and quality care of nonhuman primates. The team of facilities personnel interacts with every unit of the Yerkes Center and is responsible for providing a safe, efficient physical environment for research and animal husbandry. Services and responsibilities of the facilities department include operations and maintenance of the physical plant, fabrication of research and enrichment devices, transportation services, receiving and distribution of parcels, security, and management of new construction and alterations and renovations. The facilities unit aims to continually improve service delivery, reduce energy consumption, improve security, and improve emergency preparedness.

Significant progress made in 2016 includes:

- Numerous lighting fixtures in animal housing and common spaces were replaced or retrofitted with LED lamps providing significant savings in energy consumption and maintenance.
- Contract security presence was more than doubled and includes staffing the main reception office with a contract security guard.
- Specific Anima lLoca tion were replaced.
- The heat exchanger serving the heating hot water system of Specific Animal Location was replaced providing improved heating to the building at reduced energy consumption.
- Specific Animal Location at the Field Station.
- A new fan coil unit was installed in Specific Animal Location as part of a renovation to house two cell sorters.
- The condensate return pumps serving Specific Anima lLocation steam system were rebuilt providing for a more efficient production of steam.
- The air handler serving the 1st floor of the Main Building was updated to include new control valves, steam traps, piping, pilot positioner, preheat humidification valve and humidity sensor.
- The boiler serving one of the cage rack washers was re-tubed providing more efficient production of steam.
- Several animal housing rooms were recoated with epoxy flooring.
- Extensive site work was performed at the Main Station and Field Station to improve rodent control and erosion control.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5967

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			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						
19	O/M Director, AD, Proj Mgr, Supervisors, and Technicians	21.0			97,233.00	24,017.00	121,250.00
19	**Total Number Other Personnel**					**Total Other Personnel**	**121,250.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**121,250.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**121,250.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	121,250.00	54,563.00
		Total Indirect Costs	**54,563.00**

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)	**175,813.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Facilities Improvement (I/M)

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Facilities Improvement, previously referred to as Improvement and Modernization, is a substantial source of funding for facilities upgrades and improvement and modernization of equipment. Providing a modern, relevant physical environment for housing animals and conducting research is essential in recruiting and maintaining the best and brightest researchers. Facilities Improvement funds are critical to the Center's ability to provide facilities and equipment that are compliant, modern, efficient, and contribute to scientific discovery.

Yerkes experienced continued growth during the current funding period, which included the addition of two significant buildings: Specific Specific Animal Location Growth in physical assets provides opportunities for new programs. Facilities Improvement funds are used to ensure the relevance and efficiency of existing infrastructure and the availability of modern equipment to support ongoing programs as well as those in their nascent stage.

The list of proposed equipment and projects represents a set of needs that have been determined to be our priority areas for the achievement of the Center's mission during the proposed funding period. They represent three general categories. The first is a focus on enhancing and modernizing security systems. The second is providing a humane and enriching environment for our research animals. The third is a focus on providing modern and efficient equipment for building systems, diagnostic laboratories, clinical services, and information technology.

The Specific Aims are:

1.To continually improve security infrastructure;

2.To provide the most humane and enriching environment for research animals;

3.To maintain modern and efficient building and research equipment.

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_5968_IM.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

NOTHING TO REPORT

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

NOTHING TO REPORT

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

Continued improvement in infrastructure is planned for the next budget year with Improvement and Modernization funds. Planned equipment and projects represent our ongoing commitment to providing facilities that are modern and efficient and allow the Center to recruit and retain the brightest and most talented researchers. Providing a humane and compliant environment for our research animals is vital to our continued success and is demonstrated by the planned projects for the upcoming budget year.

B.2. Accomplishments—Facilities Improvement (I/M)

Improvement and Modernization provides vital funds for maintaining a modern and efficient infrastructure in support of the Center's mission of scientific discovery and health and well-being of primates and nonhuman primates. Projects and equipment funded by Improvement and Modernization funds aim to continually improve security infrastructure, provide the most humane and enriching environment for research animals, and maintain modern and efficient building and research equipment. Significant progress in achieving these aims has been accomplished in this budget year with the equipment purchased and projects completed. Please see section E.3 of the Overall component for a list of major infrastructure improvements made during the current budget period.

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-5968

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EF FORT			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*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description

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

Equipment Item	Funds Requested ($)*
1. FS Shower Locker trailer (equipment only)	153,100.00
2. D-Wing Style replacement Cage Racks (14 racks of 4 cages)	151,550.00
3. Replacement Siemens Panel	94,620.00
4. ARMS Legacy Hardware	57,342.00
5. 4 8.0 Cage Racks (for Field Station)	39,000.00
6. Lavoratory Vacuum system replacement in VRC	36,634.00
7. Enrichment Trailer replacement	31,200.00
8. Forklift (MS-Animal Care)	24,632.00
9. Engine Driven Welder (FS Shop)	11,922.00
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**600,000.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**600,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	0.00	0.00
		Total Indirect Costs	**0.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**600,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Asc. Dir. for Animal Resources

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

Excluded by Requester

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

The Associate Director for Animal Resources (ADAR) Excluded by Requester provides centralized administration for the Division of Animal Resources including the Center's Animal Cores and other animal-based resources. The ADAR reports directly to the Center Director and works closely with him to ensure that Center priorities are met. She liaises with the Associate Directors for Scientific Programs and Pathology, as well as Finance and Research Administration in providing high quality resource management and service. The ADAR is responsible for regulatory compliance and manages the Center's reporting for USDA, OLAW, AAALAC and other regulatory agencies. She takes a leadership role in projecting Yerkes' future animal and facility needs, including identification of funding sources and preparation of resource grant proposals. She guides the Division's independent and collaborative research priorities. The mission of this office is to ensure that the Division of Animal Resources provides the highest standards of care for all colony animals, and that these standards are maintained throughout the Center. The ADAR must work closely with other NPRCs to ensure the best management, care and use of all nonhuman primate resources and actively participates in NPRC consortia activities. [redacted] monitors Yerkes' Animal Care and Use Programs and Facilities Management to ensure regulatory compliance (USDA, OLAW, IACUC, AAALAC and USFWS). She is a member of the Emory University IACUC and serves as Yerkes Attending Veterinarian and IACUC Executive Committee member. The ADAR chairs the Yerkes Resource Allocation and Advisory Committee (RAAC) and helps project animal assignment needs working closely with the investigators to facilitate research. The ADAR liaises closely with the Yerkes Director, the Vice President for Research Administration and appointed Institutional Official for Yerkes as well as the IACUC on animal welfare and compliance issues. The future priorities and plans for the ADAR and the Division of Animal Resources will build upon the successes of the last five years focusing on the continued refinement and expansion of the Division's research support for internal and external investigators and the expansion of our collaborative and independent research activities. As a Division, it will continue to build its growing clinical research program while encouraging its clinicians and other divisional scientists to pursue clinical and collaborative research opportunities. The Division's members expect to become increasingly active research partners through their service oriented work and, to this end, one of the major priorities will be continuing the genetic and phenotypic definition of our nonhuman primate colonies in order to offer superior animal models to the research community.

The Specific Aims are:

1.To ensure animal welfare and regulatory compliance by managing all of the units in the division including; Veterinary Medicine, Animal Care, Behavioral Management, Research Services, Colony Management, Animal Records and Environmental Health and Safety Office for both the Main Station and the Field Station;

2.To facilitate research and collaboration between investigators and Animal Resource units and advance the scientific mission of the Center in concert with developing the careers of staff in the units;

3.To work closely with other internal divisions including Information Technology, Facilities Management, Public Affairs and Business Services as well as external divisions including IACUC, Office of Research Compliance, and the School of Medicine's (SOM) Division of Animal Resources to ensure communication and a global strategy for the Center.

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_5969_ADAR.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Associate Director of Animal Resources

During the last reporting period, Yerkes successfully completed an AAALAC accreditation visit with an on site visit in February 2017. The site visitors will be recommending full continued accreditation with two minor suggestions for improvement that have already been addressed. The ADAR in collaboration with Colony Management, the Virology Core and the Genetics Core recently submitted a renewal of the U42 SPF grant to support the SPF colony at Yerkes. The ADAR has worked closely with the IACUC office in implementing a new IACUC management software program and development of a new protocol submission form.

The ADAR was invited to give presentations at the American College of Laboratory Animal Medicine (ACLAM) Forum and the Association of Primate Veterinarians (APV) meetings during the last reporting period. The ACLAM presentation was part of a session on veterinarians writing infrastructure grants and focused on previous successful G20 and C06 submissions. The APV presentation was an overview of the Zika research currently being done at Yerkes as part of a special topic seminar on Zika virus. In addition, the ADAR assisted with a presentation at AAALAS on the automated feeders at the Field Station.

In Preparation

Presentations

1. Developing a "Sexy" Infrastructure Grant. Presentation at American College of Laboratory Animal Medicine Forum. St. Petersburg, FI. 2016

2. Nonhuman Primate Models of Zika Virus. Presentation at Association of Primate Veterinarians (APV). Charlotte, North Carolina. 2016

3. Excluded by Requester
   Challenges and Successes of Implementing Automated Feeders in an Outdoor Nonhuman Primate Facility. American Association of Laboratory Animal Science 67th National Meeting, Charlotte, NC, November 2016. ORAL PRESENTATION.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00
2.						Asst Dir, Animal Resources					7,134.00	1,762.00	8,896.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **20,437.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	1.2			5,128.00	1,267.00	6,395.00
1	Training Coordinator	2.4			13,120.00	3,241.00	16,361.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**22,756.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**43,193.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**45,193.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	45,193.00	20,337.00
		Total Indirect Costs	**20,337.00**

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)	**65,530.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Veterinary Medicine

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Veterinary Medicine Unit provides preventive medicine and clinical care for nonhuman primate colonies at the Main Station and Field Station, as well as management of the rodent sentinel program and treatment of clinical cases of rodents at the Main Station. In collaboration with investigators and the Research Resources Unit, the veterinary unit continues to provide research support by performing experimental interventions and imaging procedures. With continued collaboration of Field Station research and support units on the Colony Management Committee run by the Lead Veterinarian, colony breeding and management issues are addressed. Additional support and guidance are provided to investigators during the process of veterinary consultations when IACUC proposals or modifications are submitted for review. Throughout the conduct of all tasks and procedures, the unit continues to train two veterinary residents and one veterinary fellow each year to better prepare the next class of laboratory animal veterinarians. Additional involvement in research programs for veterinarians will continue as will faculty development by alternating memberships to key Emory and Yerkes committees and through faculty appointments in the Emory School of Medicine. Training programs for residents and fellows will continue to grow, as will all research and support personnel training programs.

The mission of the Veterinary Medicine Unit is to ensure the health and wellbeing of the animals in compliance with IACUC approval and in compliance with regulatory agencies including USDA, PHS, and US Fish and Wildlife Service. Members of the unit work closely with the Emory Institutional Animal Care and Use Committee, either as a member or consultant, as well as with all units within the Division of Animal Resources at Yerkes, Yerkes Facilities Management, the Yerkes Resource Allocation and Advisory Committee, administrative offices at Yerkes, and representatives of all research units at Yerkes. With the increased requirement for training of research personnel as mandated by the eighth edition of the Guide For the Care and Use of Laboratory Animals, the Veterinary Medicine Unit participates in this training and documentation as well as training veterinary residents and fellows to work in the field of laboratory medicine. The veterinarians provide consultation and support not only to investigators at Yerkes but also to outside investigators/veterinarians.

These Specific Aims are:

1.To monitor and support the health and well-being of all nonhuman primate (and rodent) colonies at Yerkes as the research portfolio develops and expands. The expansion will include development of special training and procedures for the new Biosafety Level 3 nonhuman primate facility;

2.To provide evidence-based preventive care and veterinary care to the NHP breeding colonies through annual physical examinations, reproductive health monitoring, and weight management protocols. In support of these endeavors, the veterinary unit will work closely with IT personnel to maximize the clinical utilization of Animal Research Management System (ARMS);

3.To collaborate with investigators in the fields of infectious disease, transplant medicine, reproductive medicine, and neuroscience in tandem with research support. Additionally, to enable veterinarians to serve as co-investigators and co-principal investigators for NIH-sponsored grants and obtain faculty appointments within the Emory University School of Medicine;

4.To serve as a resource for the education and training of pre- and post-graduate veterinarians and veterinary technicians in the field of laboratory animal medicine.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B2_5970_VetMed.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Veterinary Medicine

Colony Accomplishments

The Veterinary Medicine unit is responsible for reviewing all medical records for nonhuman primates entering the Yerkes colony for assignment to multiple infectious disease, transplant and neuroscience protocols. During the 2016-2017 reporting year, the veterinary staff assisted in evaluating and quarantining all nonhuman primates entering the colony from other facilities. Sixteen cynomolgus macaques entered the colony on two separate shipment dates as specified by the research needs of the investigator. Another 123 Rhesus macaques entered quarantine from a total of four different facilities in order to attempt to fulfill nonhuman primate requests for numerous IACUC approved projects. Rhesus macaques also transfer from the Field Station to the Main Station facilities on an ongoing basis in order to try to meet investigator requests.

Research Accomplishments

Project 1: The Veterinary Department collaborates with many Yerkes investigators to facilitate animal research with nonhuman primates. Specifically, the vet staff has worked closely with Excluded by Requester research laboratory to develop and refine the use of fine needle aspiration (FNA) of peripheral lymphoid tissue. Lymph node FNA allows for longitudinal evaluation of the immune response in the context of vaccine immunology studies and SIV infection in rhesus macaques. This procedure also presents an opportunity to evaluate cell subsets directly from the lymph node that are not represented in the peripheral blood. The continued collaboration between the veterinarians and the investigators has led to this procedure being successfully implemented in a number of different study protocols and has resulted in a publication in Cell Reports. Additionally, the information about this refinement technique and the knowledge gained from this collaboration has led to presentations at several conferences, including the 2016 American Association of Laboratory Animal Science National Meeting, the 2016 T Follicular Helper Cells and Germinal Centers Keystone Symposia, the 2016 HIV Vaccine Keystone Symposia, and the 2017 Comparative Medicine Seminar.

Project 2: Bacterial vaginosis (BV) has been associated with vaginal inflammation and enhanced HIV transmission in women. We have observed in previous studies that most rhesus macaques (RMs) exhibit a vaginal flora that is comparable to human BV with few lactobacilli. Submitted

Submitted

Project 3: There are several indications in nonhuman primate (NHP) medicine and research for the use of hand-held, point-of-care glucometers. Veterinary specific glucometers were recently developed for companion animals, but it is currently unknown whether human or veterinary glucometers are more appropriate for use in NHPs. Glucometers measure glucose in whole blood, but perform a calculation to estimate and report the plasma glucose level. The distribution of glucose between plasma and red blood cells varies species to species. Based on these differences, veterinary glucometers utilize the same technology as human glucometers, but apply a species-specific algorithm to estimate plasma glucose. Human studies have shown that several other factors can affect glucometer measurement including hematocrit (HCT), glycemic state and collection site. The primary aims of this study were: 1) to compare the accuracy of 2 veterinary and 2 human glucometers in 2 NHP species with naturally different HCT ranges (rhesus macaques and sooty mangabeys); 2) to determine the accuracy of 2 human glucometers during hypoglycemia and hyperglycemia; and 3) to compare glucometer performance between capillary and venous sampling sites.

Project 4: This project seeks to determine whether feeding data generated by computer-controlled automated feeding stations can be used to enhance the clinical monitoring of rhesus macaques living in large outdoor breeding groups. As animals obtain food pellets, the computer-controlled system records grams obtained in real-time by detecting RFID microchips implanted subcutaneously in each wrist of individual animals. The primary outcomes of this study include: 1) quantification of daily caloric intake according to sex, gender, and reproductive stage; 2) the association of various clinical conditions (e.g. trauma, diarrhea, retained placentas)

with a significant reduction in caloric intake; 3) association of select breeding and social behaviors with changes in caloric intake.

Project 5: This project seeks to evaluate how chronic stress may negatively affect anti-tetanus immunity among breeding female rhesus macaques (*Macaca mulatta*) and their offspring. Using rhesus macaques in large breeding troops at Yerkes National Primate Research Center (NPRC) Field Station, the aim of the current project is to determine whether and to what extent social subordination impairs the durability and prenatal transfer of anti-tetanus immunity in breeding female rhesus macaques.

Presentations

Excluded by Requester

Challenges and Successes of Implementing Automated Feeders in an Outdoor Nonhuman Primate Facility. American Association of Laboratory Animal Science 67th National Meeting, Charlotte, NC, November 2016. ORAL PRESENTATION.

Excluded by Requester A Comparison of Two Disinfectants in the Sanitation of Monkey Automated Feeders Using ATPase-based Microbiological Methods. Emory University SURE Research Symposium. August 2016. POSTER.

Publications

Excluded by Requester

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5970

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			27,765.00	6,858.00	34,623.00
2.						Associate Veterinarian					26,835.00	6,628.00	33,463.00
3.						Asst Dir, Animal Resources					21,403.00	5,287.00	26,690.00
4.						Associate Veterinarian					12,124.00	2,995.00	15,119.00
5.						Associate Veterinarian					23,985.00	5,924.00	29,909.00
6.						Associate Veterinarian					24,829.00	6,133.00	30,962.00
7.						Associate Veterinarian					11,543.00	2,851.00	14,394.00
8.						Associate Veterinarian					28,353.00	7,003.00	35,356.00
9.						Associate Veterinarian					20,670.00	5,105.00	25,775.00
10						Associate Veterinarian					20,167.00	4,981.00	25,148.00
11						Chief Veterinarian					32,890.00	8,124.00	41,014.00
12						Associate Veterinarian					22,181.00	5,479.00	27,660.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **340,113.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			2,538.00	627.00	3,165.00

16	Assist Surgery Specialist, Supervisor, Technicians	88.8	325,599.00	80,423.00		406,022.00
17	**Total Number Other Personnel**			**Total Other Personnel**		**409,187.00**
				Total Salary, Wages and Fringe Benefits (A+B)		**749,300.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	53,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Drugs	67,000.00
9. Other clinical supplies	20,000.00
10. Maintenance/repair	2,000.00
Total Other Direct Costs	**142,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**893,300.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	893,300.00	401,985.00
		Total Indirect Costs	**401,985.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**1,295,285.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Animal Care

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Animal Care Unit provides husbandry and care services for the animal colony, as well as assistance to Veterinary, Colony Management, Behavioral and Research units. These groups work together in a well-coordinated, cohesive effort to provide quality animal care. This care and management program meets and often exceeds animal welfare standards and regulations while attaining colony management and research objectives. The goals will be to increase the effectiveness and efficiency of these efforts. The mission of the Animal Care Unit is to provide for the daily care of the animals including husbandry, observing, documenting, reporting, and monitoring the general health and wellbeing, and social stability of the groups and individual animals. Another goal is for Animal Care staff to effectively and proactively communicate abnormal findings to Veterinary, Colony Management, and Behavioral Management staff for further observation and treatment. This work is critical to the overall mission of the Center. An increased focus on training of animal care staff is clearly beneficial and an important priority. As animal welfare is continually being improved with emphasis on increased socialization efforts, enrichment modifications and facility renovations for enhancing welfare, animal care staff must adapt to accomplishing their husbandry procedures with the changes in environment. Animal care staff enthusiastically supports changes for improved animal welfare and continually modify practices to meet growth and changes. Lastly, the Animal Care Unit supports the Center's educational and public outreach efforts. There are opportunities for students to gain insights and experience into laboratory animal care and facility management. Animal care technicians also provide assistance during tours and interact with neighbors during Open House events.

The Specific Aims are:

1.To continue to attain the highest standards of animal care and animal welfare as demonstrated by successful institutional and regulatory reviews and inspections;

2.To invest in educational and training resources, as well as in professional training and development opportunities for the care staff. These investments include participation through membership in national and local laboratory animal professional organizations, and through training available at the AALAS Learning Library, as well as continued and ongoing involvement with a departmental cross training program and in a behavioral management certification program. All of these programs are extremely important aspects of animal care technician training and to developing a streamlined approach to colony care and management;

3.To ensure that the care technicians have the knowledge and experience to assist with a variety of techniques and procedures that improve the health and wellbeing of the animals, thus increasing efficiency overall, integrating care technicians seamlessly in assisting Veterinary, Colony Management Research units. Select staff members at the Main Station will be trained to work in the Animal Biosafety Level 3 (ABSL3) nonhuman primate facility in order to provide highly specialized animal care support when animals are assigned to that facility;

4.To continue to monitor and enhance the security and safety of the facilities in part by continuing to receive training in disaster and emergency preparedness through participation in disaster drills and preparedness assessments.

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_5971_AC.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Animal Care

Please See Associate Director for Animal Resources component for overall accomplishment for the Division of Animal Resources.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			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						
2	Secretarial/Clerical	1.2			3,746.00	925.00	4,671.00
99	Managers (5), Supervisors (8), Technicians (86)	518.4			1,469,285.00	362,914.00	1,832,199.00
101	**Total Number Other Personnel**					**Total Other Personnel**	**1,836,870.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**1,836,870.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	300,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. NHP Bedding Supplies	50,000.00
9. Cleaning/Maintenance	86,000.00
10. Other Supplies	37,019.00
Total Other Direct Costs	**473,019.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**2,311,889.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	2,311,889.00	1,040,350.00
		Total Indirect Costs	**1,040,350.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**3,352,239.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Colony Management

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The mission of the Colony Management Unit, based at the Yerkes Field Station, is to oversee the nonhuman primate colonies in order to meet the Yerkes Center management, production and scientific needs. These responsibilities include the implementation of a colony management plan that matches resources with projected colony and research needs, ongoing genetic characterization/pedigree analysis, development and implementation of breeding plans, acquisition and disposition of animals and animal housing allocation. The Colony Management unit is charged with working closely with the Veterinary Unit, Animal Care, Research Services and the investigators to provide defined experimental animals and biological samples.

The Colony Management Unit participates in annual health surveys and quarantine procedures, reporting and tracking births, animal accessibility training, sample collection for genetic testing, viral screening and pre-screening for research protocols, contraception and immunization administration, tattooing and microchip insertion and the development of housing allocation plans to meet breeding and research needs. The group oversees the specific pathogen free (SPF) rhesus breeding program. Colony management personnel are responsible for observation and charting the complex social dynamics that exist within each social group, through both opportunistic and formal observations of behavioral interactions within the social setting and recording and plotting these data to obtain hierarchical order. This information is essential to help maintain social group stability, the formation of new groups and the introduction of animals, including breeding aged males.

The Specific Aims are:

1.To manage the established SPF breeding colony of rhesus macaques to meet the needs of researchers and maximize genetic variability of the population, as well as the continuation of collecting genetic information on parentage and phenotypes;

2.To maintain the sooty mangabey population, a natural SIV host species, with substantial value in studies aimed at the prevention and treatment of AIDS. This includes the oversight of the Breeding Plan that has been adapted to facilitate the formation of new breeding groups to maintain population growth and genetic diversity in this closed population;

3.To implement and utilize a database for enhanced access to and manipulation of genetic information;

4.To foster personnel education and training programs;

5.To publish data on primate colony management.

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_5972_ColMgt.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Colony Management

Over the last reporting period, representatives from the Colony Management Unit participated at several conferences and presented papers and posters on multiple topics. At the American Society of Primatologists, (Chicago, IL. August 2016), we presented a talk on patterns of trauma in the rhesus macaque SPF breeding colony and how rates of trauma were influenced by season and group composition. A poster on male introductions presented data on the influence of sex skin coloration and relationship between breeder males affected the success of male introductions to different social housing situations. The second poster presented data on the clinical implications of relocating rhesus macaques and the time it took for those animals to acclimate to a new environment. At the annual Southeastern branch of the American Association for Laboratory Animal Science, (Decatur, GA. March 2017), Colony Management technicians presented a talk on how to manage the clinical care of our rhesus macaque colony. Specifically, information on how to provide treatments to animals living in their social groups was discussed.

Presentations:
Conference paper: Trauma patterns in specific pathogen (SPF) Rhesus Macaque (*Macaca mulatta*) groups. Excluded by Requester American Society of Primatologists Annual Meeting, Chicago, IL. 2016

Poster: Sex skin color and male affiliative bonds facilitate the introduction of males into breeding groups of Rhesus Macaques (*Macaca mulatta*). Excluded by Requester Excluded by Requester American Society of Primatologists Annual Meeting, Chicago, IL. 2016

Poster: Clinical impacts on Rhesus Macaque (*Macaca mulatta*) social groups following relocation to a novel environment. Excluded by Requester American Society of Primatologists Annual Meeting, Chicago, IL. 2016

Management of clinical conditions in socially housed primates. Excluded by Requester SEAALAS Annual Meeting, Decatur, GA. 2017

Two abstracts were submitted for consideration to the American Society of Primatologists Annual Meeting (Washington, DC. 2017) with the first focused on how duration of breeding male residence in a social group can affect overall rates of trauma in those groups and the second focused on the methods used to form the multi-male bachelor groups that eventually are used as breeding males in the rhesus macaque colonies.

Submitted Abstracts

Submitted

Manuscripts in Preparation

In Preparation

In Preparation

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5972

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutiona Base Salary		FEORT		0.00	0.00	0.00
2.						Colony Director					18,307.00	4,522.00	22,829.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **22,829.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
13	Manager, Supervisor, Technicians	65.4			233,845.00	57,759.00	291,604.00
13	**Total Number Other Personnel**					**Total Other Personnel**	**291,604.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**314,433.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	22,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Per Diem	363,683.00
9. Maintenance/repair	1,000.00
10. Other supplies	2,000.00
Total Other Direct Costs	**388,683.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**705,116.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	705,116.00	317,302.00
		Total Indirect Costs	**317,302.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**1,022,418.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Behavioral Management

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The mission of the Behavioral Management Unit is to promote, maintain and measure primate wellbeing through collaboration among the Behavioral Management, Veterinary Medicine, Animal Care, and Research units. The Behavioral Management program includes daily implementation of animal welfare activities, the conduct of scientific investigation to advance knowledge, and responsibilities for regulatory aspects of primate welfare. Major elements of the daily program include: socialization of primates, providing environmental enrichment, applying animal training methods, and assessing behavior. Social housing throughout the lifespan of primates is the primary method to support their welfare and is the cornerstone of our mission. Enrichment methods emphasize feeding enrichment (devices, fresh produce), physical enrichment (objects, climbing structures, release into activity cages), and sensory enrichment (music, videotape viewing). A positive reinforcement animal training program facilitates animal care, research and veterinary care by reducing distress associated with common procedures, and increasing the ease of working with primates. Behavioral monitoring is done according to a defined schedule to identify behaviors of concern and to track outcomes of treatments implemented to address particular problems. Animals exhibiting psychological distress may be treated through an amplification of enrichment, training, adjustment of social dynamics, and pharmacological means, and additional behavioral monitoring is performed on these animals. The Behavioral Management program is dynamic and techniques are modified in accordance with in-house assessments and findings from the scientific literature. Behavioral research on a variety of topics is ongoing and this research contributes to the Center's strong scientific foundation that underlies improvements in primate behavioral management. Recent published studies relate to pair housing, abnormal behavior, animal training, and enrichment. Regulatory responsibilities of the Behavioral Management Unit include a review of welfare issues for each Yerkes research protocol using nonhuman primates as part of the Institutional Animal Care and Use Committee (IACUC) process. The Unit also addresses issues related to USDA and OLAW oversight, IACUC inspections, and the AAALAC accreditation process. Behavioral Management is continually striving to raise the bar for animal welfare with novel enrichment strategies, improved behavioral assessments and plans to increase socialization opportunities. Development of new strategies may require additional resources such as enrichment supplies, novel caging, new housing, and additional staff. Improvements to the program can be accomplished by staying active in the welfare science field, by frequent re-evaluation of the program to increase its efficiency, by development of enhanced record keeping systems within ARMS, by emphasizing the prevention of behavioral problems, and by seeking grant opportunities to explore behavioral issues in the colony.

The Specific Aims are:

1.To expand the daily social housing, environmental enrichment, and positive reinforcement training programs at the Yerkes Main Station and the Field Station, and improve these activities based on new research findings;

2.To enhance behavioral management education programs within and outside of Yerkes to teach others about integrating behavioral management principles into primate care programs;

3.To improve our behavioral monitoring program through enhanced automation of data collection and compilation, formal evaluation of the program, use of data for internal evaluations, and scientific assessments for publication;

4.To conduct and publish research on primate welfare to improve animal care and wellbeing;

5.To remain engaged in regulatory aspects of Behavioral Management and involved with the Behavioral Management Consortium to advance collaboration and exchange of information across NPRCs;
6.To enhance Behavioral Management staff development.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B2_5973_BMU.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit.

Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Behavioral Management

Research Completed by the Behavioral Management Unit (April 1, 2016 - March 31, 2017)

Behavioral research conducted by Behavioral Management Unit (BMU) staff members led to papers on mangabeys and rhesus macaques, in addition to some publications that are more generally about the behavioral management of laboratory primates. Excluded by Requester documented the behavioral effects of an enhanced enrichment program implemented for run-housed sooty mangabeys. The addition of a variety of types of enrichment led to species-appropriate increases in feeding/foraging and manipulation of items, and decreases in self-grooming, social affiliation, and aggression (the latter marginally significantly), while locomotion and abnormal behavior were unchanged. Since species differences in responses to enrichment can be pronounced, it is important to find effective enrichment strategies for each species housed in biomedical facilities to successfully support their psychological well-being. A review paper was published which focused on pair housing of macaques and describes partner selection factors, introduction techniques, monitoring monkeys for compatibility, and methods to employ to facilitate the long-term maintenance of pairs Excluded by Requester Excluded by Requester This review included information based on published literature, data from our Yerkes behavior records, and practical advice based on our extensive experience with forming and maintaining pairs of macaques. This paper was invited as part of a special issue of the *American Journal of Primatology* which focused on the welfare of laboratory primates. Another manuscript invited to the same special issue describes how the principles and methodologies commonly used by Applied Behavior Analysts in human clinical settings might be applied by primatologists to develop more effective ways to analyze, reduce and prevent abnormal behaviors in nonhuman primates Excluded by Requester A final manuscript was a statement by the American Society of Primatologists, the Association of Primate Veterinarians, and the American College of Laboratory Animal Medicine to propose the term "functionally appropriate nonhuman primate environments" as a more suitable descriptor and as an alternative to the previously used term, "ethologically appropriate environments" to describe environments that are suitable for nonhuman primates involved in biomedical research Excluded by Requester Excluded by Requester

Three book chapters were prepared this year by BMU staff and are currently in press. In Press In Press

Educational Programs by the Behavioral Management Unit (April 1, 2016 - March 31, 2017)

The BMU continues to work on programs to educate others at the Yerkes Center about primate behavior, as well as teaching people from outside of Yerkes. We have continued with our "Behavioral Management Certification Course" for Yerkes Animal Care staff members, which is aimed to expand their understanding of primate behavior, enrichment, animal training, social housing and animal welfare by completing modules in each of these topics. For each one of these modules, BMU staff members teach one-hour sessions weekly, for eight weeks. Information is presented through lecture, discussion, demonstrations, and group exercises which may include hands on skill development. Tests are given following each section. Upon passing, individual module certifications are earned for each topic of instruction. Once all areas are completed, a "Behavioral Management Certification" will be earned.

To date, 82 Animal Care staff members have completed the primate behavior module (8 hours of information on the natural and captive behavior of common laboratory primate species, etc.). This helps to satisfy *The*

Guide recommendation (page 53) that, “Personnel responsible for animal care and husbandry should receive training in the behavioral biology of the species they work with to appropriately monitor the effects of enrichment as well as identify the development of adverse or abnormal behaviors.” In the last year, 15 Animal Care staff members completed the enrichment module (8 hours of information on the five categories of enrichment, why it is important to use a variety of types of enrichment, the role of Animal Care staff members in the environmental enrichment program, etc.).

The BMU has also designed and taught three workshops during this time period. The “Workshop on Macaque Pair Housing” was a four-day course offered at Yerkes in May, 2016, for the first time, with participants from across the country representing other NPRCs, federal agencies, universities, and research hospitals. At the national AALAS conference (November, 2016), the BMU taught an 8-hour workshop on “Teaching Monkeys to Cooperate with Restraint: Using Positive Reinforcement Training and Temperament Testing Methods” which focused on teaching research staff members techniques for minimizing monkey stress associated with restraint. In December, 2016, the BMU provided four days of instruction on “Behavioral Management of Laboratory Primates” at the Shanghai Laboratory Animal Science Association Conference and at the Shanghai Innostar Bio-technology Company in Shanghai, China.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00
2.						Behavioral Management Head					26,177.00	6,466.00	32,643.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **32,643.00**

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						
10	Manager, Supervisor, Technicians	56.4			218,441.00	53,955.00	272,396.00
10	**Total Number Other Personnel**					**Total Other Personnel**	**272,396.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**305,039.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	30,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Foraging Devices/destructibles	10,000.00
9. Socialization panels	5,000.00
10. other supplies	5,000.00
Total Other Direct Costs	**50,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**357,039.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	357,039.00	160,668.00
		Total Indirect Costs	**160,668.00**

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)	**517,707.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Animal Records

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Animal Records Unit is responsible for the entry and maintenance of data documenting clinical, research, and regulatory records for all animals at the Yerkes Center. The mission of the Animal Records Unit is primarily to ensure the accuracy, reliability and sustainability of animal records. The information maintained includes animal history, research assignment history, colony statistics and laboratory data including select genetic profiles. Accurate animal inventory and population is a priority, and the information is maintained so as to be current and readily available to personnel. Information concerning animal assignments to research projects is maintained along with relevant Institutional Animal Care and Use Committee (IACUC) information to ensure compliance with regulatory agencies and Center policies. The recently implemented Animal Research Management System (ARMS) maintains a comprehensive animal medical record and research history with enhanced tracking and capability of performing searches. Since the fall 2013 implementation of ARMS, record keeping is an evolving process that requires the Animal Records Supervisor to liaise with other departments such as Information Technology (IT), Veterinary Medicine, Business Services, Behavioral Management, Colony Management, and Pathology, to address necessary enhancements to maintain reliability, integrity and improve efficiency. Pertinent record information is provided as required for reporting purposes to regulatory agencies such as AAALAC, USDA, USFWS and OLAW. Personnel from the unit also prepare detailed reports as needed by the Animal Resources Division, IACUC and upon request by Center personnel or by outside investigators. The information maintained in ARMS is essential for veterinary, husbandry and behavioral management of the colony and to ensure compliance with animal welfare regulations. In addition, the information contained in ARMS is critical for investigators to maintain the integrity of the research and regulatory compliance. The unit works closely with IT to develop, implement, and utilize valuable applications in an electronic environment that is conducive to sustaining operations. Quality data input is critical for reporting to USDA, AAALAC, OLAW, and other regulatory agencies. The future priorities and plans for the Animal Records Unit focus on continued utilization of ARMS. We will continue to work with IT to enhance methods for data entry. The format of information input into ARMS is designed for optimal retrieval of information in search functions. This searchable format of information is greatly beneficial for tracking and managing data and useful for all divisions. The transition to this format has required the staff to evaluate ways to streamline data input. Animal Records and IT are developing innovative solutions to address this challenge and improve efficiency. In addition to ARMS, the IACUC Topaz software will be upgrading to Elements, which will provide easier access to IACUC data in Animal Records. The unit will continue to work closely with the IACUC Office, Topaz Enterprises and Emory's School of Medicine's (SOM) Division of Animal Resources to implement this new system.

The Specific Aims are:

1.To continue to maintain an accurate record keeping system in ARMS to provide data that both facilitate daily operations and research at the Center as well as track pertinent information to maintain compliance with regulatory agencies;

2.To work closely with IT to develop innovative applications to more efficiently input information into ARMS. Real-time information is critical to the management of the colony;

3.To develop systems that allow the most up to date entry of information into ARMS, including working closely with the Research Allocation and Advisory Committee (RAAC) to maintain accurate information for animal assignments as well as participating in the upgrade process for Topaz Elements and ensuring compliance with all regulations.

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_5974_AnimalRecords.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Animal Records

Please See Associate Director for Animal Resources component for overall accomplishment for the Division of Animal Resources.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Supervisor, Records Support Staff	6.0			22,118.00	5,464.00	27,582.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**27,582.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**27,582.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**29,582.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	29,582.00	13,312.00
		Total Indirect Costs	**13,312.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**42,894.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Research Services

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Research Services Unit provides support for funded research studies through performing experimental interventions on behalf of investigators and facilitating the development of Scientific Advisory Committee (SAC) approved research proposals. A primary goal is to streamline the research process from outline to implementation for Core and Affiliate Investigators by providing a necessary service to researchers, which consists of well-trained personnel who perform the procedures to conduct research and move scientific knowledge forward. Research Services also ensures that compliance with Institutional Animal Care and Use Committee (IACUC) approved protocols is maintained. In order to fulfill these functions, the Research Services Unit liaises with Veterinary Medicine, Colony Management, Business Services and the investigators. The mission of Research Services is to provide administrative assistance as well as implementation of IACUC approved research proposals. Administrative assistance may include consultation to determine the details of project design, scheduling, budgeting, and providing assistance with protocol submissions to IACUC. This unit also coordinates the collection and delivery of specimens from colony animals in response to requests received through the Division of Pathology's Specimen Distribution Program. Research Services personnel provide a range of services and implement experimental interventions on behalf of investigators including: administration of vaccines, antiretroviral treatments and infectious agents by multiple routes; collection of biological specimens such as blood, bone marrow, CSF, and tissue biopsies; monitoring animals during minor experimental procedures; and assisting Veterinary Medicine with minor surgeries and other experimental interventions. All requested procedural interventions are referenced against the approved IACUC for that study to ensure regulatory compliance. As the research portfolio at Yerkes continues to grow, Research Services will continue to identify methods to improve efficiencies in order to maintain support for research. Lastly, Research Services will continue to expand the educational opportunities for personnel and build engagement and collaboration between staff and researchers.

The Specific Aims are:

1.To continue to provide excellent service to researchers and manage any increase in research support that is provided to internal and external investigators as Yerkes research programs continue to expand;

2.To continue close collaboration and training with Veterinary Medicine and investigators in anticipation of the need for more sophisticated procedures and to improve clinical observational skills and increase the services the unit can provide independently;

3.To continue ongoing efforts to foster communication and collaboration directly with investigators and increase the dissemination of knowledge about their research projects.

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_5975_ResSvs.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Research Services

Please See Associate Director for Animal Resources component for overall accomplishment for the Division of Animal Resources.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5975

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			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						
9	Manager, Coordinator, Supervisor, Technicians	21.6			87,924.00	21,717.00	109,641.00
9	**Total Number Other Personnel**					**Total Other Personnel**	**109,641.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**109,641.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	20,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**20,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**131,641.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	131,641.00	59,238.00
		Total Indirect Costs	**59,238.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**190,879.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Env. Health and Safety

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The mission of the Yerkes Environmental Health and Safety Office (Yerkes EHSO) is to provide oversight for the occupational health and safety programs at the Center. The primary goals of the Yerkes EHSO include creating a work environment that minimizes hazards, that reduces the risk of human illness and injury, provides comprehensive programs that support health and safety, promotes a culture of safety and accountability and assures compliance with local, state and federal regulations. The Yerkes Environmental Health and Safety Officer (Yerkes EHS Officer) reports to the Yerkes Associate Director of Animal Resources and to the Emory University Environmental Health and Safety Director. Recognizing that health and safety are critical elements in the vision and success of the organization, the Yerkes EHSO unit is responsible for ensuring that the highest standard of safety practices for all employees, students and visitors are realized. As a component of this goal, the Yerkes EHS Officer serves as Chairperson of the NIH Health and Safety Consortium group and collaborates with other NPRC colleagues via the NPRC Consortium to assure best practices. Additionally, the Yerkes EHS Officer participates with various Emory University committees to implement safety practices, is a voting member of the Institutional Biosafety (IBC) and the Research Health and Safety (RHSC) Committees, serves as a member of the University Compliance Committee and is the Environmental Health and Safety Office liaison to the Institutional Animal Care and Use Committee. Priorities for the Yerkes EHSO are to continue to strengthen our programs, monitor for opportunities for improvement and continue to strive for excellence. We will work with the University team to address challenges with the Emory Learning Management System in PeopleSoft. We will expand upon our already robust Biosafety Level 3 containment work to include the fulltime engagement of the Level 3 containment manager. We will continue to strengthen the Occupational Health Program components by moving data to the PeopleSoft system to provide employees with access to their Occupational Health data as well as add efficiency and accuracy to the documentation process.

The Specific Aims are:

1.To train employees, students and visitors in all relevant areas of Health and Safety, providing opportunities for learning via live didactic, computer based and participatory experiences;

2.To transition towards the University-supported PeopleSoft Emory Learning Management System to stream line processes and capture system-wide efficiencies;

3.To maintain a comprehensive Occupational Health Program that includes employees, students and visitors, as an indispensable objective of the Health and Safety Program;

4.To review and revise Standard Operating Procedures and Compliance monitoring to meet Yerkes EHSO goals and objectives;

5.To build upon existing programs to maintain and improve Biosafety Level 3 laboratories and Animal Biosafety Level 3 facilities to meet or exceed industry standards.

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_5976_EHSO.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Animal Resources will continue to implement the aims described in the Research Strategy of each individual unit. Overall, each unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. Each unit will continue to facilitate collaboration with other units both within the Division of Animal Resources and with other support and research divisions. The DAR will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Environmental Health and Safety

Please See Associate Director for Animal Resources component for overall accomplishment for the Division of Animal Resources.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			2,862.00	707.00	3,569.00
5	Manager, EHSO Staff	19.2			94,500.00	23,341.00	117,841.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**121,410.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**121,410.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	150,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
Total Other Direct Costs	**150,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**273,410.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	273,410.00	123,035.00
		Total Indirect Costs	**123,035.00**

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)	**396,445.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Division of Pathology

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The Division of Pathology has two main roles: 1) to provide support to the research community of the Yerkes Center, as well as to external requestors and collaborators and 2) to contribute to colony health surveillance by providing diagnostic support to the Division of Animal Resources. As such, the Division promotes an open exchange of ideas, interdepartmental and interdisciplinary collaborations, the establishment and refinement of animal models of human disease and the support of projects from external collaborators in need of nonhuman primate experimentation. There are five major units within the Division: Anatomic Pathology (includes the Necropsy/Gross Pathology and Histopathology/Electron Microscopy Laboratories), Clinical Pathology, Molecular Pathology, Biological Material Procurement Program, and Biological Material Shipping Program.

The Specific Aims are:

1.To provide outstanding technical support to Center investigators in support of their research projects including, but not limited to, postmortem examination with collection and processing of tissues, electron microscopy, in situ hybridization, fluorescence in situ hybridization and immunohistochemistry services;

2.To provide diagnostic support to the Division of Animal Resources for clinical and experimental cases involving the colony animals, promoting colony health and disease surveillance to ensure the highest level of health in our animal colony;

3.To distribute valuable resources through the Biological Material Procurement Program. The collection and distribution of these specimens make it possible for scientists to take full advantage of the materials available and allows external investigators to work with cells and tissues to which they would otherwise not have access;

4.To develop and implement scientific protocols by applying current molecular pathology, clinical pathology, electron microscopy and histological assays;

5. To maintain and enhance training opportunities for veterinary and graduate students, veterinarians, pathologists and other scientists.

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_5977_Pathology.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Division of Pathology will continue to implement the aims described in the Research Strategy. Overall, this unit will continue to provide service to facilitate research at Yerkes as well as provide veterinary care, husbandry, behavioral and colony management to promote animal welfare and personnel safety. It will continue to facilitate collaboration with other units both within the Division of Pathology and with other support and research divisions. The Division of Pathology will continue to maintain the high standards of animal care at Yerkes.

B.2. Accomplishments—Division of Pathology

Pathology Service

The Pathology unit continues to provide services for both experimental needs and clinical needs for the veterinary department. During the last reporting period the pathology unit has performed a total of 568 necropsies as detailed in the table below. The clinical pathology laboratory and histopathology and molecular pathology also continue to provide services as described in the P51 submission. A new pathologist, Excluded by Requester Excluded by was hired during the last reporting period making a total of three pathologists in the unit.

Table of Necropsies Performed over Reporting Period

	Clinical	Experimental
Apr-16	39	18
May-16	37	22
Jun-16	30	59
Jul-16	15	35
Aug-16	14	38
Sep-16	18	34
Oct-16	13	71
Nov-16	14	35
Dec-16	7	34
Jan-17	7	28
TOTAL	194	374
Total Necropsies:	568	

Pathology Research

Development of rectal enema as microbicide

During the current reporting period, we have made a significant progress in the studies understanding pharmacokinetics and efficacy of iso- (IOsm) and hypo-osmolar formulations (HOsm) of tenofovir (TFV) enemas in a macaque model. Protection from receptive anal HIV transmission by topical microbicides remains a formidable challenge. We created a unique rectal enema formulation as microbicide to deliver ART to mucosal tissue to prevent SIV/SHIV infection. Markedly higher plasma TFV concentrations were seen after administration of the HOsm high dose enema (5.28mg/ml) than all other formulations tested at all-time points. This formulation also showed higher TFV concentrations and TFV diphosphate (TFV-DP) concentrations in colorectal tissues collected at 1 and 24 hr ($p<0.05$) compared to other formulations. The data from the macaque model support the clinical development of the effective TFV enema formulation.

Left Ventricular Hypertrophy Screening Project

The NPRCs recently conducted a survey that identified many interesting phenotypes across the various NPRCs. These phenotypes involved many different diseases and conditions. Based on results of this "Extreme Phenotypes" survey, the Phenotype Mining and New Model Development working group identified Left Ventricular Hypertrophy (LVH) phenotype to advance NHP model development by coordinating the discussion and comparison of common NHP traits documented at the NPRCs.
Yerkes has made substantial progress in data mining for this project using the LVH screening protocol developed by CNPRC. The YNPRC pathologists have gathered data from 20 animals at necropsy. In addition, ten affected and three control heart samples collected at necropsy were submitted to Excluded by Requester laboratory at Baylor College of Medicine for exon sequencing and data analyses. The Pathology unit continues to collaborate with the Veterinary Department to identify potential LVH cases for the project.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5977

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00
2						Veterinary Pathologist					22,748.00	5,619.00	28,367.00
3						Veterinary Pathologist					28,215.00	6,969.00	35,184.00
4						Veterinary Pathologist					15,914.00	3,931.00	19,845.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **94,937.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
2	Secretarial/Clerical	1.2			5,920.00	1,462.00	7,382.00
15	Supervisors (3), Technicians (12)	75.6			345,264.00	85,279.00	430,543.00
17	**Total Number Other Personnel**					**Total Other Personnel**	**437,925.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**532,862.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	5,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**5,000.00**

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	60,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. HIstology/EM Supplies	20,000.00
9. Necropsy supplies	20,000.00
10. Maint/Repair/other supplies	3,000.00
Total Other Direct Costs	**103,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**640,862.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	640,862.00	288,388.00
		Total Indirect Costs	**288,388.00**

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)	**929,250.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Biomarkers Core

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The primary mission of the Yerkes Biomarkers Core is to develop, validate and execute steroid, protein and other biologically relevant assays in support of translational and clinical research performed at the Yerkes National Primate Research Center and by outside investigators. The Core has been continuously operating since the early 1980s and currently provides assays for reproductive function, stress physiology, growth, metabolism, circadian physiology, pituitary function, neuropeptides and neurotransmitters. The Core currently performs these assays though the use of ELISA, radioimmunoassay (RIA), and liquid chromatography mass spectrometry (LCMS) assays in multiple species. Assays are done for investigators and clinicians on a per sample basis in which the Core recovers cost for personnel, reagents, service contracts, and miscellaneous supplies. The facility (1000 square feet) is housed at the Yerkes Main Station and contains Thermo Fisher HPLC coupled to Orbitrap Classic mass spectrometer, Shimadzu UPLC system in tandem with an AB Sciex 6500 triple quadrupole mass spectrometer, and multiple gamma and plate readers. We perform all necessary sample processing and data analysis to provide investigators with usable data. In addition to the service work, the Core also strives to develop, implement, and validate new assays to meet new research needs. Furthermore, we strive to lower the cost and turnaround time of existing assays by validating ELISA and RIA assays on our multiple LCMS platforms whenever possible.

The Specific Aims are:

1.To develop, validate and implement an oxytocin and vasopressin LCMS assay for use in plasma, CSF and whole blood;

2.To continue to reduce cost and assay turnaround time of existing ELISA and RIA assays by implementing and validation them on LCMS platforms;

3.To provide users with robust collections of related assays such as a full thyroid panel (TSH, T4, free T4 and free T3) or a more comprehensive metabolic panel for only a slightly increased cost compared to individual LCMS assays.

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_5978_Biomarkers.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

Over the next year of funding, the Biomarkers Core has two major priorities. The first priority is to complete the development of a LC/MS assay for the quantification of oxytocin. This critical and difficult-to-quantify biomarker is a high priority for several researchers at Yerkes and Emory. Once the Core overcomes several structural barriers to development of this assay (e.g. scarcity of stable reference control molecules for oxytocin), we will have reliable access to a large number of samples for oxytocin quantification through researchers at Yerkes and Emory at large. The second priority is to expand the user base and cost recovery of the Yerkes Biomarkers Core through a targeted campaign to engage a wider range of researchers at Yerkes, Emory, and throughout the country. In this endeavor we will be leveraging our high level of expertise not only in nonhuman primate specific assays, but also in providing high quality biomarker quantitation at an economy of scale. As always, we will continue to improve our established assays and consult with our customers to provide new assays and opportunities for the research community.

2. Accomplishments—Biomarkers Core

Over the past year of funding, the Core has provided 4790 immunoassay and LC/MS tests using our standardized assays in support of research with our collaborators at Yerkes, Emory University and throughout the United States. We have validated several new imunoassays for use with rhesus and cynomologues monkeys and as well as validating our angiotensin II asssay for urine. Additionally, we have modified our Angiotensin ii, oxytocin, and vasopressin plasma/serum assays to be capable of reliable extraction from 1000ul to as little as 200ul. Additionally, the Yerkes Biomarkers Core has validated several new LC/MS methodologies for our collaborators at Yerkes. We have re-developed and validated our glucocorticosteroid LC/MS panel. The new method now uses only one-fifth of the sample volume and has a ten-fold increase in sensitivity relative to our previous protocol. By improving the extraction process, our new glucocorticosteroid LC/MS method was not limited to analyze plasma and serum, but also can be used to analyze several new substrate types (i.e. breastmilk, hair, cerebro-spinal fluid[CSF]) with much less sample volume and lower cost than traditional methods. Our primary focus for the past year has been the development of an assay to quantify oxytocin in plasma and CSF with less sample volume and higher sensitivity and specificity.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5978

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			3,378.00	834.00	4,212.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **4,212.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
3	Supervisor, Technicians	3.6			14,788.00	3,653.00	18,441.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**18,441.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**22,653.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	20,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Maintenance/repair	1,000.00
Total Other Direct Costs	**21,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**43,653.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	43,653.00	19,644.00
		Total Indirect Costs	**19,644.00**

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)	**63,297.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Comparative AIDS Core

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The purpose of the Comparative AIDS Core (CAC) is to provide resources and technical support for studies of AIDS pathogenesis, prevention, and treatment using the well-established comparative models of pathogenic simian immunodeficiency virus (SIV) infection of rhesus macaques, an Asian "non-natural" host species that develops AIDS upon experimental infection with SIV, and non-pathogenic SIV infection of sooty mangabeys, an African "natural" host species in which the infection is typically benign despite high levels of virus replication. In particular, the Core has been a unique source of SIV-infected and uninfected mangabey samples for a large number of investigators in the field, as the Yerkes colony remains the only source of such samples for the biomedical research community in the entire world. We plan to maintain the colony size at a target number of ~175 individuals, which represents the historical size of the colony and allows us to manage the population in a manner that protects both the behavioral integrity and the existing genetic diversity of the colony. Overall, the CAC is a vital component of the highly successful Yerkes research program in AIDS-related studies, and is established and designed to provide oversight and coordination for these studies, as well as the necessary technical, laboratory and animal research support.

The Core staff includes scientists, veterinarians, pathologists, and animal care technicians who work closely with Yerkes Core Scientists, Affiliate Scientists and outside collaborators to design and carry out in vivo and in vitro experiments involving specimens collected from SIV-infected and uninfected mangabeys and rhesus macaques. Currently, the Core includes all the non-investigator assigned mangabeys, as well as a large number of rhesus macaques. All donor animals have known serologic and clinical health status with weights that permit routine collections of such specimens as blood, skin, milk, gastrointestinal biopsies, bone marrow aspirates and cerebrospinal fluid in accordance with approved Emory IACUC guidelines. Of note, a pre-existing cost accounting system permits appropriate recharges to be made for the collections of requested tissue specimens. The availability and distribution of these samples has resulted in many papers in high-impact journals and has been often critical in the provision of preliminary results that were used to acquire a number of large federal and non-federal grants. Finally, the Core provides formal training as needed to scientists, staff, postdoctoral fellows and students involved in AIDS research studies using nonhuman primates.

The Specific Aims are:

1.To continue to provide partial support for the maintenance of the Yerkes sooty mangabey colony as well as dedicated groups of rhesus macaques;
2.To continue to collect and store a large number of biological samples from the assigned animals that are then provided to intramural and extramural investigators for studies of AIDS pathogenesis, prevention, and treatment;

3.To expand our focus to include a strong program of research in novel approaches to HIV/AIDS prevention and treatment, including studies in which rhesus macaques and sooty mangabeys are treated chronically with antiretroviral therapy.

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_5979_CAC.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

The Comparative AIDS Core will continue to function as a core resource of animals available to facilitate AIDS research. The core will continue to maintain rhesus macaques and sooty mangabeys assigned to the CAC and available to fill specimen requests for both internal and external investigators doing AIDS research.

B.2. Accomplishments—Comparative AIDS Core

During April 1, 2016 to January 31, 2017, 119 biological samples were provided to investigators through our Tissue Distribution Program from the Comparative AIDS Core. Of these investigators, 5 are located at Yerkes, one at Emory and six at other institutions within the United States. In addition, 378 animals were assigned to externally-funded AIDS related studies during the reporting period.

Publications during the reporting period related to the AIDS Core

Excluded by Requester

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5979

RESEARCH & RELATED BUDGET - SECTION A & B FINAL

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00
2.						Asc Dir, Animal Resources					9,255.00	2,286.00	11,541.00
3.						Chief Veterinarian					3,289.00	812.00	4,101.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **27,183.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Laboratory Manager	0.6			3,602.00	890.00	4,492.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**4,492.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**31,675.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	40,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Animal Costs	382,892.00
9. Other Expenses	45,433.00
Total Other Direct Costs	**468,325.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**500,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	500,000.00	225,000.00
		Total Indirect Costs	**225,000.00**

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

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**725,000.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Imaging Core

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The primary mission of the Yerkes Imaging Core is to provide resources and technical support for performing magnetic resonance imaging (MRI), spectroscopy (MRS) and positron emission tomography (PET), all of which are capable of visualizing high-resolution anatomical, physiological, functional and biochemical information in vivo in a non-invasive and longitudinal fashion. The main facility

Specific Animal Location

Specific Animal Location

Hardware resources include 7T animal size and 3T human size MRI scanners, a cyclotron, two microPET scanners, computation resources and MR-compatible physiological monitoring equipment. Our staff works closely with Yerkes Core Scientists, Affiliate Scientists, and outside collaborators to design and carry out imaging experiments, and to collect, analyze and interpret imaging and spectroscopic data. Our computational support includes data analysis, implementation and development of software for data analysis, and data management and storage. In addition to its service component, the Imaging Core has its own active research programs. These include ongoing implementation and development of basic and novel pulse sequences, hardware and software support for data acquisition, construction of coils/detectors, head-holders and immobilization devices, and MR-compatible physiological monitoring equipment. These resources are made available to all users. The Imaging Core provides formal training as needed to scientists, staff, postdoctoral fellows, and students. Training includes lectures on basic MR and PET physics, radiochemistry, and applications as well as hands-on MR and PET experiments and data analysis. Furthermore, the Imaging Core works closely with the Emory Center for Systems Imaging (CSI), an integrated organizational structure designed to provide synergy for various aspects of imaging research and make imaging resources easily available to the greater university community. The CSI encompasses complementary resources based at specialized imaging facilities across Emory University including Emory University Hospital, Wesley Woods, the Winship Cancer Institute and the Psychology Department on the Emory College campus.

The Specific Aims are:

1.To establish the Yerkes Imaging Core as a premiere resource in nonhuman primate diffusion and perfusion MRI and resting state functional MRI (rsfMRI);

2.To expand our focus to include a strong program of research in stroke and neurovascular function in the context of functional brain imaging through the active recruitment of an endowed faculty appointment;

3.To develop novel PET tracers and MRI contrast agents to support emerging research programs with particular emphasis on partnering with the Emory Vaccine Center and the Division of Microbiology and Immunology.

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_5980_Imaging.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

We will continue to establish the Yerkes Imaging Core as a premiere resource in nonhuman primate diffusion and perfusion MRI and resting state functional MRI. The Imaging Core has made significant progress in the development of diffusion MRI techniques (including diffusion tensor imaging (DTI), high-angular resolution diffusion imaging (HARDI), diffusion spectrum imaging (DSI) and perfusion MRI techniques (including continuous arterial spin-labeling techniques and dynamic susceptibility contrast MRI) as part of our studies in stroke imaging and nonhuman primate neurodevelopment. We have also developed standardized protocols for evaluating resting state functional connectivity in both anesthetized and fully conscious rhesus monkeys. These are two areas of in vivo imaging with significant potential across a broad range of research programs. In addition, the Yerkes Imaging Core will continue to develop and implement novel MRI techniques, such as chemical exchange saturation transfer (CEST) imaging, diffusion kurtosis imaging (DKI), susceptibility weighted imaging (SWI), hardware and software support for data acquisition and processing, construction of RF probes/detectors. These resources will be available to all users of the Imaging Core.

We will also expand our focus to include a strong program of research in stroke and neurovascular function in the context of functional

brain imaging. The major goal is to establish a preclinical program on novel stroke interventions and therapeutics that successfully translates to human use. These efforts will be supported by the recent recruitment of Excluded by Requester as the Yerkes Center's first endowed chair in the area of stroke and neuroimaging. In addition, Dr. Lary Walker is investigating the role of vascular disease in the development of dementia by determining, in aged nonhuman primates, the relationship between imaging anomalies in MRI and cerebral amyloid angiopathy. His research program is well positioned to complement our nonhuman primate stroke research and enhance our understanding of neurovascular function. In addition, Excluded by Requester has an active collaboration with Excluded by Requester to evaluate vascular anomalies associated with cocaine self-administration in squirrel monkeys.

Lastly, we will develop novel PET tracers and MRI contrast agents to support emerging research programs with particular emphasis on partnering with the Emory Vaccine Center and the Yerkes Division of Microbiology and Immunology. We are currently validating the use of biomarkers for evaluating neuroinflammation in the context of research on Parkinson's disease. These biomarkers, including F-18 labeled FEPPA, will have direct application in the study of neuroAIDS and cognitive dysfunction. In addition, we are also interested in superparamagnetic iron oxide nanoparticles (SPIONs) as they have emerged as a unique contrast agent to improve the sensitivity and specificity of MRI in detecting the abnormality of tissues or cell tracking. In particular, the exploratory studies of SPIONs for tracking HIV-specific cytotoxic T lymphocytes suggest the SPIONs may be a novel approach in in vivo monitoring of T cells and play a critical role in development of T cell-based therapies.

B.2. Accomplishments—Imaging Core

The Yerkes Imaging Core is part of the Yerkes National Primate Research Center at Emory University and focuses on the development of *in vivo* magnetic resonance imaging (MRI) and positron emission tomography (PET) to study anatomy, physiology and function non-invasively to address questions in neuroscience, neruopharmacology and neurodegenerative diseases. Research at the Imaging Core includes high-resolution structural, perfusion and functional imaging of nonhuman primates, diffusion-tensor imaging (DTI), awake monkey fMRI, quantitative perfusion imaging, quantitation of monoamine transporters and receptors, brain metabolic mapping, diffusion, perfusion and functional imaging of stroke, and image data analysis and visualization. The Imaging Core continues to support internal and external investigators with MRI and PET imaging as part of their individual research programs. In addition, we continued to commit significant resources to the development of a nonhuman primate model of ischemic stroke. A newly appointed endowed chair of stroke imaging [Excluded by Requester] joined the Imaging Core this year. We have expanded our use of diffusion tensor imaging DTI to characterize brain development in longitudinal studies conducted at the Yerkes Field Station. We have also made significant progress in establishing technical approaches that will be applicable to research programs in immunology and vaccine development. With the implementation of PET imaging, we have quantiifed the distribution of SIV virus *in vivo* and have validated biomarkers of neuroinflammation.

Significant progress has been made in imaging ischemic stroke in a clinically relevant monkey model. The long-term goal is to identify and characterize tissue at risk and functional remodeling after stroke and to cross validate against histology and behavioral assessments, to develop a mathematical model to predict outcome of stroke tissue fates using acute MRI data and to cross validate the prediction with histology, and to test pharmacological treatments in collaboration with Emory collaborators. We continue to make major advances in the neuropharmacology of abused stimulants in the context of medication development to treat stimulant addiction. As part of these efforts, we are able to routinely image fully conscious rhesus monkeys using fMRI. These advancements in awake monkey imaging will serve to enhance a variety of research programs at the Yerkes Core. Additional areas of significant interest include brain metabolic effects of neonatal medial temporal lobe lesions to characterize the neurobiology of learning and memory, the influence of psychosocial stress on the emergence of behavioral problems including anxiety depression and socially motivated behaviors, and the discovery of pharmacological interventions to slow the progression and alleviate the symptoms of Parkinsonism. More general areas of interest include anatomical imaging for placement of recording electrodes and dialysis probes, imaging neurodegenerative diseases, functional MRI of memory and cognition, PET and fMRI imaging of drug abuse, fMRI of developing monkeys, structural imaging and diffusion tensor imaging of development and aging, PET imaging of monoamine transporters and receptors associated with early life experiences and social behavior and obesity. The Yerkes Field Station offers major advantages to our imaging program including social housing, and a large number of infants and juveniles needed for developmental studies. Onsite capability to conduct PET studies without either significant disruption to the animals located at the Field Station markedly enhances the quality of science and provides unique opportunities to investigators.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5980

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			5,553.00	1,371.00	6,924.00
2.						Associate Veterinarian					13,853.00	3,422.00	17,275.00
3.						Imaging Core Assistant Director					8,044.00	1,986.00	10,030.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **34,229.00**

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	1.8			10,245.00	2,532.00	12,777.00
5	Staff Scientist, Technicians	9.6			43,948.00	10,854.00	54,802.00
6	**Total Number Other Personnel**					**Total Other Personnel**	**67,579.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**101,808.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	11,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Maintenance/repair	3,000.00
Total Other Direct Costs	**14,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**115,808.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	115,808.00	52,113.00
		Total Indirect Costs	**52,113.00**

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)	**167,921.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Virology Core

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The primary purpose of the Yerkes Virology Core is to provide serological and molecular viral diagnostic testing in support of Yerkes Research Services and Colony Management. The Core has developed a pipeline of diagnostic screens and tests which provide definitive diagnoses for the presence of infection by Simian Immunodeficiency Virus (SIV), Simian T Lymphotropic Virus (STLV), Simian type D retroviruses (SRV), and Simian Herpes B virus (Herpes-B). The presence of these viruses in rhesus macaques could confound the results of HIV vaccine and pathogenesis studies, present critical risks to human investigators accidentally exposed to rhesus macaque tissues, and could present significant health risks to the rhesus macaque colony as well. The screening pipeline consists of several tiers of increasingly stringent and sensitive tests. First, animals are screened for virus-specific antibodies using a cytometric bead array (CBA) based platform. Any animal with a positive or borderline CBA result is then tested by Western blot for the presence of antigen-specific antibodies. An inconclusive Western blot results in a third downstream virus-dependent test. For SIV and STLV, DNA is extracted from frozen peripheral blood mononuclear cells (PBMC) and a polymerase chain reaction (PCR) test is performed to detect integrated viral genomes. For SRV, a real-time, quantitative PCR is performed (currently outsourced to the California National Primate Research Center). For Herpes-B, samples are sent to the B-virus National Laboratory for analysis via competitive and recombinant ELISA. Additionally, the Yerkes Virology Core performs both custom virological assays (virus titration and growth) and kit-based CBA assays (e.g. rhesus cytokine assays) for clients across Emory University. Through the combined expertise of the leadership and technicians within this lab, and a close collaboration with the CFAR Virology and Molecular Biomarkers Core pre-clinical laboratory, the Yerkes Virology Core is extremely well-positioned to be the primary hub of virological and molecular diagnostic services across Emory University.

The Specific Aims are:
1.To continue to provide state-of-the-art viral diagnostic assays in support of the Specific Pathogen Free rhesus macaque colony (breeding) and Yerkes Animal Resources (study assignment), and expand the menu of virological services through the development, validation, and implementation of a Simian type D retrovirus quantitative real-time PCR;

2.To expand the menu of services provided for viral preparation, characterization, and diagnosis, including the growth and genetic characterization of standardized virus stocks for use in nonhuman primate studies of AIDS;

3.To develop and implement new assays to test for pre-existing immunity to viruses which could be used in pre-clinical trials of gene therapy delivery systems (AAV), candidate vaccines (CMV) or impact the health and immunological status of the primates housed at Yerkes (measles, etc.).

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_5981_Virology.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

Over the next year of funding, the Yerkes Virology Core is planning a number of new experiments to validate our SRV PCR, and several new assays for the detection of immunity several AAV serotypes and Zika virus. For further validation of our SRV qPCR, we will further delineate the detection limit of these assays in the background of primary rhesus macaque cellular DNA by diluting our plasmids in DNA extracted from rhesus macaque PBMCs. Due to the success of the SPF breeding and viral screening program, SRV(+) animals are difficult to find at the National Primate Research Centers. Therefore, we are currently using cell lines (A549 and Raji cells) infected in vitro with each SRV subtype as positive control cells for our assay until a suitable SRV DNA positive animal can be identified. Our current SRV serological positive controls are negative for SRV in our assay. This is either due to the complex relationship of SRV humoral responses and SRV DNA load or to the resolution of infection and subsequent waning of SRV DNA levels. Identification of SRV DNA positive samples at other primate facilities is ongoing. Once validated we will begin a yearlong process of external validation, comparing the results of our assay with those obtained from the Pathogen Detection Laboratory at the California National Primate Research Center. Additionally, the Core is currently validating our AAV neutralization assay for AAV1, 2, 7, and 8 serotypes. As there are several new Zika-related projects at Yerkes, we will also be using samples from these to test and validate a Luminex-based Zika virus screening protocol using commercially available kits to verify our results. As always, the Yerkes Virology Core will continue to provide high quality virological

testing services for the maintenance of the specific pathogen free colony at Yerkes.

2. Accomplishments—Virology Core

In addition to our standard specific pathogen free (SPF) testing regimen (screening more than 1600 rhesus macaques), during the last year of funding, the Yerkes Virology Core has been designing and implementing several new assays for the detection of SPF viruses and anti-viral humoral responses to viruses of considerable interest to researchers at Yerkes. First, we have begun the validation process for our SRV-specific qPCR. We have constructed plasmids containing the PCR target sequences for SRV1-4 to use as copy number standards. Using highly accurate dilution series of linearized versions of these plasmids, we have tested the efficiency of the SRV qPCR protocol (slope = ~3.3) and the ability of the primers and probe to detect each SRV subtype with similar efficiency. Our initial experiments are promising with copy number over cycle threshold (Ct) slopes ranging between 3.32 – 3.47. Additionally, our lowest standard (~10 copies per reaction) is detectable around a Ct of 37 suggesting that our qPCR protocol is capable of detecting a single copy per reaction within a 40-cycle PCR. Further iterations on our standard dilutions are needed to verify equivalent efficiencies and detection limits. Second, the Yerkes Virology Core has been providing services to screen rhesus macaques for pre-existing immunity to AAV5 by neutralization titer. Briefly, plasma from prospective animals is serially diluted and incubated with a luciferase expressing AAV of the serotype being used. This mixture is then incubated with HEK293T cells and luciferase is measured relative to AAV-negative plasma samples to determine the neutralization titer. While the Yerkes Virology Core has yet to identify animals with naturally occurring AAV5-specific neutralization titers lower than 1:40, we have identified several animals that have developed AAV5-specific antibody responses after intracranial exposure to a single high titer bolus of AAV5.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5981

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			3,378.00	834.00	4,212.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **4,212.00**

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	Technicians	2.4			9,686.00	2,392.00	12,078.00
2	**Total Number Other Personnel**					**Total Other Personnel**	**12,078.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**16,290.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	5,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Maintenance/repair	1,000.00
Total Other Direct Costs	**6,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**22,290.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	22,290.00	10,031.00
		Total Indirect Costs	**10,031.00**

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)	**32,321.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Genomics Core

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The primary mission of the Yerkes Genomics Core (GenCore) is to provide researchers in the Emory community with access to cutting-edge high throughput genomic technologies and bioinformatics. The facility (4900 sq ft) is located in the Neuroscience Building at the Yerkes Main Station and the primary computing infrastructure is housed in the Emory central IT computing racks. The primary hardware housed by the GenCore includes an Illumina HiSeq 1000 next-generation sequencing system, an Affymetrix 3000 Gene Chip Scanner, and a Fluidigm Biomark microfluidic single-cell analysis real-time PCR platform. Supporting bioinformatics and computation is a dedicated IlluminaCompute Server and Isilon storage system. Through a partnership with the Center for AIDS Research (CFAR) Virology Core, the GenCore also utilizes an Illumina MiSeq system for applications that require long read technology. The GenCore laboratory is the only core facility on the Emory campus that conducts next-gen sequencing. The Yerkes GenCore was established in 2012 with the mandate to support nonhuman primate (NHP)-based and immunology-based research. The primary users of the GenCore are monkey-model researchers at the Yerkes Center and immunologists within the Emory Vaccine Center; however, the GenCore is also utilized by members of the greater Emory community. The services offered by the GenCore include RNA-Seq and array-based transcriptomics DNA-Seq, miRNA-sequencing, microbiome 16s rRNA sequencing and sample preparation. The GenCore staff also includes a dedic bioinformaticist and provides a wide variety of analysis and computational services. Ongoing and completed projects in the GenCor laboratory include transcriptomic profiling of several pre-clinical vaccine candidates, expression monitoring of clinical trials samples undergoing novel anti-HIV therapies, and multiple small-scale RNAseq experiments in humans and several NHP species. The GenCore is the dedicated sequencing provider for the NIAID-sponsored Malaria-Host Pathogen Interaction Consortium (MaPHIC) contract (PI: Excluded by The GenCore also has an active internal research program, primarily focused on improving genomic resources and assays for NHP applications. This has included a large-scale collaboration with the Baylor Genome Sequencing Center to sequence the genome of the sooty mangabey monkey – a species housed by the Yerkes Center and used to study HIV pathogenesis. Lastly, the GenCore has provided verification analyses for the generation of a novel rhesus macaque genome sequence.

Excluded by Requester

The Specific Aims are:

1.To translate protocols for genomic profiling of the B- and T- lymphocyte receptor repertoire (TCR-Seq and Ig-Seq) for use in the rhesus macaque, and offer repertoire sequencing technology for use in SIV-vaccine studies;

2.To translate microbiome sequencing analyses to monkey models, and integrate microbiome studies into NHP applications including nutritional studies, veterinary monitoring, and SIV-vaccine trials;

3.To establish single-cell transcriptomics (scRNA-Seq) for application in monkey models and offer single-cell technology to the NHP research community, and to develop specialized scRNA-Seq for SIV/HIV latently infected cells;

4.To increase throughput, streamline project submission, billing and data retrieval for users;

5.To expand bioinformatics accessibility to the Yerkes community.

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

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B2_5982_Genomics.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

NOTHING TO REPORT

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

1.Further Decrease Turn Around Times for NextGen sequencing. Over the next 2 years, we anticipate our volume of work to approximately double due to new funding being awarded in 2016. To continually improve our turnaround time, increase service capacity and maintain competitive prices, we have evaluated several options to obtain large/medium scale automation (robotics) to handle several of our time-critical work flows. Funds permitting, we hope to obtain one of these platforms in this extended time frame.

2.Improving throughput and cost for single-cell RNA-Seq assay. One of the primary challenges in making this single-cell RNA Seq technology widely available is that the labor involved in generating the data is time-consuming and extensive. To overcome this hurdle,

we have been examining robotics platforms that automate the library prep stage. These platforms would also miniaturize assay volumes and further reduce cost. Additionally, several commercial platforms for performing 'droplet-based" single-cell RNA-Seq have become available, and we have been evaluating purchase of those.

3.Established a repertoire assay for NHP B cell Receptors/Antibodies. Maximal utility of this assay will need a high-quality reference of V,D and J sequences from the Macaca mulatta species, and an appreciation of allelic diversity in the Yerkes Colony. We are working to improve this genomic reference in two ways: (1) we are collaborating with (and have sent DNA to) Excluded by Requester (Scripps Institute) and the Specific Private Vendor to obtain long-read sequence information of the Indian Macaca mulatta immunoglobulin loci, and (2) to estimate allelic diversity, we will perform repertoire sequencing on the H-chain (using IgG constant priming) and L-chain (using K & L priming) of a set of 60 breeder animals representing a large extent of the genetic diversity of the YNPRC colony. Using a recently described bioinformatics approach (IgDiscover) we can infer the germ-line sequences of the variable gene segments and estimate allelic diversity in the colony.

4.Train users in single-cell RNA-Seq and TCR/BCR repertoire sequence analysis We do not plan on hiring additional bioinformatics staff for the Genomics Core at present. We are developing novel bioinformatics expertise in some key areas in NHP genomics, particularly in single-cell RNA-Seq analysis, and in BCR/TCR repertoire analysis of NHP samples, and we plan on training and educating users in these approaches on an individual project basis.

B.2. Accomplishments—Genomics Core

The Yerkes NHP Genomics Core Laboratory is funded at a rate of 6% from the Yerkes P51 base grant. In the current reporting period, (3/1/2016 – 2/28/2017) we accomplished the following goals that were defined in our P51 proposal.

1. Decreased Turn Around Time. To meet the increase in demand for GenCore services, we obtained a new high throughput sequencing instrument: an Illumina HiSeq3000, which became operational in March 2016. This replaced our previous "work-horse" machine, which was the HiSeq1000. The HiSeq3000 was obtained through a lease. We have also hired a 3rd laboratory technician, and have a fourth technician on staff on an interim basis to deal with our current workload. We also hired an additional 50% FTE bioinformaticist to improve the turnaround time on analyses. These have reduced average time to return sequence data to 20 days, less than half our previous turnaround time. We also instituted LIMS sample/project management software, GenoLogics, to streamline project submission and maintenance of pre-sequencing metadata. Despite these additions, the GenCore recharge recovery increased by 40% from the previous year (FY2016 recharges = $1.02 M), and our total cost recovery rose to nearly 91% over the previous two years.

2. Developed a low cost single-cell RNA-Seq assay and validated it NHPs. We developed an in-house single-cell RNA-Seq assay that sequences full-transcript RNA from single-cells in a cost effective manner. This assay can also extract the sequence data for the variable gene segments (VJ, VDJ) for individual B cells and T cells. We have also developed a computational algorithm to reconstruct these VJ/VDJ sequences correctly, and we have validated this assay to sequence the paired antigen receptor in rhesus macaque B cells.

3. Established a repertoire assay for NHP B cell Receptors/Antibodies We validated a non-commercial assay to sequence the B cell repertoire of either heavy or light chain from RNA samples, and validated it for human and rhesus samples.

4. Established a microbiome assay for NHPs We tested and validated a 16S amplicon sequencing assay for microbiome population sequencing in NHP samples. This has been performed on 3 NHP projects, and is now offered as a listed service.

5. Improved Bioinformatics Availability to Yerkes/Emory In addition to hiring another 50% FTE bioinformaticist to handle fee-for-service projects, we installed a user-dedicated workstation so that users can have access to our software licenses and analyze their own dataset under the in-person guidance of GenCore analysts. This has reduced the time to publication for projects involving the Core, as shown by Core Co-authorships on 10 published manuscripts in the last reporting period.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5982

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			4,893.00	1,209.00	6,102.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **6,102.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
5	Geneticist, Lab Mgr, Informatics Specialist, Technician	7.8			45,971.00	11,354.00	57,325.00
5	**Total Number Other Personnel**					**Total Other Personnel**	**57,325.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**63,427.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	20,000.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Maintenance/repair	1,000.00
Total Other Direct Costs	**21,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**84,427.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	84,427.00	37,992.00
		Total Indirect Costs	**37,992.00**

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)	**122,419.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: BNPD

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

The mission of the Division of Behavioral Neuroscience and Psychiatric Disorders (BNPD) is to conduct basic and translational research to better understand the neurobiological mechanisms underlying behaviors relevant to developmental and psychiatric disorders, including autism spectrum disorders, anxiety-related disorders, depression, post-traumatic stress disorders, and addiction. Faculty in BNPD use a wide range of state-of-the-art approaches in rodent and nonhuman primate (NHP) models, including rhesus macaques and new world monkeys, as well as humans to make basic science discoveries with the ultimate goal of translating these discoveries into novel therapeutic strategies to improve mental health. Investigators in BNPD use techniques that include electrophysiology, molecular genetics, epigenetics, chemogenetics (DREADDs), optogenetics, and behavioral genetics to explore the neural mechanisms underlying behaviors relevant to psychiatric disorders. All investigators in the division use rodent models, including transgenic mice, voles, and rats for high throughput rapid discoveries with the ultimate goal of translating both the discoveries and technologies to NHPs. Investigators in BNPD collaborate closely with investigators in other divisions at Yerkes as well as other National Primate Research Centers and research institutions to facilitate translating novel discoveries and technology from rodent models to NHPs. BNPD is the home of two Centers that exemplify the flow of technology and discovery from rodents to NHPs and humans. The Center for Translational Social Neuroscience is an Emory-wide Center that brings together many investigators at Yerkes across all of the neuroscience divisions as well as across Emory whose research is focused on the behavioral and neurobiological bases of social behavior or on psychiatric disorders that are characterized by deficits in social cognition. Pilot project grants, seminars and journal clubs facilitate interaction and collaboration and create a vibrant intellectual and training environment. The Silvio O. Conte Center for Oxytocin and Social Cognition is more focused on the neural mechanisms by which oxytocin enhances social cognition in voles, rats, and rhesus macaques as well as healthy and autistic human subjects. This NIH-funded center involves several highly integrative projects using parallel approaches across species to understand how oxytocin influences social cognition. The Division is led by Excluded by Requester who is the only Core Scientist in the division. All other investigators in the division are Affiliate Scientists with appointments in the School of Medicine's Departments of Psychiatry, Pediatrics, or Pharmacology. All research projects involving rodents or humans are funded by investigator-initiated federal or private foundation sources. Division scientists are highly invested in training and outreach activities, ranging from training postdoctoral fellows and PhD students to public outreach and K-12 outreach.
The Specific Aims are:
1.To enhance our scientific programs of excellence in basic and translational behavioral neuroscience relevant to psychiatry through the use of state-of-the-art technology using animal models that allow rapid scientific discovery;

2.To facilitate collaborations across Yerkes divisions, at other National Primate Research Centers and research institutions across the nation to facilitate the translation of discoveries made within BNPD to novel research in nonhuman primates;

3.To continue our significant commitment to training the next generation of scientists through undergraduate, graduate, and postdoctoral programs and to foster community outreach educational efforts.

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_5983_BNPD.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

Please see the Overall component for response.

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

Excluded by Requester

•Examine how oxytocin influences neural communication between the basolateral amygdala, nucleus accumbens and prefrontal cortex during social bonding in prairie voles using simultaneous electrophysiological techniques.
•Genotype the oxytocin receptor of wild caught prairie voles to identify the SNP that has the greatest influence on nucleus accumbens oxytocin receptor expression.
•Determine the colocalization of oxytocin receptors with markers of cholinergic neurons in the nucleus basalis of rhesus macaques.
•Finalize the study on melanocortin II examining the effect of this drug on activation of brain reward circuitry as a function of oxytocin signaling and social encounters.
•Perform Chromatin Immunoprecipitation (ChIP) assays to characterize the transcriptional landscape of the prairie vole oxytocin receptor gene.

•Submit the renewal of the Silvio O. Conte Center grant.
•Finalize the intranasal oxytocin fMRI study in autistic subjects.

Excluded by Requester

•Developing protocols for conducting single cell RNA sequencing from 1) dissociated cell suspensions of the mouse, rat, and non-human primate CNS, and 2) from neurons of each species from which we have also recorded their electrophysiological characteristics.
•Examine how the endogenous oxytocin system modulates communication between the basolateral amygdala and the nucleus accumbens and document how this communication is affected in our valproate model of autism.
•Submit an application for a P50 from the NIH Brain Initiative to develop single cell neuronal RNA sequencing involving multiple investigators at Yerkes.
•Continue collaborations with Excluded by Requester to create an opsin transgenic rhesus macaque.
Gourley
•Test the hypothesis that individual differences in cocaine self-administration in adolescence determine effects on orbitofrontal cortex (oPFC) dendritic spines, such that mice that escalate are more susceptible to spine deficiencies in adulthood. We will then assess whether ifenprodil, an NR2B-selective NMDA receptor antagonist that blocks the reinstatement of heroin-, nicotine-, and alcohol-seeking behaviors in rodent models will also have therapeutic-like effects after adolescent cocaine exposure, occluding cocaine-induced habits.
• Examine whether individual differences in cocaine self-administration in adolescence are associated with individual differences in cocaine self-administration and the reinstatement of cocaine seeking in adulthood. We expect that mice with a history of escalating cocaine exposure will respond more for cocaine as adults and be more likely to reinstate responding. In these experiments, ifenprodil will be paired with extinction training in an attempt to mitigate the reinstatement of cocaine seeking. This approach models the use of ifenprodil as a therapeutic adjunct to behavioral therapy in humans and is strongly supported by our preliminary findings.
This work builds on collaborative efforts with Excluded by Requester Yerkes NHP lab, in which we recently tested novel approaches to mitigating cocaine self-administration. The described experiments will attempt to clarify molecular mechanisms using tractable mouse models.

Excluded by Requester

•Complete the Yerkes Pilot Project examining how stress experienced by mice and rhesus macaques alters miRNA in circulating exosomes, cerebrospinal fluid (CSF) and sperm.
•Examine how parental legacies of stress influence offspring at an epigenetic level.
•Examine hormonal influences, e.g. estrogen, on memory dimensions of PTSD.

Each faculty will continue to be involved in training undergraduates, graduate students and postdoctoral fellows from a diverse background. These trainees will be encouraged to engage K-12 students through outreach programs in collaboration with the Atlanta Chapter of the Society for Neuroscience.

B.2. Accomplishments—BNPD

BNDP faculty have continued to be successful at our mission of conducting basic and translational research to better understand the neurobiological mechanisms underlying behaviors relevant to psychiatric disorders using state of the art technology, including DREADDs, optogenetics, and electrophysiology. We have continued to collaborate with other faculty at Yerkes to translate our findings in rodents into primate research. We continue to have an excellent record training a diverse group of undergraduates, graduate students and postdoctoral fellows. A brief overview of each faculty's activities and accomplishment is provided below.

Excluded by Requester In collaboration with Excluded by Requester we have used electrophysiology and optogenetics to understand how dynamic corticostriatal signaling promotes the formation of social bonds in prairie voles. We have shown that during mating, low frequency signaling from the medial prefrontal cortex modulates high frequency gamma oscillations in the nucleus accumbens, referred to as net modulation, and that the strength of this net modulation predicts the onset of huddling behavior. Under Review Under Review Under Review We have also identified a polymorphism in the prairie vole oxytocin receptor gene that predicts 80% of the expression of oxytocin receptor specifically in the nucleus accumbens. A paper describing this data was published in *Biological Pscyhiatry*. We have explored the neural mechanisms by which a melanocortin agonist facilitates social attachment in voles. Melanocortin II infused into the brains of voles activates the prefrontal cortex and nucleus accumbens only in the context of a social encounter, and this activation is abolished by co-infusion with an oxytocin receptor antagonist. This is consistent with our hypothesis that MTII evokes endogenous OT release only in the context of social stimulation. and thus similar drugs could be useful for enhancing social cognition in autism. We are collaborating with Excluded by Requester in Australia in clinical trials with a similar drug in autistic adults to determine whether it facilitates social function. Finally, we have demonstrated in voles that oxytocin receptor signaling during pair bond formation in vole acts to facilitate the coordinated activation of neurons in the social salience network.

Excluded by Requester continues to lead the Conte Center for Oxytocin and Social Cognition, which involves several projects involving NHPs as well as humans. In collaboration with Excluded by Requester we have characterized a novel small molecule oxytocin antagonist that is capable of penetrating the blood brain barrier. Excluded by Requester Co-mentors a PhD student with Excluded by Requester at Yerkes and together we are investigating whether polymorphisms in, or epigenetic markers of, oxytocin receptors in rhesus macaque are associated with variation in social behavior. Finally, Excluded by Requester has continued to make progress in a project, in collaboration with the Emory Autism Center and Excluded by Requester in which fMRI will be used to examine the effects of intranasal oxytocin on functional connectivity in the brain of autistic subjects. We have recruited all subjects, submitted an IRB and FDA IND and filed the project with ClinicalTrials.gov.

Excluded by Requester: In the past funding period, we have made significant advances in our understanding of the neural circuits and signaling cascades that contribute to stress-induced facilitation of affective disorders. Our objectives were two-fold; 1) to continue to look at the effects of chronic stress on signal transduction mechanisms in rat BNSTov neurons, and determine the relative strength of input onto BNSTov from sensory structures that process viscerosensory and interoceptive information about stress stimuli prior to manipulating these pathways with chemogenetics and optogenetics and; 2) to reproduce the anxiogenic effects of administering a high fructose diet (HFrD) during adolescence in rats and determine if any observed behavioral changes are associated with a selective change in the membrane properties, subcellular signaling pathways, and/or morphology of BLA principal neurons.

Excluded by Requester lab has also made progress characterizing at prenatal valproate rat model of autism as part of the Conte Center grant. His lab has characterized alterations in social behavior and oxytocin receptor expression in the brain as a consequence of prenatal valproate exposure. In addition, his lab has begun to examine how oxytocin influences the neural communication between the basolateral amygdala and the nucleus accumbens during social interactions.

Excluded by Requester: Excluded by Requester has been making progress understanding the neural mechanisms by which adolescence contributes to vulnerability to depression. More specifically, the Excluded by Requester lab has mapped the developmental trajectory of deep-layer neurons exposed to exogenous corticosterone (CORT), which is known to increase depressive like behavior; determined whether the novel trkB agonist, 7,8-DHF, has antidepressant-

like effects; determined the role of BDNF-trkB in the orbitofrontal cortex (oPFC) in regulating actions and habits;
and characterized the antidepressant-like effects of fasudil and their neurobiological mechanisms. These finding have been published in excellent journals including Biological Psychiatry, Neuropsychopharmacology and Journal of Neuroscience.

Excluded by Requester

Excluded by Requester

Excluded by Requester: Using a mouse model of paternal stress (Laboratory), two models of social stress in the non-human primate (Sanchez, and Wilson Laboratories), and in collaboration with the Yerkes Genomics Core, Excluded by Requester has been examining how stress experienced by mice and rhesus macaques alters miRNA in circulating exosomes, cerebrospinal fluid (CSF) and sperm. We exposed mice to olfactory stress and sequenced RNA present in circulation and sperm. In addition, we are in the process of isolating RNA from the non-human primate samples and will be sequencing this RNA within the next few months. Once these data are collected we will be using bioinformatics approaches to ascertain RNAs that are altered across these species as a function of stress. In so doing, we will illuminate conserved signatures of stress across species. Dr. Excluded by is in his second year as faculty and has submitted multiple grants to multiple funding agencies in the past year.
Training/Outreach: The four active laboratories in BNPD have trained 14 graduate students, 9 postdoctoral fellows and 12 undergraduates. These trainees include several URMs, at each level of training. BNPD trainees are actively involved in outreach activities to help generate an interest in neuroscience in K-12 students in the Atlanta Community. PhD students have organized the Atlanta Brain Bee as well as a booth at the Atlanta Science Festival, in collaboration with the Atlanta Chapter of the Society for Neuroscience. BNPD students manage a Lending Library of teaching materials in support of Brain Awareness activities in Atlanta School

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5983

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **11,541.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			2,853.00	705.00	3,558.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**3,558.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**15,099.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**15,099.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	15,099.00	6,795.00
		Total Indirect Costs	**6,795.00**

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)	**21,894.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: DCN

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Faculty in the Division of Developmental and Cognitive Neuroscience (DCN) will continue their investigator-initiated, collaborative research programs focused on the neurobiology of social behavior and cognition across the life span, providing nonhuman primate models for various neuropsychiatric disorders, including developmental disorders such as stress and anxiety, depression, schizophrenia, autism spectrum disorders, ADHD, and obesity. The faculty use state-of-the-art technology (behavior, cognition, genetics, transient inactivation, and neuroimaging, including PET) to both manipulate neurobiology and capture resulting changes in complex social and cognitive behavior. Importantly, Core Scientists within the Division will continue to serve as an intellectual resource on the psychobiology of nonhuman primates for local, regional, national and international investigators. Each Core Scientist will provide expertise to outside investigators wanting to use Center resources and those who need advice and consultation. In addition, the Core Scientists will continue to be an integral part of the training and scientific community at Emory University, with their commitments to undergraduate and graduate education, and to foster productive and successful collaborative relationships with investigators throughout the Emory campus. Importantly, the Affiliate Scientists within the Division, whose academic appointments are elsewhere, also contribute actively to the mission of the Center. The ability of the Core Scientists within the Division to provide this expertise is derived from their successful individual, extramural-funded research programs that, as detailed in the following section of peer-reviewed projects, will continue in the next five-year funding period.

The Specific Aims are:

1.To use neural inactivation methodologies (permanent lesions, pharmacological or viral-vector inactivation) coupled with neuroimaging to understand the neural connections serving memory and cognition as well as socio-emotional behavior;

2.To expand the assessment of the importance of candidate genes in the expression of a range of phenotypes including regulation of emotion and stress, cognition, adolescent brain maturation, food preference and risk for obesity, and reproductive compromise;

3.To expand use of neuroimaging tools to better understand changes in neurochemistry and neural connectivity throughout the life span in response to a number of social contexts or endocrinological manipulations;

4.To implement new standardized testing (e.g. eye tracking) to more fully examine behavioral effects of interventions; increase ad libitum testing of a number of cognitive modalities of socially housed monkeys using automated testing kiosks; and pursue the development of video capture of spontaneous social behavior of corral-housed monkeys using high-resolution IP cameras;

5.To continue our strong commitment to mentor junior faculty, graduate and undergraduate students, and postdoctoral fellows pursuing a career in behavioral neuroscience and foster productive and successful collaborative relationships with investigators throughout the Emory campus and to remain active in community outreach by conducting tours of Yerkes facilities and speaking at Center-approved community seminars.

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_5984_DCN.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

Please see the Overall component for response.

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

Aim 1: All funded developmental projects in the DCN require neurobehavioral follow-ups of the animals from birth to early adulthood, thus within each project further investigation of the animals at different time points and using different procedures will continue during the next funded period. In addition, pilot studies are underway to make the newly developed chemogenetic technique (DREADDS) available for studying the neural substrate of diverse cognitive functions as well as social behavior while the animals are maintained in social groups and across developmental periods.

Aim 2: We will pursue studies on the role of oxytocin and vasopressin on social cognition as well as genotyping for dopamine, serotonin, monoamine-oxidase and FoxP2. We will also gather data on individual variation in memory performance within a large rhesus macaque

population and examine what role genetic variation plays in these memory phenotypes. Studies will be initiated to determine the role of individual genes variation that influences complex behavioral and metabolic phenotypes using both univariate and multivariate analysis and to examine the interplay between genetic variation and age on metabolism, inflammation, oxidative stress and physiological phenotypes. Investigations on how genetic, epigenetic and social factors increase vulnerability or resilience to early adversity will be followed.

Aim 3: Almost all active and pending grants in DCN involve a neuroimaging component and we will continue to use the state-of-the-art neuroimaging tools we have developed in projects initiated in the next funding period. The Division will work in close collaboration with faculty in NND to develop and implement new databases for the collection of post-mortem brains as well as neuroimaging data.

Pending Support

Aim 5: All faculty will dedicate strong commitment in mentoring and collaborations junior faculty, graduate and undergraduate students and postdoctoral fellows pursuing a career in behavioral neuroscience and foster productive and successful collaborative relationships with investigators throughout the Emory campus; remain active in community outreach by conducting tours of Yerkes facilities and speaking at Center-approved community seminars.

B.2. Accomplishments—DCN

Aim 1: ***Non-human primate models of neurobehavioral development using brain manipulations, neonatal behavioral perturbations, perinatal drug administration and infection***: Faculty have pursued several developmental models during this funding period that are relevant to human normal and abnormal neurobehavioral development. Excluded by Requester has continued to characterize the functional development of medial temporal lobe structures using neurotoxic lesions and has found that the perirhinal cortex is a cortical structure crucial for the normal development of object recognition and cognitive inhibition. Its early insult may be relevant to the cognitive impairment observed in human cases of temporal lobe epilepsy without hippocampal sclerosis. Excluded by Requester discovered that early life stress (ELS) yields enduring impacts on brain serotonergic (5HT) function associated with increased activations of inflammatory processes, which provides novel biological mechanisms that work in parallel to increase levels of stress hormones. In collaboration with Excluded by Requester (DNND), she has begun a longitudinal, *in vivo*, neuroimaging study to examine in the same ELS animals the neurodevelopmental alterations leading to increased vulnerability to drug abuse. They have identified neurodevelopmental alterations in reward circuits that control emotional reactivity, stress responses, and motivation/reward/drug abuse. Excluded by Requester has pursued her developmental studies assessing how maternal factors, such as stress and obesity, both known to alter glucocorticoid signaling and produce a pro-inflammatory condition, influence the integrity of milk throughout lactation and consequently infant growth and health. Excluded by Requester discovered that intranasal oxytocin administration in infant monkeys increased the time spent viewing videos of facial expressions, but selectively reduced attention to the eyes in neutral faces in a dose dependent manner. The mechanism for this non-prosocial is still unknown but the results raise questions about the efficacy of implementing chronic intranasal oxytocin as a pharmacotherapy for the treatment of social deficits, particularly if given early in development. Excluded by Requester has demonstrated that early anesthesia (sevoflurane) exposure in the first month of life in rhesus macaques produces lasting cognitive and socioemotional impairments, and with faculty from the vaccine center, she has initiated a study to determine the consequences of postnatal Zika infection on neurobehavioral development. The preliminary data show significant changes in brain development and socioemotional behavior. Finally, as a refinement to our current permanent and transitory chemical lesions, we have significantly advanced the development of chemogenetic techniques (DREADDs: designer receptors exclusively activated by designer drugs) to temporarily activate or inhibit brain structures. Submitted

Submitted

Aim 2: ***Assessment of the importance of candidate genes in the expression of a range of phenotypes***: Excluded by Requester and collaborators Excluded by Requester have shown that low ranking females have more exaggerated pro-inflammatory responses to infection due to increased activity of the MyD88-dependent arm of the Toll-like receptor 4 signaling pathway while the TLR4 response in high-ranking females is polarized towards the TRIF-dependent arm, which is important in the anti-viral response. Excluded by Requester Excluded by Requester studies on ELS have also led to a recent NIH/NICHD R21 grant with Excluded by Requester to examine the longitudinal (and transgenerational) epigenetic changes that ELS produces throughout development in the same population of animals. The main goal is to understand the DNA epigenome methylation and non-coding RNA effects of ELS, and whether they predict some of the behavioral, physiological and drug abuse. Excluded by Requester and his team have established and published new paradigms that have helped to discover that rhesus monkeys possess the ability to perceive social dominance while viewing constructed artificial videos of unfamiliar monkeys interacting and to test several memory processes, such as recognition memory, recall, memory for lists, transitive inference, memory for the order of events, source memory and metamemory (ability to monitor own memory) while they remain in their social group. Finally, efforts have been made to begin a systematic and comprehensive characterization of behavioral, physiological, neurobiological and genetic phenotypes from the Yerkes breeding colony in order to facilitate subject assignments to breeding programs and research projects, and to enhance the development of nonhuman primate models of human health-related disorders and diseases. The information obtained will enhance colony management, provide leverage for NIH funding and create synergy across the multiple investigator-initiated research programs.

Aim 3: ***To expand use of neuroimaging tools***. Implementation of improved neuroimaging procedures has facilitated the realization of several projects as well as the initiation of new ones. Using the well-established, translational model of social subordination-induced chronic stress in female rhesus monkeys, Excluded by Requester has

shown that reduced binding potential of the dopamine 2 receptor (D2R) in the right orbitofrontal cortex and left dorsal lateral prefrontal cortex (PFC) is also associated with reduced functional connectivity (FC) between the left insular cortex and the anterior cingulate cortex (ACC) and this reduced FC predicts more caloric intake. Further, increased diurnal concentrations of plasma cortisol also predict reduced FC between the right and left nucleus accumbens (NAcc) and ACC that is associated with greater total caloric intake. Finally, in addition to plasma cortisol, elevations in the proinflammatory cytokine, IL-6, resulting from social subordination are associated with reduced medial PFC – NAcc FC that, in turn, predicts greater calorie intake. These patterns of FC between the PFC, insula, and striatum are not observed in females maintained on a healthier LCD, underscoring the importance of an obesogenic diet on these pathways. Further, Excluded by Requester and collaborator Excluded by Requester Georgia State University) have begun a new NIMH funded project (2016) to assess whether social dominance is differently regulated in males and females. Specifically, using PET neuroimaging, they are assessing sex differences in 5-HT receptor 1A binding to be used as predictors of stress physiology and social and emotional behavior. Neuroimaging tools have also been used to demonstrate the widespread brain reorganization following early insult to the hippocampus. Thus, these early lesions yield significant microstructural white matter changes in the hippocampal projection system (fornix, temporal stem, ventromedial prefrontal cortex and optical radiations) as assessed with Diffusion Tensor Imaging. Also, a recent resting state FMRI investigations of the same animals revealed altered functional interactions between the dorsolateral prefrontal cortex and core regions of the working memory network as well as the dorsal and ventral visual processing areas. These widespread neural changes correlate with some of the memory impairments that have been reported in the same animals. Using resting-state FMRI, Excluded by Requester showed that intranasal oxytocin in infant monkeys increased functional connectivity between the amygdala and brain regions involved in processing emotion and reward, but decreased the functional connectivity with other regions involved generally in social cognition.

Aim 4: ***The implementation of new automated procedures for animals leaving in large social group***. Eye-tracking procedures to capture the development of visual social engagement in infant monkeys have yielded significant results: (a) Through our current Autism Center for Excellence NIH grant, we have shown that the period of 4-8 weeks of age in monkeys (≈ 2-9 months for human infants) represents a critical period for the refinement of social skills, paralleled by fine-tuning of neural connections in social visual engagement pathways. The data provide a critically needed NHP model of early social development for autism that will be used in further investigations targeting gene-behavior relationships and therapeutic interventions for autism. The renewal of this P50 grant has been submitted in October 2016; (b) Studies are ongoing to investigate the cost-saving potential and clinical application of automated feeders compared to the traditional bin system; (c) during the last year, Excluded by Requester and collaborators have proceeded with developing an automated tracking system for monkeys in social groups. They have developed a prototype of a new RFID collar that will be worn by all tracked monkeys in their social group and are testing configurations for RFID sensors to be deployed in the monkey's compound.

Aim 5: Core and Affiliate Scientists in the Division have remained active in the mentoring of junior faculty, graduate and undergraduate students, and postdoctoral fellows pursuing a career in behavioral neuroscience and foster productive and continued successful collaborative relationships with investigators throughout the Emory campus. They also remained active in community outreach by conducting tours of Yerkes facilities and speaking at Center-approved community seminars.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00
2.						Core Faculty					9,255.00	2,286.00	11,541.00
3.						Core Faculty					8,901.00	2,199.00	11,100.00
4.						Core Faculty					5,922.00	1,463.00	7,385.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **41,567.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			3,616.00	893.00	4,509.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**4,509.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**46,076.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**46,076.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	46,076.00	20,734.00
		Total Indirect Costs	**20,734.00**

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)	**66,810.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: M&I

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Faculty in the Division of Microbiology and Immunology (M&I) apply a wide number of cutting-edge, interdisciplinary approaches in nonhuman primate (NHP) models to studies of the pathogenesis, prevention, and treatment of infectious diseases such as HIV & AIDS, hepatitis C, tuberculosis, group A streptococcus infection, and others. Scientists in M&I direct NIH-funded independent research programs and are heavily involved in productive and successful collaborative relationships with several research centers on the Emory campus, including the Emory Vaccine Center (EVC), the Center for AIDS Research (CFAR), and the Emory Transplant Center (ETC). In addition, faculty in M&I are very active in collaborative studies with extramural scientific institutions, both national and international (Scripps, Harvard, Penn, Rockefeller, Pasteur, and many others), to which they provide specific expertise and resources, mainly regarding the use of NHP models for studies of infectious diseases. Scientists within M&I also direct or advise a number of key core services, which include: (i) the Yerkes Virology Core, that plays a fundamental role in the colony management by testing the animals for agents such as Herpes B virus, STLV, SRV, SIV, and others; (ii) the Yerkes Genomics Core, which supports studies of NHP gene sequencing, expression and profiling by microarray as well as next-generation sequencing technology; and (iii) the CFAR Virology Core, that provides a broad range of virology assays for studies of HIV and SIV infections. Finally, scientists in M&I are an integral part of the training community at Emory University, with commitments to provide undergraduate, graduate and postdoctoral training and education, as well as community outreach efforts. In particular, they serve as members of the graduate faculty and as thesis advisors to students in the immunology, microbiology, and molecular pathogenesis programs at Emory University. The overarching goal of the M&I is to continue to develop new knowledge necessary to improve the prevention and treatment of infectious diseases that represent major threats to human health. To this end, the M&I faculty will continue to use and pioneer research techniques in the areas of cellular immunology, flow cytometry, basic virology, histology and immunohistochemistry, molecular biology, and genomics and genetics.

The Specific Aims are:

1.To enhance our scientific programs of excellence in the pathogenesis, prevention, and treatment of infectious diseases through the development and application of transformative scientific concepts, innovative technologies, and collaborative efforts with outside investigators at the national and international level;

2.To expand our focus to include a strong program in the area of tuberculosis, and to expand our current program in the area of HIV functional cure and eradication. This expansion will be conducted through active recruitment of several new faculty members for which significant resources have already been allocated;

3.To continue our significant commitment to training the next generation of scientists through undergraduate, graduate and postdoctoral programs and to foster community outreach educational efforts.

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_5990_MI.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

Please see the Overall component for response.

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

Plans: M&I scientists will continue to pursue and further expand their highly productive, cutting-edge research programs through the development of innovative scientific concepts, state-of-the-art technologies (including cell and molecular biology, flow cytometry, histology and immunohistochemistry, confocal microscopy, basic virology, transcriptome analysis, and in vivo imaging), and collaborative efforts to address key questions on the host-pathogen interaction occurring during infectious diseases such as HIV infection and AIDS, hepatitis C virus (HCV), malaria, tuberculosis, group A streptooccus, and others. This research effort will continue to fully leverage the unique NHP resources to directly test in vivo a range of concepts and products that are ultimately aimed at the prevention and therapy of these disease. In addition, M&I scientists will remain active at the national and international level with a wide range of collaborations with extramural colleagues, thus fulfilling the core mission of the Yerkes Center in terms of research resource and infrastructure. We do not anticipate any major problem in accomplishing this overarching set of goals given the well-established combination of expertise, technologies, and collaborations that is represented in the current portfolio of funded projects, or will soon be available for studies that are planned for the next funding period.

In particular, we will continue to enhance our scientific programs of excellence in the main areas of interest for M&I Core and Affiliate Scientists, which will continue to include: (i) basic, pre-clinical, and clinical studies of candidate HIV/AIDS vaccines, that we envision will continue to be conducted mainly as part of large collaborative program project grants and center grants (i.e., CHAVI-ID; CIAR; IPCAVD and HIVRAD program; etc.); (ii) basic, preclinical development of novel approaches for HIV/AIDS eradication, that we envision will continue to be highly productive in terms of high profile publications and funding of NIH grant applications. (iii) studies of AIDS pathogenesis using the comparative models of pathogenic and non-pathogenic SIV infection of RMs and SMs, respectively; (iv) studies of HCV pathogenesis and prevention,; and (iv) studies of other infectious agents/diseases, such as malaria, group A streptococcus, herpes viruses, etc. M&I scientists will also continue to serve as a resource for outside investigators who wish to establish collaborations to pursue hypothesis-driven studies in the areas of microbiology and immunology using NHP models.

We anticipate that scientists in M&I will maintain the strong scientific production that has consistently characterized the activity of the Division over the previous funding cycle (2011-2015). In this regard, we wish to emphasize that M&I is currently very well balanced in terms of experience and career stages of its Core and Affiliate scientists, with a roster that includes established, world-class investigators with large extramurally-funded programs together with very promising early stage and mid career investigators. In addition, Core Scientists within M&I will continue to direct or be actively involved in key core services with the Emory/Yerkes scientific community, including: (i) the Yerkes Virology Core, that plays a fundamental role in the colony management by testing the animals for agents such as Herpes B virus, STLV, SRV, SIV, and others; (ii) the Yerkes Genomics Core, which supports studies of NHP gene sequencing, expression and profiling by microarray as well as next-generation sequencing technology; and (iii) the Yerkes Biomarkers Core, which supports a broad range of in vivo NHP studies through the testing of many molecular biomarkers in blood and tissues; and (iv) the CFAR Virology Core, that provides a broad range of virology assays for studies of HIV and SIV infections, with an expanding focus on assays designed to measure the viral reservoirs in humans or macaques treated with antiretroviral therapy (ART). Finally, scientists in M&I will continue their significant commitment to training the next generation of scientists through undergraduate, graduate and postdoctoral programs and to foster community outreach educational efforts.

B.2. Accomplishments—M&I

Researchers in the Yerkes Division of Microbiology and Immunology (M&I) conduct studies in nonhuman primates (NHPs) that are focused on (i) understanding the dynamics of the host-pathogen interaction in the setting of infectious diseases; and (ii) developing novel strategies to prevent and treat these infections. These studies use outstanding scientific expertise, cutting-edge technology, and state-of-the-art experimental model to ultimately improve human health by lowering the burden of diseases such as HIV/AIDS, hepatitis C, Zika virus, Group A streptococcus infection, and other diseases. Scientists in M&I also hold faculty appointments at the Emory University school of Medicine, and at the Emory Vaccine Center (EVC), which is partly based within the Yerkes campus. The strong and productive interaction between M&I and EVC is emphasized by the fact that numerous EVC scientists are affiliated with M&I, and by the large number of funded projects and published articles featuring M&I and EVC scientists together. Finally, M&I scientists provide expertise to many national and international investigators seeking consultation or requesting use of Yerkes Center NHP resources for studies of infectious diseases.

Ongoing studies within M&I are focusing on the following key areas:
1. Preclinical and clinical development of novel HIV/AIDS vaccine candidates (effort led by Excluded by Requester, in which CD40L adjuvanted DNA/MVA vaccines are used in conjunction with native form of SIV or HIV envelope (Env) to optimize the cellular and humoral immune response to HIV/SIV antigens and therefore confer protection from challenge. These accomplishments are recognized with the five-year award of Consortium for Innovative AIDS Research in Non-Human Primates (NIH/NIAID UM1-AI1214436, PIs: Excluded by Requester
2. Preclinical development of novel approaches for HIV/AIDS eradication. These studies are led by Excluded by Requester and have led to successful for several NIH R01, R21/R33, and UM1 awards in the past 12 months, with projects focused on (i) targeting PD-1: PDL inhibitory pathway to achieve a functional cure for HIV infection; (ii) exploring the role of Interleukin-21, Interleukin-15, Interferon-α, and other immune-modulators to reduce the effect of residual immune activation on the size of viral reservoir in antiretroviral therapy (ART)-treated SIV-infected macaques; (iii) investigating the role of CD8+ lymphocytes in suppressing virus production and virus reactivation in the setting of short-term and long-term ART; and (iv) assessing the potential efficacy of immune interventions aimed at selectively reducing the level of virus reservoirs in cells belonging to the monocyte/macrophage linage, and particularly in the central nervous system.
3. Studies of AIDS pathogenesis using the comparative models of pathogenic and non-pathogenic SIV infection of rhesus macaques (RM) and sooty mangabeys (SM). These studies led to the completion—for the first time—of a high quality whole genome sequencing and assembly of the SM, and a genome-wide comparative analyses of transcript assemblies with RM and humans. This analysis identified a C-terminal frameshift in the SM TLR4 gene, associated with blunted *in vitro* response to TLR4 ligands, and a major structural change in exons 3-4 of ICAM-2, which abrogates its cell surface expression. These data provide a novel resource for comparative genomic studies of HIV/SIV pathogenesis and may elucidate the mechanisms by which SIV-infected SMs avoid AIDS.
4. Studies of Hepatitis C Virus (HCV) pathogenesis and prevention, led by Excluded by Requester with a major focus on (i) the definition of the structure of hepatitis C virus envelope surface glycoprotein E2, which binds to the host cell through interactions with SR-BI and CD81, and serves as a target for neutralizing antibodies, and (ii) the establishment of a novel, NHP model to better study this infection *in vivo*. These data provided unprecedented insights into HCV entry and will assist in developing an HCV vaccine and new inhibitors.
5. Studies of Zika virus infection in rhesus macaques, with focus on the development of persistent neurocognitive abnormalities and neuropathology in infants infected with Zika virus, as well as testing the protective efficacy of Zika virus-specific neutralizing antibodies as well as candidate vaccines in both adult and infant rhesus macaques.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5990

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			9,255.00	2,286.00	11,541.00
2.						Core Faculty					9,255.00	2,286.00	11,541.00
3.						Core Faculty					6,675.00	1,649.00	8,324.00
4.						Core Faculty					0.00	0.00	0.00
5.						Core Faculty					7,323.00	1,809.00	9,132.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **40,538.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			3,664.00	905.00	4,569.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**4,569.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**45,107.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**45,107.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	45,107.00	20,298.00
		Total Indirect Costs	**20,298.00**

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)	**65,405.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: NND

Component Project Lead Information:

Excluded by Requester

B. COMPONENT ACCOMPLISHMENTS

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

Faculty in the Division of Neuropharmacology and Neurologic Diseases (NND) use interdisciplinary approaches in nonhuman primate models to study a variety of translational problems in neuroscience including neurodegenerative diseases (Parkinson's, Huntington's, Alzheimer's), basal ganglia and motor function, neurobiology of drug addiction, and evolutionary biology. Our long-term goal is to develop new knowledge necessary for improved treatment of specific neurological and psychiatric disorders. Research techniques include behavioral models, neuropharmacology, neurochemistry, neuroanatomical mapping, electrophysiology, in vivo microdialysis, gene expression and profiling, transgenic models, optogenetics and functional brain imaging. The Yerkes Imaging Core plays a fundamental role in the NND, and faculty within the Imaging Core have appointments as Core Scientists or Affiliate Scientists within NND. Core Scientists within NND serve as an intellectual resource for the study of neuroscience in nonhuman primates for local, regional, national, and international investigators. Each staff scientist provides expertise to outside investigators seeking consultation or requesting use of the Yerkes Center resources. In addition, the Core Scientists are an integral part of the training and scientific community at Emory University with commitments to provide undergraduate, graduate, and postdoctoral training and education and foster productive and successful collaborative relationships with other investigators on the Emory campus. Most research scientists in NND are members of the graduate faculty at Emory University and serve as thesis advisors to students in the neuroscience and the molecular and systems pharmacology training programs. Lastly, there is a strong commitment to community outreach efforts at local area schools and educational organizations.

The Specific Aims are:

1.To enhance our scientific programs of excellence in neurodegenerative diseases, drug addiction and evolutionary biology through the development and application of innovative technologies and collaborative efforts with outside investigators at the national and international level;
2.To expand our focus to include a strong program of research in stroke and neurovascular function in the context of functional brain imaging through the active recruitment of an endowed faculty appointment;

3.To continue our significant commitment to training the next generation of scientists through undergraduate, graduate, and postdoctoral programs and to foster community outreach educational efforts.

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_5994_NND.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

Please see the Overall component for response.

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

NND scientists will continue to enhance their research programs through the development of innovative technologies and collaborative efforts. Several ongoing studies are directed towards a better understanding of the role of changes in thalamic activity in Parkinson's disease. Optogenetic techniques will be further refined and employed to examine the functional effect of the thalamostriatal projections in normal and parkinsonian rhesus monkeys. Additional efforts will evaluate the neuroprotective properties of anti-inflammatory agents on MPTP-induced loss of midbrain dopaminergic neurons in rhesus monkeys. The Yerkes Imaging Core recently validated a PET ligand that is sensitive to microglia activation in response to neuroinflammation. Hence, a tool is available for in vivo evaluation of neuroinflammation in the MPTP model of parkinsonism. The Emory Udall Parkinson's Disease Center headed by Excluded by Requester is expected to continue to play a significant role in fostering collaborations with outside investigators, including the Udall Center component at Vanderbilt University. Additional studies will focus on NHP models of human inherited neurodegenerative diseases, including Huntington's and Alzheimer's, developing transgenic reporter cells for noninvasive MRI, and developing personal stem cells for cell therapy. These animal models are expected to lead to a greater understanding of the underlying biology of these neurodegenerative diseases and to the development of potential therapies. Research efforts focused on drug addiction will pursue the evaluation of MDMA and amphetamine analogs as prosocial drugs with therapeutic potential. Social deficits and social anxiety are often present with major components of many common psychiatric disorders such as PTSD, autism, and depression. Studies previously conducted in squirrel monkeys will be extended to rhesus monkeys in the context of fMRI in fully conscious subjects.

We are committed to expand our research focus to include a strong program of research in stroke and neurovascular function in the context of functional brain imaging. We recently recruited the Yerkes Center's first endowed chair in the area of stroke and neuroimaging. Excluded by Requester joined the NND faculty and holds a joint appointment in the Department of Neurology. The major goal of Excluded by Requester research at Yerkes is to establish a preclinical program on novel stroke interventions and therapeutics that successfully translates to human use. In addition, Excluded by is investigating the role of vascular disease in the development of dementia by determining, in aged nonhuman primates, the relationship between imaging anomalies in MRI and cerebral amyloid angiopathy. His research program is well positioned to complement our nonhuman primate stroke research and enhance our understanding of neurovascular function. In addition, Excluded by Requester has an active collaboration with Excluded by to evaluate vascular anomalies associated with cocaine self-administration in squirrel monkeys.

Lastly, we will continue our significant commitment to training the next generation of scientists through undergraduate, graduate, and postdoctoral programs and to foster community outreach educational efforts. As noted above, NND Core Scientists and Affiliate Scientists are an integral part of the training and scientific community at Emory University with commitments to provide undergraduate, graduate, and postdoctoral training and education. Our faculty are highly engaged in seminars, lectures in ethics, student retreats and other program activities. Our faculty also host undergraduate students through various mechanisms to gain research experience during the summer months. Lastly, there is a strong commitment to community outreach efforts at local area schools and educational organizations. Many of these activities are coordinated through the Yerkes Office of Public Affairs and focus on educating the public on the importance of animal and nonhuman primate research in science and medicine. Our faculty are committed to continue these efforts in training and community outreach.

B.2. Accomplishments—Division of Neuropharmacology and Neurologic Diseases (NND)

Researchers in the Yerkes Division of Neuropharmacology and Neurologic Diseases (NND) are working to advance the understanding of brain function through studies focusing on the development and function of the nervous system and anatomical differences seen when neurological disorders are present. Faculty in the Division use interdisciplinary approaches in nonhuman primate models to study a variety of translational problems in neuroscience, including neurodegenerative diseases (Parkinson's, Huntington's and Alzheimer's), basal ganglia and motor function, neurobiology of drug addiction, and evolutionary biology. Our long-term goal is to develop the knowledge necessary for improved treatment of specific neurological and psychiatric disorders. Our scientists are highly collaborative with researchers in other Yerkes Divisions, and they provide expertise to regional, national and international investigators seeking consultation or requesting use of Yerkes Center resources.

Ongoing studies within NND have identified pharmacologic targets that could serve to develop new treatments for the long-term therapy of Parkinson's disease. Specific efforts have been directed at the role of striatal glutamatergic transmission in the pathophysiology of abnormal responses to levodopa. Additional findings have advanced our understanding of the importance of striatal neuron pathology in the transmission and integration of corticostriatal information in Parkinson's disease. An ongoing project uses a combination of anatomical and electrophysiological approaches to determine the plastic changes induced in the synaptic microcircuitry of the striatum due to spine loss and its functional consequences on the physiology of the corticostriatal system. These major accomplishments were recognized with the five-year renewal of the Udall Parkinson's Disease Center at Emory University: Circuitry to Therapy (NIH/NINDS P50, PI: Excluded by Requester Excluded by Requester. This P50 continues a Center of Excellence in Parkinson's disease research at Emory University focused on translational studies of the basal ganglia-thalamocortical circuitry and the development of new medication therapies for Parkinson's disease. Research focused on Alzheimer's disease has directed efforts toward phenotyping cases of Alzheimer's disease, with a growing focus on proteomic analysis of Alzheimer's disease cases and animal models. Ongoing efforts focused on Huntington's disease have produced and characterized second generation Huntington's disease in nonhuman primates and two have confirmed germline transmission. The Principal Investigator, Excluded by Requester recently received a five-year competing renewal of this R24 grant to continue these high impact studies in a nonhuman primate transgenic model of Huntington's disease.

There is significant interest in ketamine as a therapeutic for a number of diverse psychiatric disorders, including drug addiction. The general aim of a project headed by Excluded by Requester s to validate a constant-infusion ketamine model using fMRI in fully conscious rhesus moneys to examine activation/deactivation profiles of ketamine in brain regions known to be associated with drug addiction. The protocols developed will have significant utility in defining drug mechanism of action at a neurochemical and brain circuit level of analysis. Lastly, NND Core Scientists and Affiliate Scientists are an integral part of the training and scientific community at Emory University with commitments to provide undergraduate, graduate, and postdoctoral training and education. Most scientists in NND are members of the graduate faculty at Emory University and serve as thesis advisors to students in the neuroscience and pharmacology training programs. This has proven to be an excellent opportunity for students to interact with well-known researchers in their field of interest. Moreover, the Udall Center provides educational opportunities for students, postdoctoral fellows, and neurology/neurosurgery residents and fellows, such as lectures and hands-on training.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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-5994

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

ORGANIZATIONAL DUNS*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.		Excluded by Requester				Project Lead	Institutional Base Salary	EFFORT			3,702.00	914.00	4,616.00
2.						Core Faculty					7,199.00	1,778.00	8,977.00
3.						Core Faculty					6,052.00	1,495.00	7,547.00
4.						Core Faculty					9,129.00	2,255.00	11,384.00
5.						Core Faculty					9,255.00	2,286.00	11,541.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **44,065.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
1	Secretarial/Clerical	0.6			2,438.00	602.00	3,040.00
1	**Total Number Other Personnel**					**Total Other Personnel**	**3,040.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**47,105.00**

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**47,105.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	47,105.00	21,197.00
		Total Indirect Costs	**21,197.00**

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)	**68,302.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Pilot Projects

Component Project Lead Information:

JOHNSON, R. PAUL

B. COMPONENT ACCOMPLISHMENTS

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

The overarching goal of the Yerkes Pilot Research Project Program is to support innovative biomedical or behavioral pilot research projects involving nonhuman primates. The process of obtaining NIH funding for translational research projects involving nonhuman primates in today's funding environment is extremely challenging. The success rates of NIH proposals remain quite low and without preliminary data, the prospects for funding are negligible. Moreover, the barriers to generate preliminary data for research projects involving nonhuman primates, especially for investigators not previously experienced in nonhuman primate research, are considerable. However, the continued advancement of translational research requires a sustained influx of new ideas, new approaches and new investigators. The goal of the Yerkes Pilot Research Program is to facilitate the translation of new ideas and new approaches, as well as the involvement of new investigators into NIH-funded research proposals involving nonhuman primates. These projects, by their nature, are developmental and higher risk, but also high reward, in that they form the foundation for future grant proposals and for future advances in the use of nonhuman primate models to address basic and translational problems in human health.

The Specific Aims are:

1.To promote basic and translational biomedical and behavioral pilot research projects involving nonhuman primates;
2.To promote these developmental projects by providing both seed funding and the critical expertise of Yerkes Core Scientists in the conduct of nonhuman primate research and the development and optimization of nonhuman primate disease models;
3.To support the career development of young investigators by prioritizing the funding of young investigators without prior R01-equivalent funding.

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_5995_Pilots.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

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

File uploaded: B4_c Training.pdf

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

Please see the Overall component for response.

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

The Pilot Research Program RFA for the next project period will be released in February 2018. The RFA will be broadly distributed, both within the Emory community and beyond, as described in detail under the Accomplishments section (B2). In addition, the announcement will be distributed nationally by posting on the Yerkes website as well as the NPRC Consortium website hosted by Excluded by Requester

Following the receipt of applications, the review of applications will be carried out by the Yerkes National Scientific Advisory Board (NSAB). Each member will be assigned between 5 to 7 applications and asked to provide an overall impact factor using the standard NIH 1-9 scale, and using the standard review criteria, along with brief written comments. The collated scores and comments will be reviewed by the Center Director and the Associate Director for Scientific Programs for the selection of final projects. Applications from early career investigators will be given particular consideration. Applicants will be notified and projects initiated in May 2018.

We will continue to explore ways to increase the breadth of distribution of the Yerkes Pilot Project RFA, especially to engage investigators outside Yerkes and those who have not previously used nonhuman primates.

B.2. Accomplishments—Pilot Research Program

Overview

The goal of the Yerkes Pilot Research Program is to facilitate the translation of new ideas and new approaches, as well as the involvement of new investigators into NIH-funded research proposals involving nonhuman primates. These projects, by their nature, are developmental and higher risk, but also high reward, in that they form the foundation for future grant proposals and for future advances in the use of nonhuman primate models to address basic and translational problems in human health.

The Specific Aims, which are unchanged, include:

1. To promote basic and translational biomedical and behavioral pilot research projects involving nonhuman primates.
2. To promote these developmental projects by providing both seed funding and the critical expertise of Yerkes Core Scientists in the conduct of nonhuman primate research and the development and optimization of nonhuman primate disease models.
3. To support the career development of young investigators by prioritizing the funding of young investigators without prior R01-equivalent funding.

Description of the Pilot Project Program

The Yerkes Pilot Project Program is operated in accordance with the Office of Research Infrastructure Programs (ORIP) guidelines and designed to fund projects that aim to solve problems related to human health, as well as paving the way for subsequent independent grant support. The Yerkes Pilot Research awards each currently provide one year of support, up to $70,000 in direct costs. In addition, projects must meet the following criteria:

- Pilot research funds may not be used to provide interim support for established projects or for investigations funded from other sources;
- All Pilot Research Projects must be planned, conducted, and carried out under the supervision of at least one Core Scientist at the NPRC. A Core Scientist must assume responsibility for overall management, coordination and progress reports;
- All activities related to the use of NHPs must be conducted on-site at Yerkes. Other activities can be performed at other sites, depending on the nature of the pilot project.

The Pilot Research Program RFA is released in February or March. The RFA is broadly distributed, both within the Emory community and beyond. The RFA is distributed to the Emory School of Medicine Faculty listserv, the Yerkes Faculty listserv, the Emory CFAR listserv, the listserv for the Georgia CTSA, as well as the listserv for the Woodruff Health Science Research Administrators (which includes the School of Medicine, the Rollins School of Public Health, the School of Nursing and the Winship Cancer Center) and also to the Research Deans of the Laney Graduate School and the Emory College of Arts and Sciences for distribution to their faculty. These research administrators and/or Deans in turn distribute to their internal and external distribution lists. It is also distributed to the Atlanta Veterans Affairs Medical Center. In addition, the announcement is distributed nationally by posting on the Yerkes website as well as the NPRC Consortium website hosted by Excluded by Requester

Following the receipt of applications, the review of applications is carried out by the Yerkes National Scientific Advisory Board (NSAB). Each member is assigned between 5 to 7 applications and asked to provide an overall impact factor using the standard NIH 1-9 scale, and using the standard review criteria (Significance, Approach, Innovations, Investigator, Environment), along with brief written comments. The collated scores and comments are reviewed by the Center Director and the Associate Director for Scientific Programs for the selection of final projects. Applicants are then notified and projects are typically initiated in May.

We received 17 applications for our 2016 cycle of pilot projects. Following review by our NSAB, the three projects below (which include one PI outside of Yerkes and one Early Career Investigator), were selected for funding. Project summaries for each of these projects follow.

Neurodevelopmental consequences of Zika virus infection in infant rhesus macaques

PI: Excluded by Requester Core Scientist: Excluded by Requester

Performance Period: 05/01/2016-04/30/2017

Summary: Zika virus (ZIKV) infection can have devastating neurologic consequences for infants infected in utero. Little is known, however, about the impact of ZIKV infection close to the time of delivery or in the period of infancy. To address this gap, we developed a model of postnatal ZIKV infection in infant rhesus macaques (RMs). Six infant RMs were challenged with ZIKV with peak viral loads in plasma at day 2-3 that cleared by day 10 after infection. Infant RMs developed anti-ZIKV binding IgG and IgM antibodies as well as neutralization titers in plasma. Structural T1-weighted magnetic resonance imaging (MRI), resting-state functional MRI, and Diffusion Tensor Imaging (DTI) performed at three and six months of age revealed increased size of the lateral ventricles, microstructural alteration in the corpus callosum, and reduction in the functional connectivity of the primary motor (M1) and somatosensory (S1) cortices in ZIKV-infected infant RMs as compared to age-matched controls. ZIKV-infected infants also showed emotional dysregulation during the Human Intruder task, failing to demonstrate the species-typical freezing behavior in response to an acute social stressor as compared to similarly reared controls. In summary, Submitted

Submitted

Developing a novel optogenetic monkey model

PI (and Core Scientist): Excluded by Requester

Performance Period: 05/01/2016-04/30/2017

'Optogenetics', the introduction of light-sensitive channels into specific neurons that allows researchers to modulate the activity of these neurons by light in subsequent neurophysiological experiments, has revolutionized physiologic experimentation in rodents, facilitated by the availability of mature genetic tools and large numbers of transgenic rodent strains. However, the application of this technique to non-human primates (NHPs) has significantly lagged behind, in part because transgenic NHP lines are not readily available. Our ultimate goal is to develop a genetically modified NHP model to accelerate the application of optogenetic techniques in NHPs. This pilot study will allow us to develop and validate the necessary constructs and vectors, and generate preliminary data that will then enable us to apply for federal funding for this project.

We have created conditional expression constructs for expressing opsin expression. cDNA for two constructs were cloned into lentiviral vectors (LVs), both under the regulation of the Ubi promoter. These include (1) a construct for red fluorescent protein (DsRed) with a STOP codon flanked with two loxP sequences and a fusion gene containing the sequence for green fluorescent protein (GFP) and Jaws (Jaws/GFP) named "LV-floxed-Jaws", and (2) a construct for yellow fluorescent protein (YFP) with a STOP codon flanked with two loxP sequences and a fusion gene containing the td-Tomato (tdT) and Chronos (Chronos/tdT) sequences, named "LV-floxed-Chronos". To create LVs for expressing Cre-recombinase under tyrosine hydroxylase (TH) promoter control, cDNA of Cre-recombinase and mOrange fluorescent protein (mO) was co-expressed by 2A peptide and cloned into the LV under the regulation of the TH promoter, generating the "LV-TH-Cre/mO" vector. All vectors have been created and currently assessing conditional expression of opsins.

Biological signatures of stress in mice and macaques

PI: Excluded by Requester Core Scientist: Excluded by Requester

Performance Period: 05/01/2016-04/30/2017

Adverse natural and anthropogenic events contribute to the development of neuropsychiatric disorders not only in individuals directly exposed to these events, but also in descendant generations, as reflected in recent studies of offspring of Holocaust survivors. Identifying and reversing biological mechanisms that underlie the development of neuropsychiatric disorders in these vulnerable populations requires an understanding of the

biological signatures of stress exposure within somatic and germ cells of the population directly experiencing stress. Using a mouse model of paternal stress ([redacted] Laboratory), two models of social stress in the non-human primate ([redacted] Laboratories), and in collaboration with the Yerkes Genomics Core, the goal of this proposal is to examine how stress experienced by mice and rhesus macaques alters miRNA in circulating exosomes, cerebrospinal fluid (CSF) and sperm.

We exposed mice to olfactory stress and sequenced RNA present in circulation and sperm. In addition, we are in the process of isolating RNA from the non-human primate samples and will be sequencing this RNA within the next few months. Once these data are collected we will be using bioinformatics approaches to ascertain RNAs that are altered across these species as a function of stress. In so doing, we will illuminate conserved signatures of stress across species.

B.4. Training and Professional Development Opportunities

Please see the overall component for response.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	Dr	Robert	Paul	Johnson		Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

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

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

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

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

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

RESEARCH & RELATED BUDGET - SECTIONS F-K

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Pilot Projects $70,000 x 3	210,000.00
Total Other Direct Costs	**210,000.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**210,000.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	210,000.00	94,500.00
		Total Indirect Costs	**94,500.00**

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)	**304,500.00**

J. Fee	Funds Requested ($)*
	0.00

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

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

Budget Justification

The budget request for the upcoming period is submitted in accordance with the peer reviewed P51 renewal approved in 2016. Justification for each budget category was also peer reviewed and approved at that time, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Outreach

Component Project Lead Information:

JOHNSON, R. PAUL

B. COMPONENT ACCOMPLISHMENTS

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

The Yerkes Public Affairs (PA) Office directs the Yerkes Research Center's Outreach and Community Engagement as well as its Public Relations. For the purpose of this P51 Base Grant submission, there will be two related components: this Outreach component and a separate component for Public Affairs/Public Relations under the Administrative component.

The PA Office is responsible for increasing recognition of Yerkes as a premier research center dedicated to conducting essential basic science and translational research to advance scientific understanding and to improve human health and wellbeing. To achieve this mission, the PA Office works proactively in the multiple, complementary areas of Outreach and Public Relations. Specific activities that fall under Outreach include:

•Tours
•Community and Educational Outreach, including speakers' bureau placements
•Educational internships
•Yerkes website
•Lunch and Learn programs
•Special Events, Meetings and Presentations
•Publications
•Government Relations
•Special Projects as strategically determined and/or requested by the Center Director

In the arena of educational initiatives, PA coordinates tours of the Main Station and Field Station for educational, community and other groups as appropriate, and offers at least two Field Station Open Houses annually for neighbors, community talk participants and others. In addition, PA facilitates approval of tour requests Yerkes employees submit for their family, friends, colleagues and others. PA also places speakers in the community and at schools, coordinates educational internships at the Center, manages the Yerkes website and also educates employees about Center research and other topics via the Lunch and Learn program. Each year, the Yerkes PA Office coordinates National Primate Research Center representation at the annual Society for Neuroscience meeting to educate researchers about the expertise and resources that the National Primate Research Centers offer. The Yerkes PA Office provides information to Emory publications to educate the greater Emory community about the Yerkes Research Center and provides information to elected officials to keep them informed about our Center.

The Specific Aims are:

1.To maintain a proactive approach to outreach;

2.To continue organizing community and educational outreach opportunities, and to use those opportunities to connect the Center's research whenever possible to improvements in human health;

3.To partner with other National Primate Research Centers, organizations and others strategically identified to extend the reach of Yerkes-related information.

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_5996_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?

Please see the Overall component for response.

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

During the next year, the Yerkes National Primate Research Center PA Office will continue to be proactive in its approach to educating employees, the Emory community, the greater metro Atlanta community and others about the Yerkes Research Center as well as the NPRC program.

We are again organizing a continuing education eight-part series about Yerkes-based research; this time, most speakers are Yerkes graduate students and post-doctoral fellows. We are also planning for our next Field Station Open House and are in discussion with organizers of the Atlanta Science Festival to begin planning a Yerkes presence at the March 2018 expo event.

As this report is being submitted, organizers of this summer's Institute on Neuroscience are reviewing applications; a goal for the teacher-developed curriculum materials is for them to make a clear connection between research with animals and the promise of improved human health. Also, we want to ensure the materials can be adapted for use in middle school as well as high school. Reaching more middle school students is a goal.

Another goal is to partner with other organizations to extend the reach of Yerkes information. The NPRCs are working with SfN to determine how we can extend our reach to the organization's membership and annual meeting attendees, and Yerkes Chief of Public Affairs now serves on the board of Americans for Medical Progress, which is providing opportunities to share animal research and Yerkes-specific messages with representatives from non-profit, research and corporate entities.

Soon, we will be able to give these new contacts a feature article about Yerkes. Emory's Woodruff Health Sciences Center is reviving its Emory Health magazine, and Yerkes research will be highlighted in the first issue.

B.2. Accomplishments—Outreach

The Yerkes Public Affairs (PA) Office is responsible for increasing recognition of Yerkes as one of the seven National Primate Research Centers fighting disease and improving human health by making breakthrough discoveries possible. To achieve this, the PA Office directs the center's Outreach and Community Engagement. PA staff also works in the areas of media relations, issues management, emergency preparedness in collaboration with Yerkes Facilities Management, and special projects, all of which are reported in another section within this progress report.

Falling under Outreach and Community Engagement are: Tours; Community and Educational Outreach, including speakers' bureau placements; Educational internships; Yerkes website; Special Events, Meetings and Presentations; Publications; Government Relations; and Special Projects as strategically determined by the Center Director.

This year, the center reached more than 1,250 people via our tour program, including our two Field Station Open Houses and a tour for science teachers from across Georgia who attended the annual Georgia Science Teachers Association meeting. We also coordinated two continuing education eight-part series featuring Yerkes researchers and again partnered with Georgia State University and Emory University to offer the Institute on Neuroscience, which gives high school students and middle and high school teachers hands-on research experience during the summer.

Again this year, the Yerkes PA Office coordinated the National Primate Research Center's participation in the annual Society for Neuroscience meeting, including managing our sponsorship of the Animals in Research panel. Also, the Yerkes PA Office provided information to Emory publications to educate the greater Emory community about the Yerkes Research Center and worked with Emory's Government Affairs department to provide information to elected officials to keep them informed about our Center and our research advancements.

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	Dr	Robert	Paul	Johnson		Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

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

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	5,014.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**5,014.00**

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*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	300.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Expenses	5,100.00
Total Other Direct Costs	**5,400.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**10,414.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	10,414.00	4,686.00
		Total Indirect Costs	**4,686.00**

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)	**15,100.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: H_5996 Budget Justification.pdf
(Only attach one file.)

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

Budget Justification—Outreach

The budget request for the upcoming period is submitted in accordance with the budget discussed with and approved by the program director. The budget request for this component includes the Outreach and Public Relations working group budgets, and there is no significant change in this budget request from previously approved levels.

A. COMPONENT COVER PAGE

Project Title: Consortium

Component Project Lead Information:

JOHNSON, R. PAUL

B. COMPONENT ACCOMPLISHMENTS

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

The mission of the Nonhuman Primate Research Centers Consortium is to strengthen communications, leverage system-wide resources and facilitate sharing of information and best practices. The Consortium Working Groups comprise experts from major disciplines within each center who collaborate to address priority issues, challenges and opportunities that the National Primate Research Center Directors identify at national and local levels.

The Nonhuman Primate Research Centers Consortium began in 2007 to enhance cooperation between the National Primate Research Centers and the NIH Office of Research Infrastructure Programs. The Consortium now has nine Working Groups with representation from all of the National Primate Research Centers and two additional Working Groups with focused representation.

The National Primate Research Center Directors oversee the Consortium in conjunction with the NIH Division of Program Coordination, Planning, and Strategic Initiatives. This oversight includes monitoring progress and reviewing and approving annual budgets.

The Specific Aim is:

1.To continue to strengthen the NPRC Consortium and each of its Working Groups as resources to National Primate Research Center faculty and staff, the NIH and researchers nationwide.

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_5997_Consortium.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?

Our overarching goal continues to be to strengthen the NPRC Consortium and each of its Working Groups as resources to National Primate Research Center faculty and staff, the NIH and researchers nationwide.

Each Working Group submits annual plans to the NIH Division of Program Coordination, Planning, and Strategic Initiatives. Portions of those plans specific to the Yerkes Research Center are listed below.

Behavioral Management
The Yerkes Behavioral Management unit will continue to contribute to the Behavioral Management Working Group by writing joint publications, conducting grant-supported, collaborative research on animal management, sharing staff training information, finalizing the welfare report and working to ensure that this Consortium Working Group is a national resource.

Breeding Colony Management
The Yerkes Colony Management unit will continue to contribute to the ongoing efforts of the Breeding Colony Management Working Group. In addition, Yerkes will collaborate with the Behavioral Management Working Group to help prioritize future projects and provide information as requested.

Clinical and Surgical Techniques
Yerkes veterinary personnel will continue helping develop the lecture schedule, participating in monthly conferences and discussions, and developing guidelines through the use of surveys, questionnaires and discussions. Yerkes will also continue to provide written narratives and presentations for the Working Group's library.

Genetics & Genomics
The Yerkes team will continue to optimize the Fluidigm EP1 SNP genotyping platform to improve throughput and decrease cost for these analyses. They will also continue to facilitate the distribution of nonhuman primate genetic material.

Integrity-Compliance

The Yerkes Veterinary Medicine unit will contribute to the Integrity and Compliance Working Group by continuing to participate in quarterly calls, sharing information about the topics discussed and participating in discussions about the role of a training program in maintaining and monitoring compliance.

Occupational Health & Safety
The Yerkes Environmental Health and Safety unit will continue to chair the Occupational Health & Safety Working Group. This responsibility includes developing meeting agendas, chairing calls and the annual meeting, and taking minutes. Yerkes personnel will also continue to maintain contact with the B-virus lab at Georgia State University and share SOPs, data about injury and illness, and costs for supplies.

Outreach
The Yerkes Public Affairs unit will contribute to the Outreach Working Group by continuing to participate in monthly calls and the annual meeting, sharing information, representing all National Primate Research Centers at the annual Society for Neuroscience meeting and managing the Centers' two-year sponsorship of its Animals in Research panel, and continuing to provide information to and promote the nprcresearch.org website.

Public Relations
The Yerkes Public Affairs unit, which chairs the Public Relations Working Group, will continue to participate in monthly calls and the annual meeting, leading efforts to coordinate national public relations activities, and providing information to and promoting the nprcresearch.org website, as well as the public-facing website, which is currently in development.

Pathology
The Yerkes Division of Pathology will continue fulfilling and supporting the Working Group's goals to: provide instruction to lab animal and pathology residents, as well as veterinary students enrolled in the McClure Training Program; facilitate collaboration with and provide support to veterinary pathologists from the other National Primate Research Centers and schools of veterinary medicine; facilitate consultation with other veterinary pathologists and researchers; and serve as a repository of digital slides from classic pathological conditions of nonhuman primates.

Phenotype Mining and New Model Development (PMNMD)
Yerkes participants in the PMNMD will help advance NHP model development by coordinating the discussion and comparison of common NHP traits documented at the NPRCs. Specific phenotypes being examined on a cross-center basis include Behavioral Inhibition/Anxiety, Left Ventricular Hypertrophy (LVH), and SIV Elite Controllers.

Rigor and Reproducibility Working Group
The Rigor and Reproducibility Working Group is still getting underway, so the full scope of activities have yet to be defined, but Yerkes personnel will participate actively to help define the scope of activities and to help identify best practices across the NPRCs that will help support the NIH's goal of ensuring the highest degree of rigor and reproducibility for NHP research.

Training
The two residents currently in training within the Yerkes Veterinary Medicine unit will continue to present to their colleagues, focusing on either a clinical case or the results of their research projects with nonhuman primates. Clinicians will continue to participate in the monthly Virtual Grand Rounds.

Zika
Yerkes members of the Zika Working Group will continue to work together with the other members to assure data sharing; coordinate Zika research projects among Centers; discuss the potential for sample storage and sample sharing, both ongoing and at necropsy; promote the sharing of SOPs for diagnostic assays; and promote the harmonizing of Zika virus diagnostic assays.

B.2. Accomplishments—Consortium

The Nonhuman Primate Research Centers Consortium began in 2007 to enhance cooperation between the National Primate Research Centers and the NIH Office of Research Infrastructure Programs. The Consortium now has 13 Working Groups with representation from all of the National Primate Research Centers and two additional Working Groups with focused representation. The mission of the Nonhuman Primate Research Centers Consortium is to strengthen communications, leverage system-wide resources and facilitate sharing of information and best practices among the NPRCs. The Consortium Working Groups comprise experts from major disciplines within each center who collaborate to address priority issues, challenges and opportunities that the National Primate Research Center Directors identify at national and local levels. The National Primate Research Center Directors oversee the Consortium in conjunction with the NIH Division of Program Coordination, Planning, and Strategic Initiatives. This oversight includes monitoring progress and reviewing and approving annual budgets.

The overall Specific Aim, which is unchanged, is to continue to strengthen the NPRC Consortium and each of its Working Groups as resources to National Primate Research Center faculty and staff, the NIH and researchers nationwide.

Yerkes employees participate in a number of the NPRC Consortium Working Groups; specific members for each of the groups are listed below.

Working Group	Yerkes Representative/s
Behavioral Management	Excluded by Requester
Breeding and Colony Management	
Clinical And Surgical Techniques	
Genetics and Genomics	
Integrity/Compliance	
Occupational Health and Safety	
Outreach	
Pathology	
Phenotype Mining and New Model Development	
Public Relations	
Rigor and Reproducibility	
Training	
Zika	

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*: 066469933

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	Dr	Robert	Paul	Johnson		Project Lead	Institutional Base Salary	EFFORT			0.00	0.00	0.00

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **0.00**

B. Other Personnel

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

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

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

ORGANIZATIONAL DUNS*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	7,542.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**7,542.00**

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*: 066469933
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: EMORY UNIVERSITY

Start Date*: 05-01-2017 **End Date*:** 04-30-2018

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

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**7,542.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. MTDC	45.0	7,542.00	3,394.00
		Total Indirect Costs	**3,394.00**

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)	**10,936.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: H_5997 Budget Justification.pdf
(Only attach one file.)

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

Budget Justification—Consortium

The budget request for the upcoming period is submitted in accordance with the budget discussed with and approved by the program director. The budget request for this component includes the following working group budgets:

- Behavioral Management Consortium (BMC)
- Breeding Colony Management Consortium (BCMC)
- Genetics and Genomics Working Group (GGWG)
- Occupational Health and Safety (OHS)
- Rigor and Reproducibility Working Group (RRWG)
- Zika Working Group

There is no significant change in this budget request from previously approved levels.