BIOLOGICAL MATERIALS RESOURCE GRANTS **Federal Award Date:** 12/22/2018

Department of Health and Human Services
National Institutes of Health

OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Grant Number: 5P40OD012217-32
FAIN: P40OD012217

Principal Investigator(s):
Melween I. Martinez, DVM

Project Title: CARIBBEAN PRIMATE RESEARCH CENTER

Ms. Gloria Cruz
University of Puerto Rico Medical Science Campus
PO BOX 365067
San Juan, PR 00936

Award e-mailed to: enga.rcm@upr.edu

Period Of Performance:
Budget Period: 12/01/2018 – 11/30/2019
Project Period: 04/15/1987 – 11/30/2020

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $2,283,320 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF PUERTO RICO MED SCIENCES in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

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

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number P40OD012217. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

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

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

Sincerely yours,

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

Additional information follows

SECTION I – AWARD DATA – 5P40OD012217-32

Award Calculation (U.S. Dollars)

Salaries and Wages	$706,265
Fringe Benefits	$406,624
Personnel Costs (Subtotal)	$1,112,889
Equipment	$25,000
Materials & Supplies	$112,115
Travel	$2,817
Other	$254,998
Subawards/Consortium/Contractual Costs	$34,091
Federal Direct Costs	$1,541,910
Federal F&A Costs	$741,410
Approved Budget	$2,283,320
Total Amount of Federal Funds Obligated (Federal Share)	$2,283,320
TOTAL FEDERAL AWARD AMOUNT	$2,283,320
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$2,283,320

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
32	$2,283,320	$2,283,320
33	$2,258,320	$2,258,320

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:	1660433762A6
Document Number:	POD012217G
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020
OD	8014500	$2,283,320	$2,258,320

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

NIH Administrative Data:
PCC: CMR03 / **OC**: 414E / **Released**: eRA Commons 12/21/2018
Award Processed: 12/22/2018 12:01:38 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P40OD012217-32

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 – 5P40OD012217-32

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

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants

Policy Statement, including addenda in effect as of the beginning date of the budget period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

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

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

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

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

This award has been assigned the Federal Award Identification Number (FAIN) P40OD012217. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

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

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

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

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 5P40OD012217-32

Clinical Trial Indicator: No

This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

SUBJECT FOA
This award is subject to the conditions set forth in PAR-14-005, "Animal and Biological Material Resource Centers (P40)," which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link: http://grants.nih.gov/grants/guide/pa-files/PAR-14-005.html
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ORIP FUNDING PLAN FOR FY2018
This non-competing award reflects the NIH Fiscal Policy for Grant Awards for FY2019 (see NIH Guide Notice NOT-19-031) and the implementation of the ORIP FY2019 grants funding policy: https://orip.nih.gov/funding/awards-funding-policy
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CONSORTIUM
This award includes funds awarded for subcontractual/consortium activity with **University of Texas at Rio Grande Valley** in the amount of $34,091 total costs ($23,463 direct costs + $10,628 facilities and administrative costs). Consortia are to be established and administered as described in the NIH Grants Policy Statement (NIH GPS). The referenced section of the NIH GPS, Part II Chapter 15 is available at: http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf
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PROGRAM INCOME REPORTING
Program income is gross income earned that was directly generated by the grant-supported activity or earned as a result of the award. Program income may be used only for allowable costs in accordance with the applicable cost principles and the terms and conditions of the award. The amount of program income earned and the amount expended must be reported on the appropriate annual FFR in the Program Income section of the FFR (lines 10 L – O). Any costs associated with the generation of the gross amount of program income not charged to the grant should be deducted from the gross program income earned, and the net program income should be the amount reported. For awards under SNAP, the amount of program income earned must be reported in the non-competing continuation progress report. Refer to Part II, Chapter 8: http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf
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PRIOR APPROVAL REQUEST
Any prior approval request (e.g., changes to key personnel as noted on the award, changes in human and animal subjects requiring prior approval, carryover requests) must be submitted to the assigned Grants Management Specialist and Programmatic Official. Please refer to Part II Chapter 8 the NIH Grants Policy Statement for the activities and/or expenditures that require NIH approval at http://grants.nih.gov/grants/policy/nihgps/nihgps.pdf
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NON-COMPETING RENEWAL (NON-SNAP)
The NIH requires the use of the Research Performance Progress Report (RPPR) for all Type 5 progress reports. The RPPR and other documents applicable to this Non-SNAP grant are due the first of the month preceding the month in which the budget period ends (e.g., if the budget period ends 11/30, the due date is 10/1). Please see http://grants.nih.gov/grants/rppr/index.htm for additional information on the RPPR.
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COMMUNICATIONS/PRESS RELEASE

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

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

STAFF CONTACTS

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

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

Program Official: Miguel A. Contreras
Email: contre1@mail.nih.gov **Phone**: 301.594.9410

SPREADSHEET SUMMARY
GRANT NUMBER: 5P40OD012217-32

INSTITUTION: UNIVERSITY OF PUERTO RICO MED SCIENCES

Budget	Year 32	Year 33
Salaries and Wages	$706,265	$706,265
Fringe Benefits	$406,624	$406,624
Personnel Costs (Subtotal)	$1,112,889	$1,112,889
Equipment	$25,000	
Materials & Supplies	$112,115	$112,115
Travel	$2,817	$2,817
Other	$254,998	$254,998
Subawards/Consortium/Contractual Costs	$34,091	$34,091
TOTAL FEDERAL DC	$1,541,910	$1,516,910
TOTAL FEDERAL F&A	$741,410	$741,410
TOTAL COST	$2,283,320	$2,258,320

Facilities and Administrative Costs	Year 32	Year 33
F&A Cost Rate 1	50%	50%
F&A Cost Base 1	$1,482,819	$1,482,819
F&A Costs 1	$741,410	$741,410

A. COVER PAGE

Project Title: CARIBBEAN PRIMATE RESEARCH CENTER	
Grant Number: 5P40OD012217-32	**Project/Grant Period:** 04/15/1987 - 11/30/2020
Reporting Period: 12/01/2017 - 11/30/2018	**Requested Budget Period:** 12/01/2018 - 11/30/2019
Report Term Frequency: Annual	**Date Submitted:** 10/01/2018
Program Director/Principal Investigator Information: MELWEEN I MARTINEZ , DVM **Phone number:** (787) 756-6540 **Email:** melween.martinez@upr.edu	**Recipient Organization:** UNIVERSITY OF PUERTO RICO MED SCIENCES UPR Medical Sciences Campus Office of Sponsored Programs, PO Box 365067 SAN JUAN, PR 009365067 **DUNS:** 948108063 **EIN:** 1660433762A6 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: IRMA ELVIRA ROMANGARCIA Medical Center Area, Mail Building B-622A San Juan, PR 00935 **Phone number:** 787-758-2525 Ext 7042 **Email:** irma.roman@upr.edu	**Signing Official:** IRMA ELVIRA ROMANGARCIA Medical Center Area, Mail Building B-622A San Juan, PR 00935 **Phone number:** 787-758-2525 Ext 7042 **Email:** irma.roman@upr.edu
Human Subjects: No	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

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

The major goal of this application is to improve and maintain the CPRC's unique research resources through support of operations, administration, veterinary care, and research. The proposed program will maintain a unique national and international research resource for comparative studies in the biomedical and behavioral sciences.

There are three specific aims to the proposed project:

Aim1: To maintain the conventional indian-origin rhesus macaque resources that can provide high quality animals to support numerous PHS-funded research projects.

Aim2: To provide animals genetically and virologically characterized in order to improve their utility as research models

Aim 3: To promote, conduct, and support research in a variety of areas including the establishment of the Translational Science Initiative (TSI) as part of the Applied Research Component.

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: ACCOMPLISHMENTS CORE GRANT 5940OD012217-31.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
3P40OD012217-29S2		Redacted by agreement of the CPRC Pathology Section plays an essential role in maintaining the health of the rhesus monkeys colony as well as in preserving the skeletons of each deceased animal. However, the air conditioning of the facility does not meet the laboratory standards of engineering control as required. The aim of this supplement is to renovate the air conditioning and ventilation system of Redacted by agreement needed to provide an adequate environment while performing necropsy as well as bone maceration procedures.	The renovation of the ventilation system at the necropsy was delayed by the aftermath of Hurricane Maria . Electricity at Redacted by agreement Redacted was recovered in July, after 10 months of the hurricane.Lack of electricity, communication and internet at Redacted by agreement made impossible the continuation of the project before November 30, 2017. However we expect to complete the project by November 30, 2018.

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

File uploaded: Professional Development and Trainings.pdf

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

The outreach program of CPRC has the mission to promote public awareness of local research. The goal is to create educational opportunities and community activities to foster a better understanding of primates and research at CPRC within Puerto Rico. It provides education and resources to the Puerto Rican community to stimulate research opportunities. The CPRC staff offers interactive presentations in community schools and libraries, as well as participates with an informational table at community health fairs, and hosts educational visits to our facilities for high school teachers, students, and community groups. Web site was updated and offers information about the CPRC (www.cprc.rcm.upr.edu).Additionally, we established a collaboration with the Municipality of Humacao to offer educational outreach to the local community from the recently developed community computer and internet laboratory established in an

annex building to the CPRC Cayo Santiago offices. The Center, specially Cayo Santiago, has been exposed through TV special programs, news, presentations and social media. The outreach accomplished as a result of Hurricane Maria effects on the Center has been significant, allowing others to learn about the Center's scientific and educational importance.

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

With the help of a CO6 grant recently awarded by NIH , the plans for the next reporting year will be concentrated in continue recovering, restoring and modernizing the Center after the severe damage that both facilities suffered by Hurricane Category4/5 María. For Redacted Redacted by agreement we will work towards the immediate needs for facility improvements traced in our 2017 – 2027 Master Plan and the reconstruction and replacement of the infrastructure destroyed by the hurricane. We will take into consideration the necessary renovations needed to accomplish the proposed goals, as well as any technological improvements that are necessary to modernize the Redacte The pilot population density control study planned for 2017 has been postponed. However, we plan to perform the annual trapping from October 15- December 21, 2018. A complete group will be removed, and new animals tattooed. Redacted by Redacted by agreement as well as the activities planned at the Translational Science Initiative (TSI). Also will continue participating in different NPRCs working groups, as well in scientific meetings. In general, the CPRC will continue to maintain a strong animal care and use program according to regulations. As part of the Program, it will continue providing genetically and virological characterized healthy rhesus macaques to support numerous PHS-funded research projects as well as other scientific initiatives. The CPRC hopes to become stronger after all the recovery and renovation activities as part of Hurricane Maria aftermath.

A. Overall Component:

With the support of the P40 grant, the Caribbean Primate Research Center (CPRC) has continued providing healthy rhesus macaque monkeys of known genetic background to support research activities. Sales of animals to mainland supporting mainly PHS- funded projects continued successfully throughout the year. Animals from Redacted by agreement were allocated to different researches locally as well as nationwide.

The free-range rhesus macaque colony at Redacted by agreement continued its long history of 80 years maintaining excellent health and condition. The island continued to provide a unique scientific scenario to perform behavioral and non-invasive biomedical research. It currently supports 12 research projects from different national and international universities studying topics related to lifetime histories, kinship, decision making, cognition, among others. Throughout this reporting period various publications were generated using the extensive demographic database that dates to 1956 together with pedigree data collected systematically since the early 1990's For various of these publications CPRC staff took active participation that resulted in co-authorships.

Following the creation of the 2017 – 2027 Master Plan, during this reporting period we began the digitalization of historical visual census data with a collaboration between master students of Liverpool Johns Moore University and the UPR. Students digitized nearly 20 years of monthly census sheets. We will continue this task by establishing similar exchange programs and until all historical archives are scanned and stored in a cloud base platform.

On September 20, 2017 Hurricane Maria hit Puerto Rico, entering through the town of Punta Santiago, where Redacted by is located causing unprecedented damage to at least 98% of our field site. Hurricane Maria was the tenth most intense and possibly the deadliest natural disaster to have ever strike the Atlantic. Cayo Santiago took a direct hit from Hurricane Maria, causing mass destruction to the Redacted by agreement and denuding all vegetation. The lack of natural vegetation has caused prolonged reduction in the availability of food, water, and shade from the intense sun. For months after the hurricane and due to the scarcity of vegetation and freshwater, the monkeys were observed ingesting ocean water, and consuming more seaweed and soil. Although the population survived sustained winds of over 155 mph, it experienced a spike in mortality rates during the following month. The facility suffered major destruction with the loss of vehicles, laboratory, buildings, corrals, and equipment. So far, we have completed the reconstruction of rain roof collectors that provide drinking water for the monkeys and the replacement of the cistern tanks that preserve the drinking water, we

have obtained via donations a floating dock, a used pickup truck, water tanks, two all-terrain vehicles, a generator, power tools, and building materials. With the assistance of two rounds of National Primate Research Center skilled teams we have rebuilt the rain roof collectors and have built two small enclosures that can serve as a space to trap monkeys during the upcoming trapping season that will allow to tattoo the two cohorts that were not possible to tattoo (n=567 monkeys), collect a blood sample for genetics, and cull one social group for population control purposes. In terms of how research was affected post-hurricane, due to the lack of paths and total devastation, Redacted by agreement remained closed for nearly six months with research and data collection officially restarting on February 14, 2018. The closing of our facility affected the research, for example the initiation of the newly approved research project from Redacted by agreement from the University of Washington, who is leading a study on Social environmental effects on aging and immune function in rhesus macaques funded by NIH grant K99AG051764 was delayed until corrals can be rebuilt.

Not only Redacted was severely affected by Hurricane Maria, but Redacted by agreement Redacted by agreement as well. The Station was without electrical power for 10 months, making the continuous use of a diesel –generator, a real challenge. Repair and maintenance of animal housing at Redacted by continued during this period. Examples include refurbishment of corrals and quarantines areas, installation of ceramic tiles in the corrals, replacement of cyclone fencing, galvanized pipes, gates, metal roof and replacement of perches, among others. The maintenance of the enclosures is continuous. In general, the Center is still in a recovery phase , dealing with the restoration of the infrastructure. The Infrastructure of the Laboratory of Primate Morphology, as well as the Virology Laboratory were not affected directly by the hurricane. The Laboratory of Morphology continued providing support to researchers and students that uses such an important skeletal collection. Collaboration is in place with New York University, Anthropology Department. Part of the collection continues to be transferred to their facilities. In there, the collection will have a better exposure to the scientific community. The Virology Division provided support to researches related to SIV, Dengue and Zika.

In spite of such a harsh and challenging year, the CPRC has been resilient, giving continuation to its objectives.

B. Core Component:

Note- The data for 2018 Progress Report corresponds to the 2017 to 2018 (fiscal year: July1st-June 30th).

Redacted by agreement As of June 2018, the free-ranging rhesus

population on CS numbers 1,814 individuals which are divided into 6 social groups, ranging in size from 71 to 522 Many of these monkeys are the subjects of several studies supported in this application. Since 2012, the Cayo Santiago (CS) population has increased by 68% from 1081 to 1,814. The live birth rate for, 2015, 2016, 2017 and 2018 was 86%, 89%, 70% and 82% respectively. The mortality rate for Cayo Santiago during the years 2015, 2016, 2017 and 2018 was, 7.8%, 7.4%, 9.6% and 7.5% respectively. During this four-year reporting period, a total of 352 monkeys were transferred from CS to Redacted by So far, since 2017 we have had 334 births corresponding to the 2018 birth season.

Redacted by agreement The number of animals in the Conventional colony at Redacted by has remained approximately at 1,081 (2015), 996 (2016) ,779 (2017) and 667 (2018) individuals. The number of animals in the Conventional colony decreased due to the need of space for the expansion of the two closed SPF colonies, and the housing Conventional macaques transferred each year from CS to Redacted by agreement

1. Births: Annual births in the conventional colony have decreased. This decrease is due to a combination of factors including the aging population at Redacted by and population control strategies like male vasectomies.

2. Breeding: From July to Jun 2018 the live birth rate was 84% (32/38).

3. Mortality rate at the Redacted by for the fiscal year 2017 was approximately 13% (76% of these animals were euthanized), and the mortality rate for the year 2018 is 11% (73% by euthanasia).

4. Morbidity at the Conventional Redacted by agreement

FY 2018(July 2017 – June 2018)

MORBIDITY	# of cases	Percentage
Trauma	92	13.8%
Diarrhea	124	18.6%
Other diseases	70	10.5%
Total number of sick animals	286	43%
*Total number of animals in conventional colony in SSFS	667	

Trauma cases: the main reason for this percentage is that new, non-breeding groups are made to remove animals from single housing situations. Like any new social group, aggression will occur. Diarrhea cases: in addition to chronic diarrhea cases, animals brought in from Cayo Santiago can develop transient diarrhea due to the change in environment. Also as new, non-social groups are made, stress-related diarrhea can occur in lower ranking animals. Morbidity: morbidity overall in this colony is impacted by an aging population with older animals being predisposed to neoplasia, organ failure, degenerative diseases, among others

Division of Virology and Genetics:

Number of diagnostic tests performed at the CPRC Virology Laboratory:

Test	# Assays
Herpes B	2,763
STLV-1	2,763
SIV	2,763
SRV	2,763
Measles	2,763
SV40	0

Supplements:
Necropsy Area A/C

The renovation of the ventilation system at the necropsy area was delayed by the aftermath of Hurricane Maria . Electricity at Redacted by agreement was recovered in July, after 10 months of the hurricane. Lack of electricity, communication and internet at Redacted by agreement made impossible the continuation of the project before November 30, 2017. However we expect to complete the project by November 30, 2018.

C.Applied Research Component

The Applied Research Component include the Translational Science Initiative (TSI). To meet the mission, the TSI is implementing four fundamental pilot projects.

This initiative, as the whole Center's operation were impacted by the Hurricane Maria that swamped Puerto Rico on September 20, 2018, exactly one year ago. In spite of the constrains and multiple challenges we have to overcome, we are proud to report outstanding scientific results for this period.

Project No.1 Outcome of Zika infection in dengue pre-exposed animals. Project Leader: Redacted by agreement

This project is part of the Zika Research Initiative at the CPRC. Results from the first phase of this project were published in the high impact Journal Nature Communication in June 2017 (DOI: 10.1038/ncomms15674).
During the period covered by this progress we have advanced in the phase 2 covered under the topic: Time: Key Factor for Dengue and Zika Interactions.

Partial results have been presented during the VI Pan American Dengue Research Network Meeting in Galveston 2018 and during the Zika Working Group, Face to Face Meeting, NIH August 2018. Unpublished

The time between a primary and a secondary dengue infection is relevant to the clinical presentation. A short interval between infections usually results in protection while an extended period of time is associated with severe dengue. Virus-specific antibodies are prevalent in flavivirus naïve subjects, while cross-flavivirus antibodies are present in individuals previously exposed to dengue or other flaviviruses [1]. Nevertheless, the presence of cross-reacting antibodies does not prevent the production of ZIKV specific antibodies [2,3]. Few is still known about the contribution of virus-specific versus the cross-reacting antibodies or the cellular immune response developed during a primary dengue infection into the viremia and pathogenesis during a secondary ZIKV infection in vivo [4]. On the other hand, the quality of the antibodies showed to be essential to control ZIKV infection in vivo. Swanstrom et al proposed that the presence of EDE-1or EDE1-like antibodies may be responsible for cross-neutralizing activity of ZIKV in DENV-immune individuals [5]. While it has been suggested that the magnitude of these cross-reactive immune response may depend on the length of time separating the 2 infections and the frequency of previous flavivirus exposures it is not clear the temporal association of the quantity and effectiveness of those antibodies with the longevity of the immune response [1].

Recently we showed that previous dengue immunity of more than 2 years does not result in an increase in Zika viremia or pathogenesis [6]. Interesting DENV-immune animals showed to have a non-significant but shorter viremic period compared to DENV-naive macaques. In this work, we explored the role of the longevity of DENV immune status in a secondary ZIKV infection including the

Zika viremia and pathogenesis in macaques.

In this work we found that a previous immunity of 12 months but not of 3 months was able to reduce significantly the peak viremia and the average viremia days (Figure 1).

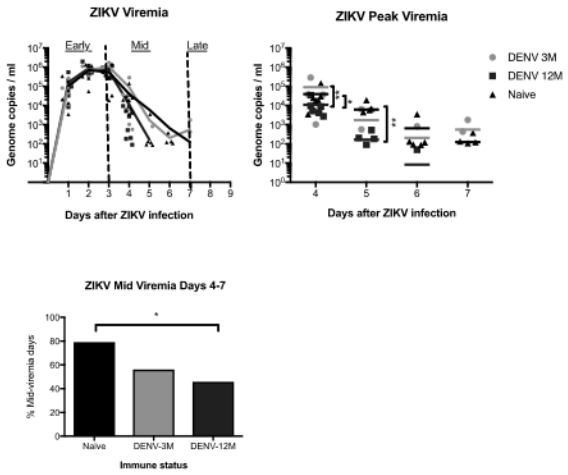

Figure 1

We looked at quality of the neutralizing antibodies against Zika and dengue in all groups.

As showed in figure two there were not differences in the potency neutralizing ZIKV among groups. However the DENV-mid convalescent group showed to have a population of nAbs with a significantly higher potency against DENV when compared to the early convalescent group (Figure 2).

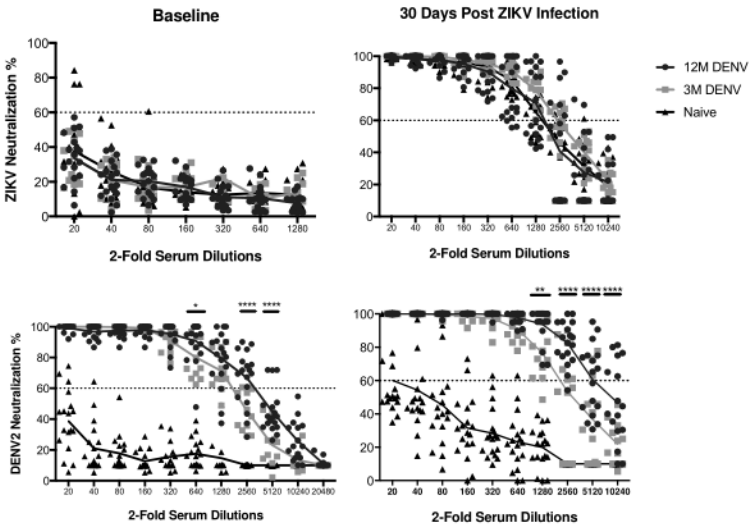

Figure 2

Macaques provides a reliable model to study the immunological profile after sequential flaviviruses infections [6-8]. Previously we showed that 2.8 years immunity to dengue did not enhanced Zika infection. Moreover, that period of convalescence results in an immune status that trend to control Zika viremia and the increase of liver enzymes after the infection [6]. In this work we aimed to establish the contribution of the convalescent period in the immune response to ZIKV in subjects with previous immunity to DENV. It is well documented that the cross-reacting Abs and the magnitude of the nAbs to other flavivirus after ZIKV infection is higher in flavivirus immune than in naïve individuals [1-3,9]. Previously it has been showed that the plasmablast response during secondary DENV infection is mainly MBC derived and that the B cell response rapidly generated after secondary DENV infections contains plasmablasts with memory B cell origin resulting in a mature response with antibodies that are largely crossreactive but also neutralizing in vitro [10]. From our work we found that the magnitude of the cross-reactivity to the primary infecting flavivirus, both at binding and neutralizing level are significantly affected by the time elapse between the DENV and ZIKV infections (figure 2). This difference may be related to the maturity of the MBCs and the affinity of the antibodies they produce. However there is very limited studies on how the affinity maturation develops during the first encounter with the virus and whether the affinity of MBCs is modified during a secondary heterologous infection [11] or as in this work, during a secondary infection with ZIKV.

We also confirmed the presence of highly cross-reacting but non-neutralizing antibodies to ZIKV in the DENV-immune groups [2,3]. However, those antibodies were significantly higher only in the group within the early convalescent period (3 months) after DENV infection compared both to the naive and to the middle DENV convalescent (12 months) groups. This confirm the high frequency of ZIKV cross-reacting antibodies during the early DENV convalescence that wane during the middle and late convalescence periods. From the results we are presenting here and before [6], we can conclude that the neutralization against ZIKV is very limited or absent in all samples we tested after DENV infection, regardless the convalescence status. Our results are in agreement we recent findings by Montoya et al. [9] and in partial agreement with other reports using human samples [2,5,12,13]. We conclude that the disagreement is mainly related to the dissimilar definition of convalescence period in those previous works.

This finding has enormous implications for the diagnostic interpretation and the epidemiological considerations during a flavivirus epidemic and to properly dissect the immune response to ZIKV. Several works have been published so far and seminals conclusions have been made without considering that the results

may be bias or incomplete by overlooking the contribution of the length of time between the two infections to those results. The above-discussed results provide novel insights on the dynamic of the antibodies response to ZIKV in a population previously exposed to DENV.

In our work, the role of the cellular immune response in the significant decrease of ZIKV middle peak viremia (days 4 to 7) is patent. Particularly relevant is the significant preexistent combination of high and lower frequencies of TEM and TCM respectively, in the group exposed to DENV one year before the Zika infection. It has been established that protective memory is mediated by TEM that migrate to inflamed peripheral tissues and display immediate effector functions, whereas reactive memory is mediated by central memory T cells (TCM) with more limited effector function [14]. The group of animals better controlling the Zika viremia and with a significant lower levels of the liver enzymes, showed a significant higher frequency of preexisting effector $CD4^{+}CD3^{+}CD28^{-}CD95^{+}$ cells that were sustained throughout day 3 after ZIKV infection, the last time point it was measured (figure 3).

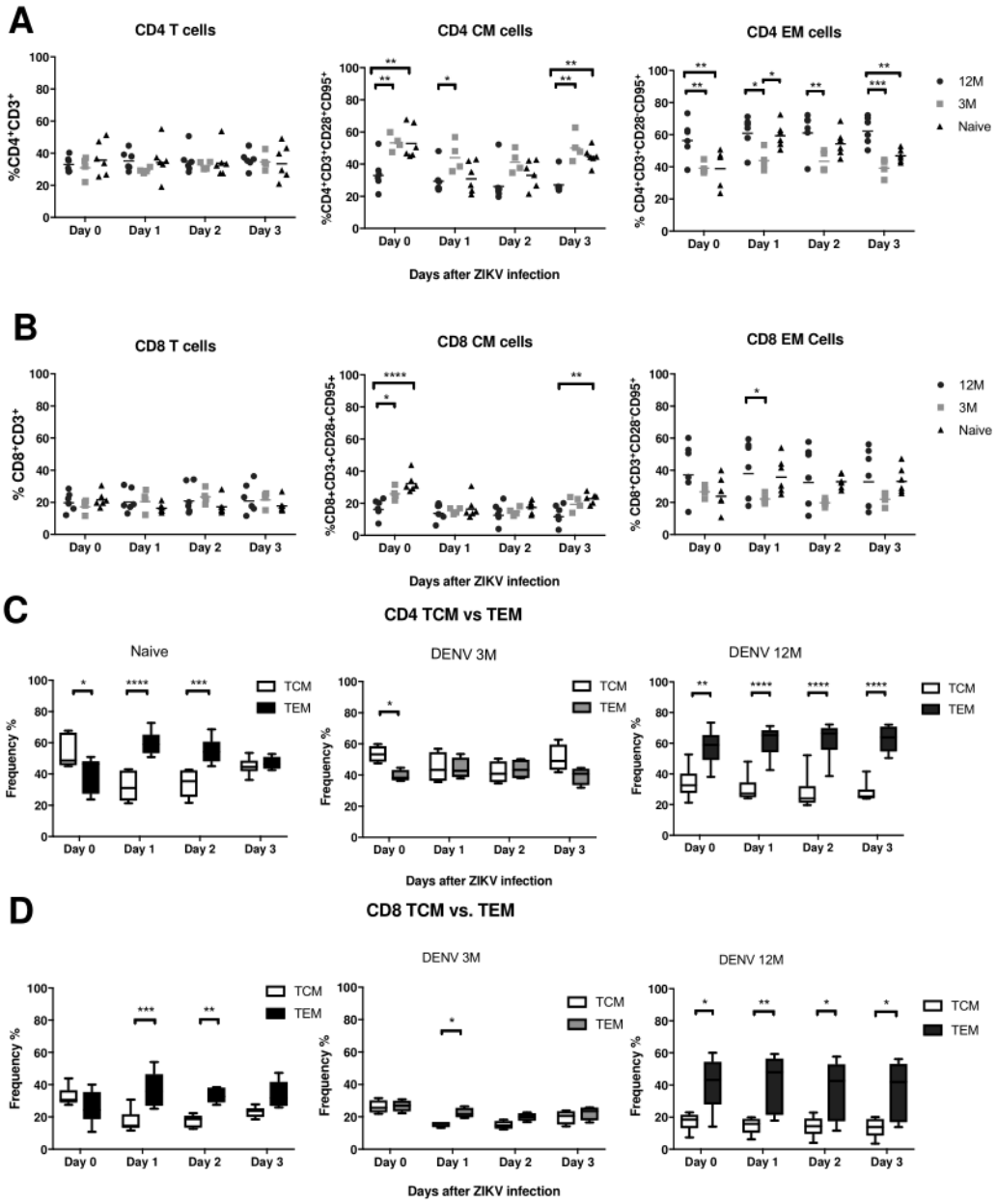

Figure 3

It has been documented that in antigen-primed individuals, tetanus toxoid-specific CD4 T cells can be detected in circulating TCM and TEM up to 10 years after antigenic stimulation, and their frequencies increase following booster immunization [15].

Limited but significant proliferation was noted two days after the infection only in the CD4 TCM cells in the 12M DENV-immune and in the naïve groups compared to the 3M DENV-immune group. However, proliferating CD4 and $CD8^+$ T-cells have been reported by 6–8 days post ZIKV infection [7,16,17]. As we were unable to

collect samples from day 7 until day 30 p.i. we missed to test for that peak in our cohorts. To circumvent that challenge, we estimated the relation between central and effector memory $CD4^+$ and $CD8^+$ T cells after ZIKV infection. In all cases, after ZIKV infection we detected a simultaneous contraction and expansion in the CD4 and CD8 TCM and TEM cells respectively, confirming that the changes in magnitude in those types of cells were specific for the ZIKV infection. A ZIKV-dependent compartment displacement from the central to the effector memory cells was also confirmed by the fact that most of the animals with lower frequencies of TCM cells showed the higher frequency of TEM cells. However, in our study the animals exposed to DENV only three months before ZIKV showed significant lower frequency of TEM cells compared to the 12M DENV-immune group and very limited changes in the frequency of the TCM endorsing that the convalescent period that separate the two flavivirus exposition has significant consequences in the immune response and in the outcome of the secondary infection. This time-dependent effect has bee previously well characterized for the humoral immune response to secondary dengue infections [18-20].

The role of CD4 T cells in flavivirus infection has been extensively documented [21] and their particular role in response to ZIKV infection have been confirmed with samples from few human cases [22-24]. In our work CD4 T cells are of high relevance not only because their effector memory role, if not, in their cytotoxic capabilities. We showed that CD4 T cells CTL activity, determined by the expression of the degranulation marker CD107a, showed higher frequency and magnitude in the 12 months dengue immune animals compared to the naïve group. Interesting the reactivity of these cells, one year after DENV in vivo priming, showed a switch. From being highly responsive to the whole DENV virus before the ZIKV infection (characterized by a significant higher frequency of IFN-g production and CD107a expression) they turner in to highly responsive to ZIKV envelope and non-structural proteins 30 days after ZIKV infection. That switch was a trend, but not significant in animals with 3 months of previous exposition to DENV. Interesting it has been shown that higher frequency of DENV-specific IFN-g producing T cells are associated to subclinical manifestations in children suffering of secondary DENV infection [25]. Our results confirms that the T cells were mature enough after 12 months but not after only three months of exposition to DENV antigens.

The key role of the T cells controlling Zika replication and liver damage in the animals exposed to dengue 12 months before Zika infection is reinforced by the significant increase of circulating cytolytic protein perforin at day 7 post infection. This denotes the acquisition of cytotoxic function of the T cells [26] in that group compared to the other two groups. Previously we confirmed a serum perforin

peak at day 6 after ZIKV infection in animals with 2.8 years of previous immunity to DENV [6]. Others has shown that Granzyme B expression, an activation marker, in macaques CD4 and CD8 T cells peaked between 7 and 10 days post ZIKV infection [17] . It is known that frequency of DENV CD4 T cells are detectable early following DENV infection and the frequency of DENV-specific CD107a+ CD4 T correlate with enhanced protection against dengue disease [27,28]. In this work we confirm that, after a middle time of convalescence (12 months) the CD4+ T-cells differentiated in effector memory and continues its differentiation to play a protective role by acquiring cytotoxic and cytokine-producing profiles. The protective role of the cellular immune response controlling the viral burden of ZIKV in mice have been reported [29,30]. More recently have been proven that prior DENV immunity can protect against ZIKV infection during pregnancy in mice, and CD8+ T cells are sufficient for this cross-protection [31]. Currently it is well documented that preexposure to DENV both in macaques and humans results in a qualitative modification of the humoral and cellular immune response to ZIKV [1,6,32,33]

The uniqueness of our report is that we established that the magnitude and the breath of that modification depend on the convalescent status with significant consequences. In the presence of previous DENV infection, the increase in the frequency of the specific TEM cells and of the cytotoxic CD4 T cells may occurs at any time after ZIKV infection. However, playing a significant role controlling ZIKV viremia and liver damage happens only after a mid-convalescent period of about one year, but not too early (3 months) or too late for cytotoxicity property (2,5 years) after the primary DENV infection.

We are confirming that previous encounter with a flavivirus not only modify the magnitude and the quality of the immune response to ZIKV over the time, if not, that those changes can have significant implication controlling the ZIKV infection.

Our findings have enormous impact for the epidemiological models anticipating the magnitude of new ZIKV epidemics in DENV endemic areas and most important in the ZIKV and DENV vaccines design and schedule.

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Project 2: Induction of Mucosal Immunity in Macaques by Global Vaccine Adjuvant. Project Leaders: Redacted by agreement and Redacted by agreement Redacted by agreement This project was approved by the IACUC on September 6, 2016. This protocol was also approved by the Medical Science Campus Biosafety Committee.

However after several considerations and to limitation in the adjuvant availability we decided to close this project. In March 2018, this project was replaced by the following project: **Evaluation of verdinexor, an orally bioavailable exportin-1 inhibitor, in cell-based and primate infections of HIV/SIV**

This is a proof-of-concept studies in collaboration with Karyopharm Therapeutics. Leaders: Redacted by agreement University of Puerto Rico-Medical Sciences Campus (UPR), Redacted by agreement School of Medicine, UPR and Redacted by agreement Redacted by agreement

With this protocol we aim to determine the efficacy of KPT-335 (verdinexor) in an ex vivo model of SHIV and SIV infection. Peripheral blood mononuclear cells (PBMCs) will be isolated from non-human primates (NHP; Indian-origin Rhesus macaques) and ex vivo infected with strains of SIV and SHIV. Serial dilutions of verdinexor will be added either pre- or post-treatment in a concentration range from 1µM to 0.4nM by 3-fold dilutions. Cell health, percentage and types of cells infected and magnitude of infection will be determined by flow cytometry (+/- gate and mean fluorescence intensity). Cytokine release will be measured by multiplex luminescence-based assay, and the quantification of Rev protein will be determined by western blot and the localization of the SHIV/SIV Rev protein will be determined by immunofluorescence cell staining.

In spite of the short period of time running this project, for this period we can report the following results.

The selective inhibitor of nuclear export (SINE) compound KPT-335 (verdinexor) developed by Karyopharm Therapeutics, has shown antiviral properties in animal models of influenza A virus infections. The pharmacological mechanism consists of inhibiting the activity of the host cell nuclear protein exportin-1. HIV replication is reliant on the viral protein Rev to shuttle unspliced or partially spliced mRNAs from the nucleus to the cytoplasm (including Rev transcripts), thus treatment of HIV-infected cells with verdinexor would result in a reduction of Rev protein levels in cells. In order to test this, we are attempting to develop a reliable detection method for Rev protein expression using flow cytometry and commercially available anti-rev antibodies. Rev detection using the REV4 clone was non-specific as we were able to detection staining signals in uninfected cells. We also tested drug cytotoxicity in uninfected cells using a flow cytometry cell viability assay, and found that 63nM was at the higher end of cell tolerability. Future tests will include another commercially available and flow cytometry untested clone, REV6, as well as comparative cell viability stages among different infection conditions.

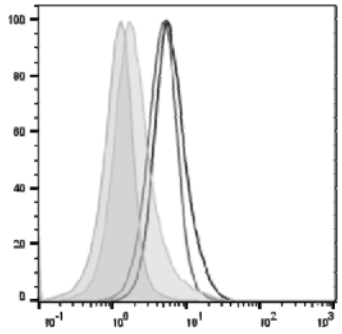

Figure 1
REV4 clone does not reliably label Rev protein on SIV-infected CEMx174 cells. Flow cytometry expression measurements of Rev protein on fixed and permeabilized CEMx174 cells 48hrs post-infection with simian immunodeficiency virus (SIV). Anti-Rev (REV4 clone, Santa Cruz) labeling shows Rev detection on both SIV-infected and uninfected cells, irrespective of infection status.

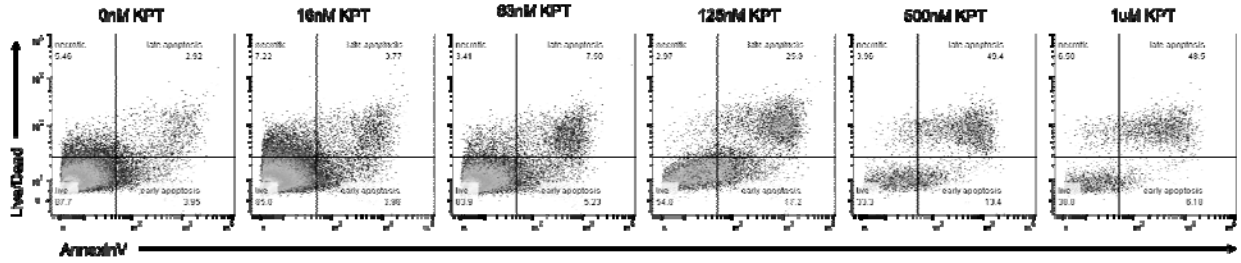

Figure 2
Testing KPT-335 cytotoxicity studies on CEMx174 cells. Flow cytometry viability measurements on fixed/permeabilized CEMx174 human lymphoblastoma cells treated for 48hrs with different KPT-335 (KPT) concentrations,. AnnexinV (BioLegend) and Live/Dead (Invitrogen) combined staining allows for the identification of different cell viability stages.

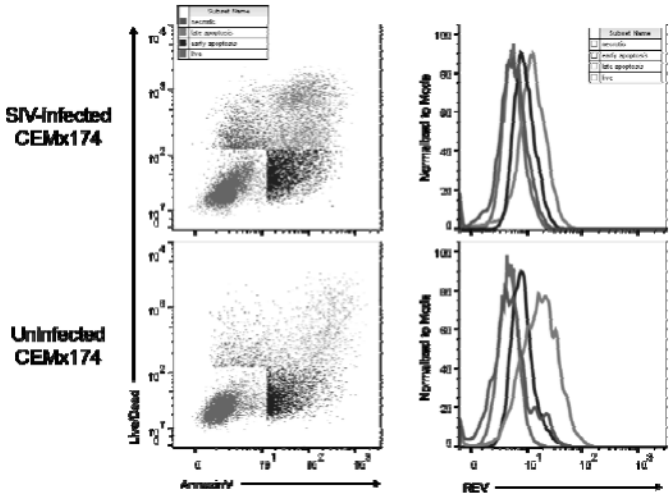

Figure 3: REV4 clone does not reliably label REV protein on SIV-infected CEMx174 cells irrespective of viability stage. Flow cytometry viability and expression measurements of REV protein on fixed and permeabilized CEMx174 cells 48hrs post-infection with simian immunodeficiency virus (SIV). AnnexinV (BioLegend) and Live/Dead (Invitrogen) combined staining shows different cell viability stages, while anti-REV (REV4 clone, Santa Cruz) labeling shows REV detection on both SIV-infected and uninfected cells.

Project 3: Development Of Rhesus Monkeys As A Model Of Pre-Diabetes.
Project Leader: Redacted by agreement and Melween Martinez, DVM, CPRC-UPR-MSC.-

OBJECTIVES:
Our main objective is to develop a rhesus model of pre-diabetes to test novel interventions that may reverse pre-diabetes and to decipher mechanisms involved in pre-diabetes and insulin resistance.

ACCOMPLISHMENTS:

1. Selection of prediabetic and healthy rhesus monkeys

After screening 50 animals we completed the selection of middle-aged pre-diabetic rhesus monkeys (n=8) and healthy middle-aged nondiabetic monkeys (n=6). These animals are on an Ad libitum, non-high fat diet. Our criteria for selection of pre-diabetic monkeys was based on high fasting glucose levels and/or compensatory hyperinsulinemia. Monkeys were screened two times to confirm the prediabetic status. Additional parameters that we measured were BMI and blood pressure.

2. Mitochondrial bioenergetic phenotype of rhesus monkeys

Standardization and optimization for simultaneously measuring oxidative phosphorylation and glycolysis in PBMCs from rhesus monkeys: We used an

Extracellular Flux Analyzer to establish optimal conditions to measure mitochondrial bioenergetics using peripheral blood mononuclear cells (PBMCs) from rhesus monkeys. We established optimal concentrations of cells and of the drugs (FCCP and oligomycin) used in the measurement of oxygen consumption rates and glycolysis by performing dose-response experiments. Next we measure the bioenergetic profile in our cohort of rhesus monkeys (see below).

Age-related decreases in oxidative phosphorylation but not in glycolysis in rhesus monkeys: We performed experiments to measure the bioenergetic phenotype of rhesus monkeys by simultaneously measuring oxygen consumption rate (indicative of oxidative phosphorylation) and glycolysis, the pathways that generate ATP in the cells. To establish the mitochondrial bioenergetic phenotype we analyzed PBMCs from middle-aged (10-12 years; n=3) and old (17-20 years; n=3) rhesus monkeys and found that: (i) Basal oxygen consumption rate (OCR) was significantly ($p<0.05$) reduced (a 34% reduction) in 17-20-year old animals compared with 10-12 year old monkeys; (ii) Maximal OCR was significantly ($p<0.05$) reduced (a 68% reduction) in 17-20 year old rhesus compared with 10-12 year old monkeys; and (iii) No significant changes between groups were observed in the spare respiratory capacity or the rate of glycolysis. Our results suggest that aging leads to the loss of mitochondrial bioenergetics.

Prediabetic but not healthy rhesus monkeys exhibit lower spare respiratory capacity: We found that prediabetic monkeys (n=7) exhibit a significant ($p=0.03$) 75% reduction in the mitochondrial spare respiratory capacity (SRC) compared to healthy middle-aged monkeys (n=4). The SRC is the reserved energy that a tissue requires in response to an insult. If the SRC is not sufficient to provide the required ATP during a period of increased energy demand, cells may undergo senescence and function. Our results suggest that PBMCs from prediabetic rhesus monkeys exhibit a bioenergetic deficit that may represent a prodromal stage of diabetes.

Significance: There is an urgent need to identify new approaches for the prevention and treatment of metabolic diseases such as diabetes. Moreover, it is critical to start the intervention before the onset of the disease, specifically, during the prediabetic stage. Our main objective is to develop in the Caribbean Primate Research Center a rhesus model of prediabetes that can be used to test new pharmacological interventions and decipher mechanisms involved in age-related metabolic diseases. By establishing the bioenergetic profile of rhesus monkeys, we create a novel and accurate model for conducting translational research to study the impact of pharmacological interventions to prevent the development of age-dependent metabolic disease.

COLLABORATION: This research program prompted collaboration with Redacted by agreement Redacted by agreement University of North Carolina at Chapel Hill) to identify novel pathways/networks that underlie the differential response between losartan/prediabetic and control/prediabetic groups using whole genome expression analysis. Redacted by agreement a Ph.D. student working in this project last summer visited the laboratory of Redacted by agreement to participate in a gene expression and analysis workshop. He will be applying this year the knowledge acquired in our study for sample analysis.

CHALLENGES ENCOUNTERED: Our project was negatively impacted after hurricane María hit the island of Puerto Rico. First, the postdoctoral fellow working in this project left the Island and went back to Argentina, her country of origin. In addition, the graduate student working in the project was out of the laboratory for almost a year due to delays related to the completion of the comprehensive exam. Now Redacted by agreement is back to the laboratory and this year he will be completing the gene expression studies. Fortunately, a new graduate student Redacted by agreement joined my laboratory and this year she will be working in the completion of the molecular characterization of the insulin signaling pathway in our cohort of rhesus monkeys.

Project 4: Assessing the anti-inflammatory role of Fasciola hepatica Fatty Acid Binding Protein in a Non-Human Primate Septic shock Model: Project Leaders Redacted by agreement PhD, UPR-MSC and Redacted by agreement DVM, CPRC-UPR-MSC **.**

The central hypothesis of this project is that a recombinant protein of 14.5kDa belonging to the fatty acid binding protein family from the parasitic helminth *Fasciola hepatica* (Fh15) will be able to prevent or ameliorate the lethal symptoms of sepsis / septic shock in a non-human model septic shock model.

Aim-1: Scale-up the expression and purification of Fh15 and characterize its anti-inflammatory capacity **(Completed)**

This aim was completed during the first year of project and the results published with acknowledgment to the P40 of PR-CPRC in Scientific Reports 7 (1): 5455, 2017, DOI: 10.1038/s41598-017-05735-w.

Redacted by agreement *Recombinant Fasciola hepatica fatty acid binding protein suppresses toll-like receptor stimulation in response to multiple bacterial ligands.*

Aim-1.1. Study the effect that Fh15 exert on the cytokine production of PBMC from naïve *Rhesus macaques* stimulated with LPS in vitro.

During the first two quarterly of the 2nd year of project we still had difficulties to perform *in vivo* experiments because of logistic and/or lack of human resources availability at the CPRC. To advance the project we then focused in determining whether our molecule (Fh15) could suppress the production of inflammatory cytokines from PBMCs of naïve Rhesus monkeys stimulated *in vitro* with *Escherichia coli*-LPS. These experiments were performed with blood collected from two naïve animals of the Rhesus colony of the UC Davis Primate Center, where my PhD-student Redacted by agreement had the fortune to receive 1-month training as part of the relief effort unfold by UC Davis to help to graduate students of UPR-MSC.

PBMC culture. Whole blood (5-ml) from two-rhesus macaque (*Macaca mullatta*) was collected in CPT tubes with sodium heparin and centrifuged 1hr to collect buffy coat as described by manufacturer. Isolated PBMCs were cultured in RPMI 1640 supplemented with glutamine, 10% FBS and 1% Penn-strep. Cells were plated in duplicated at a final concentration of 5 x 10^5 cells/well in 24 wells plate and stimulated with PBS as negative control or LPS (100ng/ml) as positive control. In an initial experiment cells were treated with different Fh15 concentrations ranging among 5 to 20µg. In a second experiment cells were treated with the same Fh15 concentrations and 1h later stimulated with LPS (100ng/ml). Cells were incubated by 20h at 37°C, 5% CO_2. After incubation, cell supernatant from each well was collected and used for cytokines determination. Redacted by agreement at Redacted by agreement San Antonio Texas, performed the cytokine determinations by Luminex. Results were expressed as fold changes of the concentration for each single cytokine relative to the concentration of the same cytokine produced by LPS.

RESULTS

As expected, cells stimulated with LPS produced high levels of all cytokines and chemokines studied. Regardless the Fh15 concentration used, cells treated only with Fh15 produced levels of cytokine or chemokine very similar to the PBS-background. This indicates that Fh15 is unable to induce the secretion of any pro-inflammatory cytokine or chemokine, which is consistent with our previous studies *in vitro* using THP1-Blue CD14 cells (human monocyte cell line) or murine bone marrow derived macrophages [34]. However, despite Fh15 does not induce any cytokine production it was able to progressively suppress the LPS-induced cytokine production with the increasing of the concentration, reaching maximal cytokine suppression at Fh15 concentration of 20µg/ml (data not

shown). At these experimental conditions, Fh15 suppressed the LPS-induced TNFα (**p=0.0013), MCP1 (*p=0.0128), IL12p40 (***p=0.0010), IFNγ (*p=0.0117), MIP1α (**p= 0.0047), MIP1b (**p=0.0036), IL-6 (**p=0.0058) and CXCL (*p=0.0121) (**Figure-1**).

By using an XTT-assay we demonstrated that the optimized Fh15 concentration is not toxic for cell and that the suppression of cytokine production observed *in vitro* is a real effect and not an effect caused by toxicity.

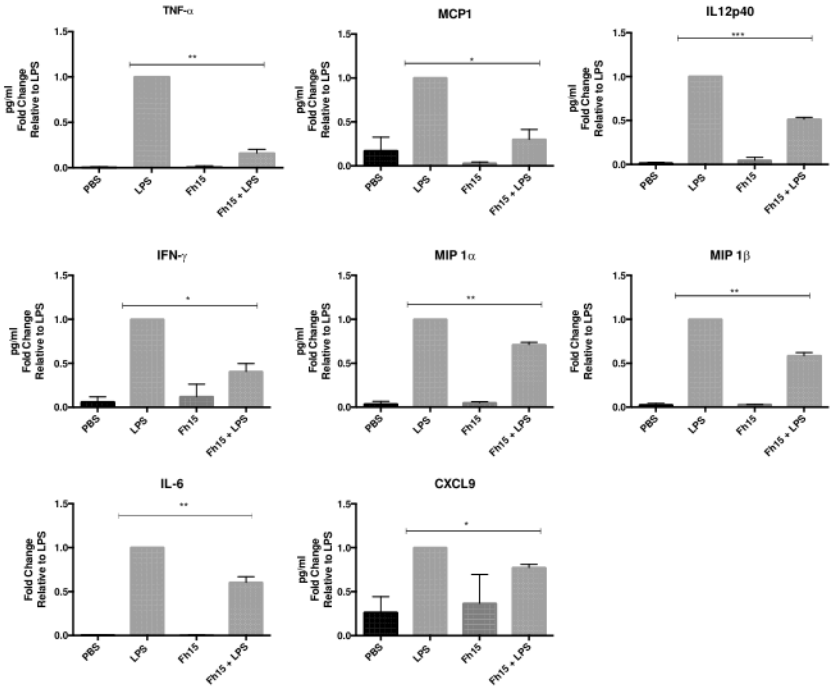

Figure-1. Cytokine determinations. PBMCs were isolated from whole blood collected to two different naive Rhesus macaques. Cells were seeded at the concentration of 5 x 10^5 cells /well in 24-well culture plates. Cells were stimulated with PBS, Fh15 (20µg), LPS (100ng/ml) or Fh15 (20µg) 1h prior LPS estimulation. After 20h of incubation at 37°C, 5% CO_2 cell supernatant was collected from each well for meaurig the concntration of secreted cytokines / chemokines.

CONCLUSIONS

Our previous published studies and the results obtained herein with cells from non-human primates cells collectively support our hypothesis that Fh15 will be able to exert similar anti-inflammatory effect when it can be tested *in vivo*. To test the anti-inflammatory capacity of Fh15 *in vivo* using *Rhesus macaques* it is strongly necessary to establish a well-standardized model of septic shock within this animal specie.

Aim 2. Develop a controlled septic shock model in *Rhesus macaque* to study the change pattern of cytokines during early phase of septic shock.

To develop a septic shock model in non-human primates we used animals from the Rhesus macaques colony of the PR-CPRC following a protocol described in the only paper published to date that uses live *Escherichia coli*-infusion for inducing septicemia [35]. Despite the multiple difficulties and limitations that suffered our University and in particular the CPRC with the pass of the Maria's Hurricane this aim was significantly advanced during the current 2nd year of project.

For this part of the study we proposed to use a minimum of 4 conventional adult *Rhesus macaques* (3-4-years-old) either sex. Due to logistic issues only a monkey can be handled at a time. To date two monkeys have been used and the data obtained was analyzed separately.

Bacteria. The *E. coli* strain used for inducing the septic shock was purchased from the American Type Culture Collection (ATCC (*E. coli* 086a: K61 serotype; ATCC 33985). Prior to experiment a fresh *E. coli* was cultured for 24 hours; harvested and washed five times to remove free endotoxin. The day of the experiment; a sample of the bacteria suspension was collected and quantified to set the bacteria concentration at 10^{10}CFU/kg body weight using pyrogen-free isotonic saline. Just prior to apply the infusion the bacteria suspension was re-suspend in a volume of 50 ml isotonic saline (room temperature) to increase the volume in order to allow a slow administration.

Animal preparation. The day before experimentation the animals were sedated with ketamine hydrochloride (AST Pharma, Oudewater, the Netherlands); transported to the operation chamber and fasted overnight. During the experiment the animals were placed on their side on a temperature-controlled heating pad to support body temperature. Body core temperature was monitored during the experiment. Animals were intubated orally and allowed to breathe freely. To inject the isotonic saline, live *E. coli* infusion and antibiotic a cannula was inserted in the femoral or cephalic vein. An infusing of isotonic saline containing 2·5% glucose at a rate of 3·3 ml/kg/h was used to compensate fluid loss. To avoid discomfort, the animals remained anaesthetized during the entire experimental window (8-h) using O_2/N_2O/ Isoflurane inhalation anesthesia.

***Sepsis induction Animal # 1*:** One-hour prior the bacterial infusion the baseline physiologic parameters (normal levels) such as: heart rate, blood pressure and body temperature were recorded. The bacterial infusion (10^{10} CFU/kg body weight of live *E. coli*) was applied i.v. slowly over a period of 2 h, followed immediately by an intravenous (i.v.) administration of the bacteriostatic agent enrofloxacin [Baytril 2·5%) dose: 9 mg/kg] to neutralize surviving bacteria and to

synchronize shock induction. This dose was selected based on previous published dose-infection studies performed in similar non-human primates model [35]. Animal remained connected to a BIONET monitor to measure blood pressure, blood oxygen saturation, ECG, temperature and respirations. During the experiment period, a veterinary doctor supervised the heart rate, blood pressure, body temperature and other clinical markers to determine the development of the septic shock. Observations of these parameters were performed every 10 minutes during the complete time-course of the experiment (8h). At this time point the animal was euthanized to analyze organ damage. Blood samples of 5-ml were taken at 30 min, 2h, 4h, 6h and 8h.

***Sepsis induction Animal # 2*:** Identical protocol to described above but without applying enrofloxacin after the *E. coli* infusion.

***Blood processing*.** Blood samples anti-coagulated with EDTA-Na was centrifuged at 1,500 rpm/min x 10 min to separate plasma from cells. The plasma was tested for the presence and fluctuations of characteristic biomarkers such as *C*-reactive protein (CRP), procalcitonin (PCT) and also for analyzing a panel of pro-inflammatory cytokines/chemokines using Human Cytokine Array / Chemokine Array. We also measured the endotoxin concentration using Chromogenic Limulus Amebocyte Lysate (LAL) QCL-1000 Assay (Lonza, Walkersville, MD) and bacteremia by spreading a small aliquot of whole blood in agar plate, which was incubated overnight at 37^{o}C.

RESULTS

Physiological Parameters and post-euthanasia observations

After monitoring every 10 min for 8h the body temperature, heart rate, diastolic / systolic rate, arterial pressure, respiratory rate and blood oxygenation of animals no significant changes in any of these parameters were noticed (**Figure-2**). After 8h of LPS infusion, animals were euthanized and necropsied to examine macroscopically the organs. Portions of some organs, such as adrenals grand, spleen, lung, and heart were preserved in formalin for further histological analysis. At first view, no significant organ damage was noticed in the tissues collected when were compared with those collected from a healthy animal. The histochemical analyses are still pending to be performed. These observations indicated that the current experimental conditions are not enough to develop a septic shock in our experimental animals.

Bacterial Load and Endotoxin levels

Blood samples from both euthanized animals were cultured in agar plate for

determining bacterial load during the experimentation period. Both animals showed a different bacteremia dynamic. In Rhesus-1 the bacteremia was detected from 30 min and peaked at 2h of experimentation. Given this animal received a successful treatment with enrofloxacin immediately after the *E. coli* infusion (at 2h), bacteremia was not longer detected in the subsequent time-points. In contrast, Rhesus-2, that did not receive the antibiotic treatment, had detectable levels of bacteremia from 30 min but bacteremia was gradually increasing and peaked at 8h of experimentation. These results indicate that at euthanasia bacteria was actively replicating in the blood of this animal (**Figure-3**).

The plasma samples collected at different experimental time points were tested for determining the endotoxin levels. **Figure-3** only shows the levels of endotoxin for Rhesus-1. Determinations for Rhesus-2 are pending because the kit is in backorder until mid of September.

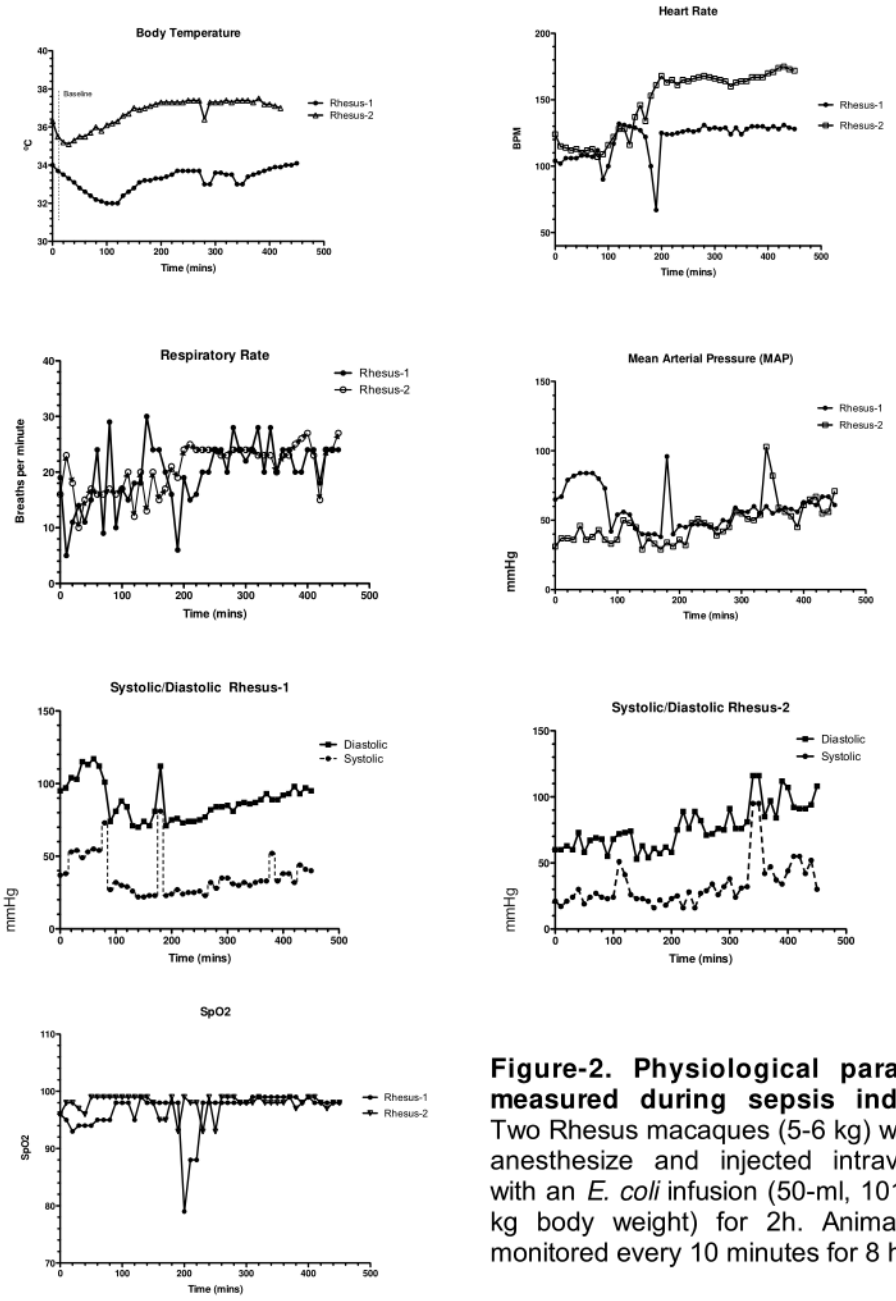

Figure-2. Physiological parameters measured during sepsis induction. Two Rhesus macaques (5-6 kg) were fully anesthesize and injected intravenously with an *E. coli* infusion (50-ml, 1010 CFU/ kg body weight) for 2h. Animals were monitored every 10 minutes for 8 hours.

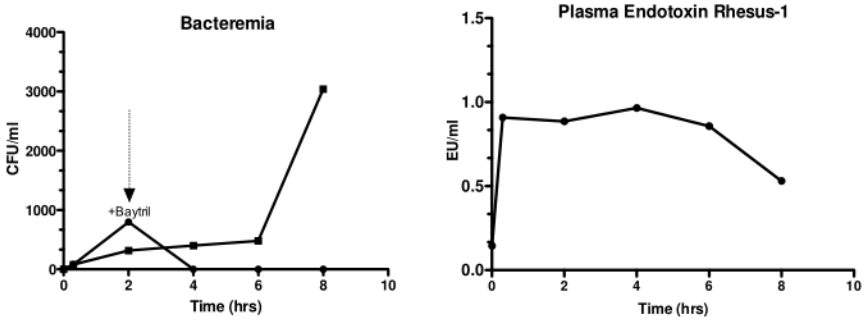

Figure-3. Bacteremia and endotoxin assessment. Blood collected from Rhesus monkeys subjected to the septic shock induction showed significant amount of bacteremia, which droped drastically in Rhesus-1 after the antibiotic application (arrow) whereas the Rhesus-2, which no received antibiotic had significantly higher bacteremia with maximal values at 8h of *E. coli* infusion.

Levels of procalcitonin and C-Reactive Protein

Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin that is secreted by a number of parenchymal tissues and differentiated types cells of body. PCT function as a biomarker of higher specificity than other pro-inflammatory markers (e.g. cytokines) in identifying patients with sepsis and can be used in the diagnostic of bacterial infections [36]. C-reactive protein (CRP) is a blood marker for inflammation in the body. CRP is produced in the liver and is classified as an acute phase reactant, which means that its levels will rise in response to inflammation [37].

Rhesus-1, which received the antibiotic after the *E. coli* infusion had very low levels of PCT that were not different from the baseline. However, this animal showed a significant increase of CRP by 6 hours after the infusion confirming the induction of a pro-inflammatory status.

The low levels of PCT as predictor of bacterial infection are consistent with the low bacteria load caused by the antibiotic application in Rhesus-1. Rhesus-2, that did not receive treatment with antibiotic, had levels of PCT and CRP that were three-fold higher compared to Rhesus-1 (**Figure-4**). These results confirm that at euthanasia both animals were suffering of an acute inflammatory process as consequence of the *E. coli* infusion.

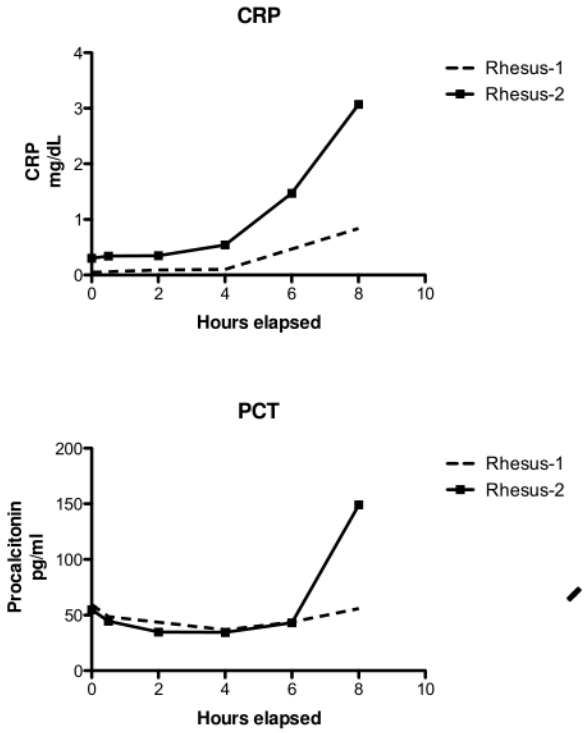

Figure-4. Levels of procalcitonin and C-reactive protein in plasma. Plasma of Rhesus collected at different time periods after i.v. *E. coli* infusion were tested for measuring levels of procalcitonin (PCT) and C-reactive protein (CRP). Both animals showed significant levels of both infflammatory indicators.

Cytokine Profiling

Luminex was used to study a panel of pro-inflamatory cytokines in the plasma samples collected from each experimental animal. These determinations were performed with the collaboration of Redacted by agreement at the South West Foundation, San Antonio, Texas. Results demonstrate that most cytokines / chemokines were detectable at high levels after 2h of *E. coli*-infusion and remained at very high levels during the entire experimental window (**Figure-5 & 5B**). TNFα, and MIP1b, which is a cytokine and a chemokine of early secretion, respectively, peaked at 2h after the infusion and further their concentrations in plasma decreased becoming undetectable at the end of the experiment. The kinetic of cytokines and chemokines was the same in both animals. However, the concentration of some cytokines was higher in Rhesus-1 than in Rhesus-2 or vice verse. Variations in the concentrations of cytokines could be an effect of the enrofloxacine. Each cytokine determination was performed in duplicate and results were expressed as a mean value for each determination. Thus, the standard deviations showed on the bars of figure-5 and 5B don't represent

variations among biological samples but variations between experimental replicates.

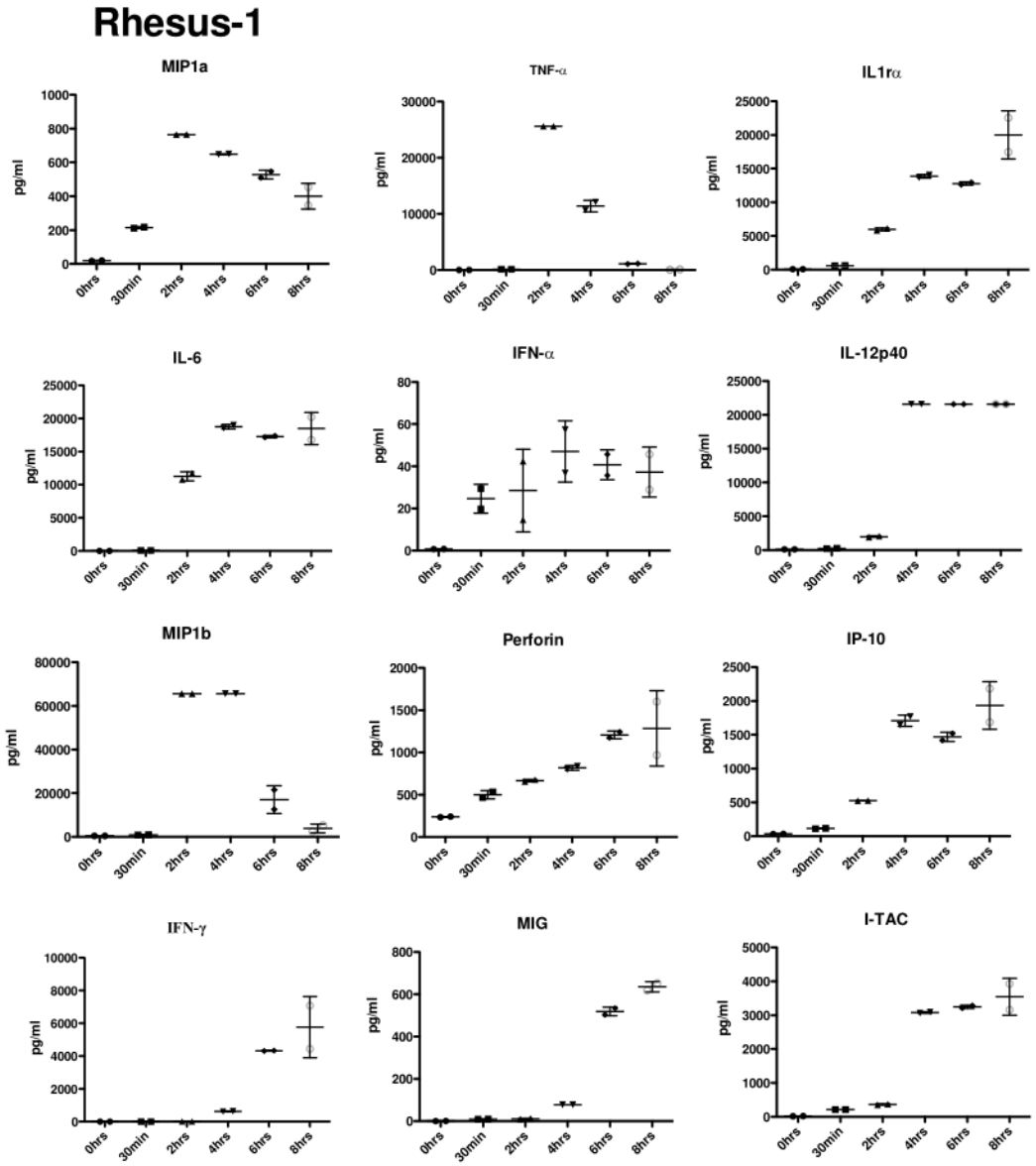

Figure-5. Cytokine/chemokine profile. Plasma from Rhesus macaque- # 1 was tested by a panel of pro-inflammatory cytokines / chemokines using Luminex. The duration of the i.v. *E. coli* infusion was 2h. Most cytokines /chemokines reached detectables levels after this time.

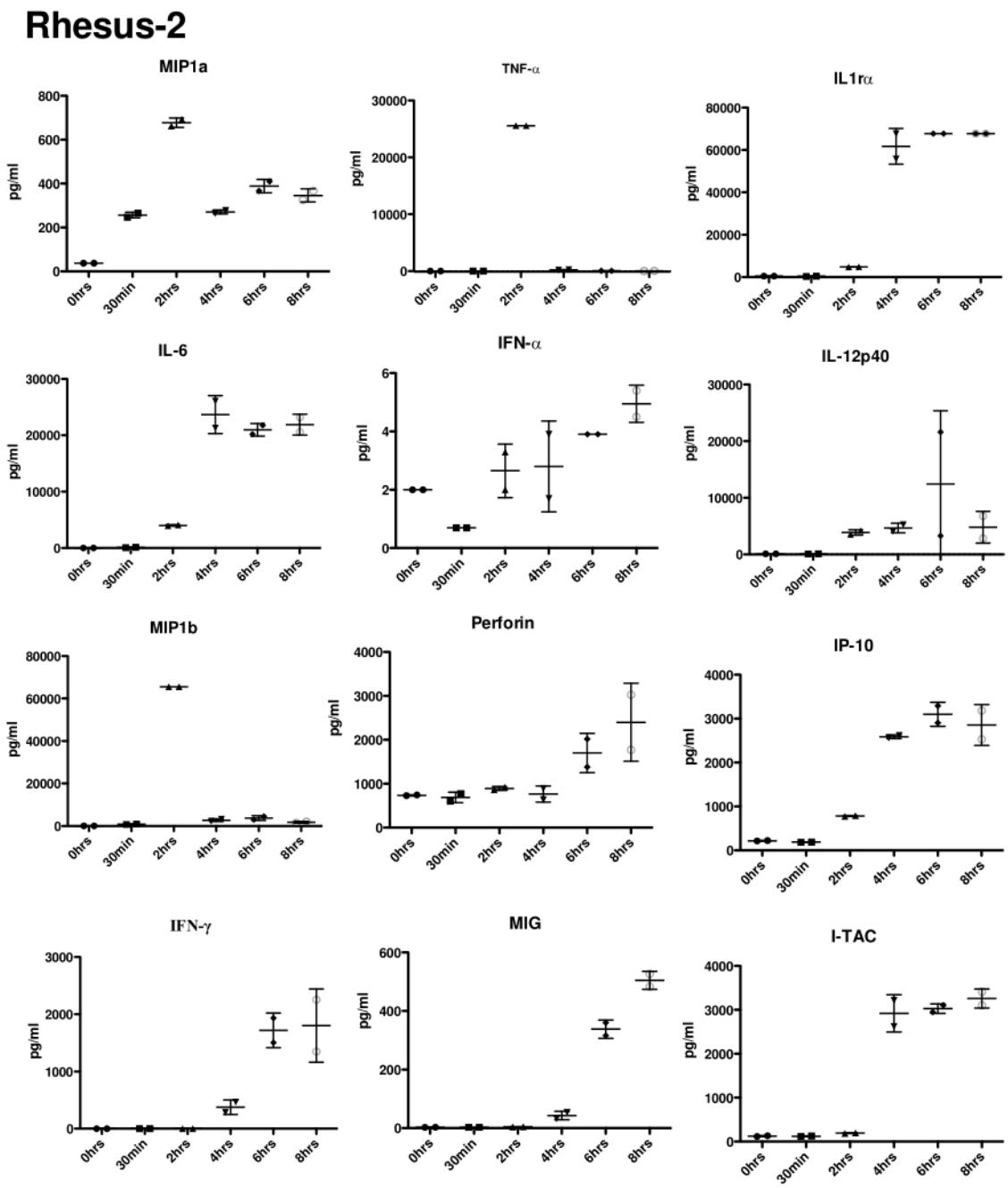

Figure-5B. Cytokine/chemokine profile. Plasma from Rhesus macaque- # 2 was tested by a panel of pro-inflammatory cytokines / chemokines using Luminex. The duration of the i.v. *E. coli* infusion was 2h. Most cytokines /chemokines reached detectables levels after this time.

CONCLUSIONS

1. Although the macroscopic observation of organs collected at necropsy as well as the physiological parameter measured during the 8 hours after *E. coli* infusion indicated that animals do not developed the septic shock, the high levels of PCT, CRP, endotoxin, bacterial load and pro-inflammatory cytokines observed in these animals clearly demonstrate that both animals were incubating an acute and severe inflammatory process. Evidently, to observe the pathological and lethal effect of a septic shock in these animals a longer monitoring of at least 24-h would be necessary.

2. Differences between the protocols (presence or absence of antibiotic immediately after bacteria infusion) provoked marked differences in the bacterial load, levels of PCT and in lesser extension in the concentration of some cytokines or chemokines. Therefore, it would be highly recommendable to replicate the experiment in absence of enrofloxacin.

3. To confirm the data obtained with Rhesus-2 and perform the proper statistical analysis with at least 2-3 biological replicates two additional animals must be performed.

4. Despite a short experimental window of 8-h is insufficient to develop the septic shock in *Rhesus macaque*, we have identified 4 or 5 parameters that could serve as inflammation markers to test the ability of Fh15 to prevent or suppress the inflammatory responses during an ongoing inflammatory process caused by sepsis. The proposed inflammation markers are: PCT, CPR, TNFα at 2h post-infusion and IL-6 and / or IL12p40 at 8h post-infusion.

Professional Development and Trainings:

The Caribbean Primate Research Center [Redacted by agreement] serves as a Placement Learning Provider for undergraduate and graduate students. [Redacted by agreement] offers professional training within the established research program and serves as a one-on-one mentor to the students. Students has the opportunity, during the twelve months of the placement, to perform technical tasks such as census taking, caretaker activities, as well as to work as behavioral research assistants. However, training mentorship in [Redacted by] was interrupted due to the recovery efforts after Hurricane Maria. Training opportunities are expected to be resumed during the upcoming trapping season starting in October, 2018.

During the period covered by this progress report, we continue providing training on molecular virology at the Virology Laboratory (VL)- CPRC to three undergraduate students for the University of Puerto Rico.

Also, under the mentorship of [Redacted by agreement] the VL continues providing an excellent environment for the PhD students. In August 2018, the first PhD student funded by the P40, graduated with excellent academic record. Currently, the other two previous PhD students from the Microbiology and Medical Zoology Department of the Medical Sciences Campus-UPR, continue their thesis' dissertation- work at the Virology Lab. In addition, two new students were accepted and taking the basics courses and learning the techniques. In total, the CPRC-Virology lab, hosted four PhD, and three undergraduate students .All four PhD students are working under project 1 of the Translational Science Initiative of the Applied Research Component of this Grant. At this time, Unpublished

[Redacted by agreement] presented at the VI Pan American Dengue Research Network Meeting in April 2018, and as an Invited Speaker at University of Texas Medical Branch (UTMB), in January 2018.The students also delivered oral presentation in local and national forums, and presented posters in other meetings.

The Laboratory of Primate Morphology (LPM) has also served as a platform for graduate students conducting PhD investigations. A student from New York University , Department of Anthropology, is using the skeletal collection in a project which is part of a wider research program. The study aimed at understanding the role sexual selection plays in trait evolution among primates, including humans, and at identifying the factors explaining intra- and inter-specific variation in sexually-selected traits. One interesting avenue is to explore how genetic and environmental factors influence the development of secondary sex characters such as body size, muscle strength and canine length, and whether it covaries with behavioral tactics in live animals over their lifetime. Understanding how sexual selection processes lead to variation in morphology will also inform debates concerning sexual dimorphism and inferred mating systems in extinct primates in general, including hominids. Another student from the American Museum of Natural History- Vertebrate Paleontology, studied taxon-specific patterns of locomotor ontogeny to which fossil hominin remains

may be compared and assessment of the phylogenetic signal of those patterns: A comparative analyses of trabecular bone characteristics in the hands and feet in different dentally-defined age groups. She visited the LPM to select specimens for MicroCT scanning. The selected specimens were split into four batches. The first batch has been was sent and returned. The second batch has been sent to the Museum of Natural History. The scanning is in progress. Several tours were given through the year, in where participants could observed the rhesus skeletal collection. Redacted by agreement also received students to perform clinical or scientific work. Dr. Martinez participated at the bi -annual NIH Director's meeting, and gave a presentation of the situation of the CPRC after Hurricane Maria at the American Primatology Society's annual meeting.

In general, in spite of the challenges from the hurricane aftermath, several students benefited for training or professional experience at the CPRC, in Redacted by agreement Redacted by agreement Cayo Santiago, Laboratory of Primate Morphology and the Virology Laboratory. Among them are veterinary medicine, veterinary technologists, graduate and undergraduate students.

Due to Hurricane Maria aftermath, less students were received this year, however the Center continues to be a platform for student's research and clinical development.

NAME	INSTITUTION	DEGREE	DATES PARTICIPATING
Redacted by agreement	UPR-RP	Biology	August 2017-present
	UPR-RP	Biology	August 2017-present
	UPR-RP	Antropology & Biology	August 2016-present
	UPR-RP	Biology	March 2018-present
	UPR-MSC	Veterinary Technology	August-December 2017
	UPR-MSC	Veterinary Technology	August-December 2017
	UPR-MSC	Veterinary Technology	August-December 2017

Redacted by agreement	UPR-MSC	Veterinary Technology	August-December 2017
	UPR-MSC	Veterinary Technology	August-December 2017
	UPR-MSC	Veterinary Technology	August-December 2017
	UPR-MSC	Veterinary Technology	August-December 2017
	UPR-MSC	Veterinary Technology	August-December 2017
	Tri Institutional Training Program NY	Lab Animal Residency Rotation	October, 2017
	UPR-MSC	Veterinary Technology	January-February 2018
	UPR-MSC	Veterinary Technology	January-February 2018
	UPR-MSC	Veterinary Technology	January-February 2018
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	UPR-MSC	Veterinary	January-February

		Technology	2018
Redacted by agreement	UPR-MSC	Veterinary Technology	January-February 2018
	UPR-MSC	Veterinary Technology	January-February 2018
	UPR-MSC	Veterinary Technology	January-February 2018
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	UPR-MSC	Veterinary Technology	January-February 2018
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	UPR-MSC	Veterinary Technology	February 2018 – present
	UPR-MSC	Veterinary Technology	February 2018 – present
	UPR-MSC	Veterinary Technology	February 2018 – present
	UPRRP	Biology	August-present

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Brent LJ, Heilbronner SR, Horvath JE, Gonzalez-Martinez J, Ruiz-Lambides A, Robinson AG, Skene JH, Platt ML. Genetic origins of social networks in rhesus macaques. Scientific reports. 2013 January 9;3:1042. PubMed PMID: 23304433; PubMed Central PMCID: PMC3540398.
Complete	Petersdorf M, Dubuc C, Georgiev AV, Winters S, Higham JP. Is male rhesus macaque facial coloration under intrasexual selection?. Behavioral ecology : official journal of the International Society for Behavioral Ecology. 2017 November;28(6):1472-1481. PubMed PMID: 29622929; PubMed Central PMCID: PMC5872909.
Complete	Harding JD. Nonhuman Primates and Translational Research: Progress, Opportunities, and Challenges. ILAR journal. 2017 December 1;58(2):141-150. PubMed PMID: 29253273; PubMed Central PMCID: PMC5886318.
Complete	Mandalaywala TM, Petrullo LA, Parker KJ, Maestripieri D, Higham JP. Vigilance for threat accounts for inter-individual variation in physiological responses to adversity in rhesus macaques: A cognition × environment approach. Developmental psychobiology. 2017 December;59(8):1031-1038. PubMed PMID: 29071705; PubMed Central PMCID: PMC5690846.
Complete	Brent LJN, Ruiz-Lambides A, Platt ML. Persistent social isolation reflects identity and social context but not maternal effects or early environment. Scientific reports. 2017 December 19;7(1):17791. PubMed PMID: 29259240; PubMed Central PMCID: PMC5736592.
N/A: Not Journal	Benderlioglu Z, Guatelli-Steinberg D. Exploring a connection between matriline dominance rank and linear enamel hypoplasia in Cayo Santiago rhesus monkeys. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Bezanson M, Menamara A. Trashing the field: field site and species bias in primatology. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Coyne SP. Predictors of age at first reproduction in adolescent female rhesus macaques. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Cunningham A, DeLeon VB. Morphological integration of hyoid and skull through ontogeny in Macaca mulatta. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Dechow PC. Understanding human craniofacial bone properties and biomechanics - a perspective on macaques, baboons, and beyond. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Ebersole JL, Nagarajan N, Gonzalez OA. Gingival Gene Expression Profiles to Stage Progression of Periodontitis: Of Monkey and Man?. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Eller AR. Developmental pacing in Macaca mulatta from two types of managed environments: captive and free-ranging. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Glowacka H, Schwartz GT. A test of the 'Brain Pleiotropy Hypothesis' for the relationship between brain size and dental development in rhesus macaques. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.

N/A: Not Journal	Hardin AM. Genetic correlations in the canine-premolar honing complex of the rhesus macaques of Cayo Santiago. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Higham JP. Sexual selection in male rhesus macaques: genes, physiology, morphology, behavior, life-history. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Kimock CM, Higham JP, Decasien AR, Dubuc C. Intra-specific variation in skeletal traits of free-ranging rhesus macaques (Macaca mulatta). 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Kohn LA, Ricci B, Turnsquist JL, Kessler MJ, Berard JD. Morphological integration in macaque limb development: implications for understanding human development. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Li H, Luo W, Feng A, Tang ML, Kensler TB, Maldonado E, Gonzalez O, Kessler MJ, Dechow PC, Ebersole JL, Wang Q. Odontogenic Abscesses in Rhesus Macaques (Macaca mulatta) of Cayo Santiago. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Platt ML. Modeling the Genetic, Epigenetic, and Neural Mechanisms Mediating Variation in Complex Human Social Behavior in Rhesus Macaques. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Raveendran M, Harris R, Rogers J. Functional genetic variation among rhesus macaques (Macaca mulatta): A newly recognized and powerful tool for research. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Rothschild BM, Wang Q, Turnquist JE, Derousseau JC, Kessler MJ, Pritzker KP. Arthritis in Rhesus macaques (Macaca mulatta) from Cayo Santiago. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11.
N/A: Not Journal	Ruiz-Lambides A, Giura-Negru B, Caraballo G. The rhesus macaque (Macaca mulatta) population of Cayo Santiago post-hurricane Maria: social groups, distribution, current research situation.. American Society of Primatologists meeting; 2018.
N/A: Not Journal	Taboada H, Anton SC, Williams SA, Laird MF, Stock MK, Villamil CL, Bauman S, Gonzalez-Velez O, Schmitt CA, Dubuc C, Higham J. Intra-demic morphological variation: using the Cayo Santiago macaques to model plasticity in the fossil record. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
N/A: Not Journal	Wang Q. Macaques in the Study of Human Conditions – In Celebration of 80 years of Cayo Santiago. 87th AAPA (American Association of Physical Anthropologists) meeting; 2018 April 11; Austin, TX, USA.
Complete	Larson SM, Ruiz-Lambides A, Platt ML, Brent LJN. Social network dynamics precede a mass eviction in group-living rhesus macaques. Animal behaviour. 2018 February;136:185-193. PubMed PMID: 29887618; PubMed Central PMCID: PMC5990275.
Complete	Gonzalez OA, Kirakodu S, Novak MJ, Stromberg AJ, Orraca L, Gonzalez-Martinez J, Burgos A, Ebersole JL. Comparative analysis of microbial sensing molecules in mucosal tissues with aging. Immunobiology. 2018 March;223(3):279-287. PubMed PMID: 29066255; PubMed Central PMCID: PMC5821569.
Complete	Weiß BM, Kücklich M, Thomsen R, Henkel S, Jänig S, Kulik L, Birkemeyer C, Widdig A. Chemical composition of axillary odorants reflects social and individual attributes in rhesus macaques. Behavioral ecology and sociobiology. 2018 March 28;72(4):65. PubMed PMID: 29606788; PubMed Central PMCID: PMC5871651.
In Process at NIHMS	Madlon-Kay S, Montague MJ, Brent LJN, Ellis S, Zhong B, Snyder-Mackler N, Horvath JE, Skene JHP, Platt ML. Weak effects of common genetic variation in oxytocin and vasopressin receptor genes on rhesus macaque social behavior. American journal of primatology. 2018 June 21;:e22873. PubMed PMID: 29931777.
Complete	Al-Attar A, Alimova Y, Kirakodu S, Kozal A, Novak MJ, Stromberg AJ, Orraca L,

	Gonzalez-Martinez J, Martinez M, Ebersole JL, Gonzalez OA. Activation of Notch-1 in oral epithelial cells by P. gingivalis triggers the expression of the antimicrobial protein PLA₂-IIA. Mucosal immunology. 2018 July;11(4):1047-1059. PubMed PMID: 29515164; PubMed Central PMCID: PMC6030509.
Complete	Ebersole JL, Novak MJ, Orraca L, Martinez-Gonzalez J, Kirakodu S, Chen KC, Stromberg A, Gonzalez OA. Hypoxia-inducible transcription factors, HIF1A and HIF2A, increase in aging mucosal tissues. Immunology. 2018 July;154(3):452-464. PubMed PMID: 29338076; PubMed Central PMCID: PMC6002220.
In Process at NIHMS	Kanthaswamy S, Oldt RF, Ng J, Smith DG, Martínez MI, Sariol CA. Determination of major histocompatibility class I and class II genetic composition of the Caribbean Primate Center specific pathogen-free rhesus macaque (Macaca mulatta) colony based on massively parallel sequencing. Journal of medical primatology. 2018 July 4. PubMed PMID: 29971797.
In Process at NIHMS	Which male and female characteristics influence the probability of extragroup paternities in rhesus macaques, Macaca mulatta?. Animal behaviour.
In Process at NIHMS	Periodontal Disease Susceptible Matrilines in the Cayo Santiago Macaca mulatta Macaques. Journal of periodontal research.

Non-compliant Publications Previously Reported for this Project

Public Access Compliance	Citation
Non-Compliant	Milich KM, Georgiev AV, Petersen RM, Emery Thompson M, Maestripieri D. Alpha male status and availability of conceptive females are associated with high glucocorticoid concentrations in high-ranking male rhesus macaques (Macaca mulatta) during the mating season. Hormones and behavior. 2018 January;97:5-13. PubMed PMID: 28954215.

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

Category	Explanation
Other	Berger MW. Thrashed by Hurricane Maria, Monkey Island Tries to Rebuild, Bolstered by Support From Scientific Community. [Internet]. Penn News2017 September. Available from: https://penntoday.upenn.edu/news/thrashed-hurricane-maria-monkey-island-tries-rebuild-bolstered-support-scientific-community.
Other	Press A. Hurricane damages Monkey Island center. [Internet]. Texarkana Gazette2017 October. Available from: http://www.texarkanagazette.com/news/national/story/2017/oct/07/hurricanedamages-monkey-islandcenter/694575/.
Other	Bhat R. Social Isolation Is Not All Doom and Gloom for Some Macaques. [Internet]. THE WIRE2018 February. Available from: https://thewire.in/science/social-isolation-not-doom-gloom-macaques.
Other	Press A. After Maria, Scientists race to save Monkey Island. [Internet]. Tampa Bay Times2017 October. Available from: https://www.tampabay.com/incoming/after-maria-scientists-race-to-save-monkey-island/2340282.
Other	Winter S. Hurricane Maria rescue mission launched to save 1,000 monkeys hit by storm. [Internet]. Express2017 September. Available from: http://www.sciencemag.org/news/2017/02/you-can-thank-your-fruit-hunting-ancestors-your-color-vision.
Other	Phillips A. Puerto Rico's Irreplaceable Monkey Island Needs Human Help Now. [Internet]. Earther.com2017 October. Available from: https://earther.gizmodo.com/puerto-rico-s-irreplaceable-monkey-island-needs-human-h-1819104004.
Other	McKellips P. FEMA PUBLIC AFFAIRS FEMA TRANSCRIPT. [Other]. FEMA2017 October. Available from: https://www.fema.gov/media-library-data/1507917867029-c690b36086e8fc4c8791d220686d37ae/MonkeyIslandTranscript.txt.

Other	Yong E. Rescuing Puerto Rico's Monkey Island. After a unique macaque colony off the island's coast was hit by Hurricane Maria, its caretakers are rushing to save it—and themselves.. [Internet]. The Atlantic2017 September. Available from: https://www.theatlantic.com/science/archive/2017/09/the-uncertain-fate-of-puerto-ricos-monkey-island/541080/.
Other	Huang Y. Puerto Rico Deserves Better. [Internet]. The Campus Times (Uiverstity of Rochester, NY)2017 October. Available from: http://www.campustimes.org/2017/10/02/puerto-rico-deserves-better/.
Other	Baeza Bickel N. Scientists seek to save Puerto Rico's Monkey Island. [Internet]. Global Michigan-University of Michigan2017 October. Available from: https://global.umich.edu/newsroom/scientists-seek-to-save-puerto-ricos-monkey-island/.
Other	Unkown. Buscan más medidas de seguridad para Cayo Santiago. [Internet]. NotiUno.com2018. Available from: https://notiuno.com/buscan-mas-medidas-de-seguridad-para-cayo-santiago/.
Other	Rosati A. The race to save Monkey Island: Researchers reveal devastation of Puerto Rico home of 1,500 rhesus monkeys. [revised 2017 October]. [Internet]. Mail Online2017 October. Available from: https://www.dailymail.co.uk/sciencetech/article-4946170/The-race-save-Monkey-Island.html.
Other	Unkown. Urgen se provean medidas para restringir acceso a Cayo Santiago. [Internet]. TACTICALRESOLUTION.COM2018 January. Available from: https://www.tacticalresolution.com/noticias/urgen-se-provean-medidas-para-restringir-acceso-a-cayo-santiago-15143/.
Other	Skrabut M. Project Monkey Island. [Internet]. IPS2017 November. Available from: https://www.projectmonkeyisland.org/.
Audio or video	Unkown. A Race to Save Monkey Island in Puerto Rico. [Video]. AP News2017 October. Available from: https://www.apnews.com/4ef721896b1b416586741cb4cabd05f4.
Other	Morton J. "Looking stressed can help keep the peace: First research to suggest scratching may have evolved as a communication tool to help social cohesion." . [Internet]. Science Daily2018 September. Available from: https://www.sciencedaily.com/releases/2017/09/170911095925.htm.
Other	Vergano D, Sacks B. Scientists Are Trying To Rescue 1,500 Monkeys In Puerto Rico. [Internet]. 2017 September. Available from: https://www.buzzfeednews.com/article/danvergano/monkey-island-rescue.
Other	Howard L. Researchers Rally to Help Puerto Rico's Monkey Island. [Internet]. Speaking of Research.com2017 November. Available from: https://speakingofresearch.com/2017/11/07/researchers-rally-to-help-puerto-ricos-monkey-island/.
Other	Press A. Hurricane Mauled PR's Renowned Monkey Island Research Center. [Internet]. Voa News2017 October. Available from: https://www.voanews.com/a/hurricane-mauled-prs-renowned-monkey-island-research-center/4059709.html.
Other	Wadley J. U-M professor part of effort to save monkeys displaced by hurricane. [Internet]. Michigan News2017 October. Available from: http://record.umich.edu/articles/u-m-professor-part-effort-save-monkeys-displaced-hurricane.
Other	Knapton S. Time running out for 'Monkey Island' devastated by Hurricane Maria. [Internet]. The Telegraph2017 October. Available from: https://www.telegraph.co.uk/science/2017/10/08/time-running-monkey-island-devastated-hurricane-maria/
Other	Noticel. Necesidades de los Rhesus en Cayo Santiago tras el paso de María. [Internet]. Noticel2017 December. Available from: https://www.noticel.com/el-tiempo/huracanes/necesidades-de-los-rhesus-en-cayo-santiago-tras-el-paso-de-mara/672971501.
Other	Rose S. Autism research on Puerto Rico island threatened by hurricane aftermath. [Internet]. CNN2017 October. Available from: https://edition.cnn.com/2017/10/13/health/autism-research-puerto-rico-

	hurricane/index.html.
Audio or video	Kessler M, Rawlins R. Cayo Santiago & The Origins NIH NPRC Program with Hurricane Maria update. [Video]. 2018. Available from: https://www.youtube.com/watch?v=LCgkFZ7RIyc&feature=youtu.be
Other	Tacopino J. This plea for help in Puerto Rico is heartbraking. [Internet]. 2017 September. Available from: https://nypost.com/2017/09/25/this-plea-for-help-in-puerto-rico-is-heartbreaking/.
Other	Nazario A. Ley para la Promoción Educativa y Científica de la Colonia de Monos de Cayo Santiago.. [Other]. 2018. Available from: http://www.lexjuris.com/lexlex/Leyes2018/lexl2018128.htm.
Other	Eckart K. Scientists come to the aid of Puerto Rican community, research station . 2017 September. Available from: https://www.washington.edu/news/2017/09/26/scientists-aid-puerto-rican-research-station/.
Other	WEISSENSTEIN M. Hurricane mauled PR's renowned Monkey Island research center. [Internet]. The Gazette2017 October. Available from: https://gazette.com/hurricane-mauled-pr-s-renowned-monkey-island-research-center/article_5713e8fc-ebc3-5919-84a9-423d4b90eac6.html.
Audio or video	Unkown. Rescuing Monkey Island: Daily Planet. [Video]. Discovery Canada2017 December. Available from: https://www.youtube.com/watch?time_continue=78&v=0OZmH_J9XYI.
Other	Unkown. From the Field: Cayo Santiago, Puerto Rico. [Internet]. Leakey Foundation2017 September. Available from: https://leakeyfoundation.org/from-the-field-cayo-santiago-puerto-rico/.
Other	Unkown. Monkey Island devastated by Hurricane Maria. [Internet]. 2017 September. Available from: https://sites.lsa.umich.edu/cognitive-evolution/2017/09/27/monkey-island-devastated-by-hurricane-maria/.
Other	Howard L. Scientists Rally to Help Unique Research Facility Destroyed by Hurricane Maria. [Internet]. UCDAVIS OFFICE OF RESEARCH2017 October. Available from: https://research.ucdavis.edu/cayosantiago/.
Audio or video	Unkown. Puerto Rico Moves Forward: Macaque Monkeys Adapt After Hurricane Maria. [Video]. Nova PBS2018 September. Available from: https://www.youtube.com/watch?v=5j1ezxH0hAQ.
Other	Espinosa R. Friday October 6, Our World in Pictures-PUERTO RICO — Monkeys Roam Island. [Photograph]. Brooklyn Daily Eagle2017 October. Available from: http://www.brooklyneagle.com/articles/2017/10/6/friday-october-6-our-world-pictures.
Other	Rivera Y. La ciencia no se rinde en Cayo Santiago. [Internet]. 2017 December. Available from: https://www.elvocero.com/actualidad/la-ciencia-no-se-rinde-en-cayo-santiago/article_d75e53fc-e465-11e7-8c46-2ff8aae1ea38.html.
Other	Unkown. Some monkeys prone to isolation. [Internet]. AAAS 2017 December. Available from: https://www.eurekalert.org/pub_releases/2017-12/uoe-smp121817.php.
Other	Kaplinsky C. Rebuilding Cayo Santiago Eight months after Hurricane Maria, this unique field site is still in recovery.. [Internet]. Natural History 2018 August. Available from: http://www.naturalhistorymag.com/features/083530/rebuilding-cayo-santiago.
Other	Al dia MicroJuris. Presentan medida para fortalecer legado científico en Cayo Santiago. [Internet]. MicroJuris.com2017 December. Available from: https://aldia.microjuris.com/2017/12/14/presentan-medida-para-fortalecer-legado-cientifico-en-cayo-santiago/.
Other	Hanson H. Scientists Scramble to Save 1,000 Primates on Puerto Rico's "Monkey Island". [Internet]. 2017 October. Available from: https://www.motherjones.com/politics/2017/10/scientists-scramble-to-save-1000-primates-on-puerto-ricos-monkey-island/.
Other	Dickson C. Primates on Puerto Rico's 'Monkey Island' research station narrowly survived Maria. [Internet]. Yahoo News2017 September. Available from:

	https://www.yahoo.com/news/monkeys-puerto-ricos-monkey-island-research-station-narrowly-survived-maria-203845783.html.
Other	Press A. Island ravaged by Maria could hold mysteries of human mind. [Internet]. New York Post2017 October. Available from: https://nypost.com/2017/10/06/why-scientists-are-rushing-to-save-monkey-island-in-puerto-rico/.
Other	Ruiz A. Official Cayo Santiago Biological Field Station Facebook Page. [Internet]. 2017. Available from: https://www.facebook.com/CayoSantiagoBFS/.
Other	Price M. You can thank your fruit-hunting ancestors for your color vision. [Internet]. 2017 February. Available from: http://www.sciencemag.org/news/2017/02/you-can-thank-your-fruit-hunting-ancestors-your-color-vision.
Other	Hubler D. Return to Monkey Island: Repairing Damage from Hurricane Maria. [Internet]. EDM DIGEST2018 May. Available from: https://edmdigest.com/recovery/monkey-island-damage-hurricane-maria/.
Other	McMaster A. Scientists in Puerto Rico Are Trying to Save 1,500 Monkeys for This Important Reason. [Internet]. 2017 October. Available from: https://www.globalcitizen.org/en/content/puerto-rico-cayo-santiago-monkey-island-hurricane/.
Audio or video	Kincade L. Autism research in danger after Maria. [Video]. CNN2017 October. Available from: https://edition.cnn.com/videos/world/2017/10/12/puerto-rico-monkey-island-research-hurricane-maria-kinkade.cnn.
Other	Unkown. Urgen trabajos y medidas de seguridad en el Cayo Santiago en Humacao tras María. Walo Radio2017 December. Available from: http://waloradio.com/urgen-trabajos-y-medidas-de-seguridad-en-el-cayo-santiago-en-humacao/.
Other	WEISSENSTEIN M. Scientists race to save Monkey Island research center. [revised 2017 October]. [Internet]. The Detroit News2017 October. Available from: https://www.detroitnews.com/story/tech/science/2017/10/06/hurricane-maria-monkey-island/106361830/.
Other	Rosati A. Scientists join forces to save Puerto Rico's 'Monkey Island'. [Internet]. 2017 October. Available from: http://theconversation.com/scientists-join-forces-to-save-puerto-ricos-monkey-island-84960
Audio or video	Unkown. Puerto Rico's Monkey Island research centre ravaged by hurricane. [Video]. 2017 October. Available from: https://www.youtube.com/watch?v=kNa5c4t-lqA.
Other	Devitt J. Researchers Work to Save "Monkey Island" Damaged by Hurricane Maria. [Internet]. 2017 September. Available from: https://www.nyu.edu/about/news-publications/news/2017/september/researchers-work-to-save-monkey-island-damaged-by-hurricane-mari.html.
Other	Baeza Bickel N. Científicos unen fuerzas para salvar la "Isla de los Monos" en Puerto Rico. [Internet]. Michigan News2017 October. Available from: http://espanol.umich.edu/noticias/2017/10/03/cientificos-unen-fuerzas-para-salvar-la-isla-de-los-monos-en-puerto-rico/.
Other	Coyne SP. The Ontogeny of Sexual Maturation: Factors Affecting the Development of Sexual Signal Production, Perception, and Behavior in Adolescent Female Rhesus Macaques. [Other]. 2017.
Other	Glowatz E. Hurricane Maria Aftermath: The Monkey Science Island In Puerto Rico. [Internet]. Internarional Business Times2017 October. Available from: https://www.ibtimes.com/hurricane-maria-aftermath-monkey-science-island-puerto-rico-2596958.
Other	Hathaway B. Researchers mobilize to save storm-ravaged Monkey Island. [Internet]. 2017 September. Available from: https://news.yale.edu/2017/09/26/researchers-mobilize-save-storm-ravaged-monkey-island.

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

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

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
eRA Commons User Name	Y	Martinez, Melween I.	DVM	PD/PI	EFFORT					NA
Redacted by agreement										NA
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Redacted by agreement			NA
			NA
			NA
			NA
			NA
			NA

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

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

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

No

D.2.b New Senior/Key Personnel

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

No

D.2.c Changes in Other Support

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

No

D.2.d New Other Significant Contributors

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

No

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

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

No

E. IMPACT

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

Not Applicable

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

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. 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

Restoration of the infrastructure, as well as the normal research activities, specially at Redacted by agreement represent a challenge. We have plans in place to restore the infrastructure with funding provided by NIH.

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. SPECIAL REPORTING REQUIREMENTS

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

File(s) uploaded:
TABLE OF SALES FY 2018Completed.pdf
PROGRAM INCOME & EXPENSES REPORTING FY 2018.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: Caribbean Primate Research Center, UPR-MSC	948108063	00-000	UPR Medical Sciences Campus PO Box 1053 SAN JUAN PR 009365067
UNIVERSITY OF PUERTO RICO MEDICAL SCIENCES CAMPUS	948108063		UPR Medical Sciences Campus Office of Sponsored Programs, PO Box 365067 SAN JUAN PR 009365067

Caribbean Primate Research Center, UPR-MSC	948108063	00-000	UPR Medical Sciences Campus PO Box 1053 SAN JUAN PR 009360000
UNIVERSITY OF PUERTO RICO MEDICAL SCIENCES CAMPUS	948108063		UPR Medical Sciences Campus Office of Sponsored Programs, PO Box 365067 SAN JUAN PR 009365067
Caribbean Primate Research Center, UPR-MSC	948108063	00-000	UPR Medical Sciences Campus PO Box 1053 SAN JUAN PR 009365067
UNIVERSITY OF PUERTO RICO MEDICAL SCIENCES CAMPUS	948108063		UPR Medical Sciences Campus Office of Sponsored Programs, PO Box 365067 SAN JUAN PR 009365067
Caribbean Primate Research Center, UPR-MSC	948108063	00-000	UPR Medical Sciences Campus PO Box 1053 SAN JUAN PR 009360000

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

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

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

Yes

Anticipated Amount	Source(s)
900000	Monkey sales & bench fees

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

TABLE OF SALES FY 2018
(July 2017-June 2018)

Principal Investigator/Contact Person	Institution	Source of Support	Number of animals assigned
Redacted by agreement			8
			35
			31
			13
			50
			30
			16
			39
			11
			24
			13
			8
			25
Total FY 18			**303**

WNPRC: Washington National Primate Research Center

INCOME FY18

$	854,240.00	MONKEY SALES
$	16,530.35	BENCH FEES
$	10,389.60	BD
$	6,950.00	CELL PROLABS, BIOPRO, BRIAN C. BROSDAHL (KIDNEYS)
$	7,488.88	OTHER
$	**895,628.83**	

PROGRAM INCOME EXPENSES FY 2018

	EXPENSES	ENCUMBRANCES	TOTAL
SALARIES & FB	$ 598,366.47		$ 598,366.47
OFFICE MATERIAL	$ 13,396.87	$ 2,187.74	$ 15,584.61
SANITARY MATERIALS	$ 29,317.88	$ 7,226.66	$ 36,544.54
LABOTATORY MATERIALS	$ 13,784.81	$ (8,761.09)	$ 5,023.72
PEST CONTROL	$ 49,004.80	$ 30,693.70	$ 79,698.50
FRUITS & VEGGIES ADJUSTMENT	(2,444.33)	$ (738.75)	$ (3,183.08)
WATER & ICE FOR EMPLOYEES	$ 213.75		$ 213.75
UNIFORMS	$ 13,156.93	$ 3,106.54	$ 16,263.47
SMALL TOOLS	$ 5,000.03	$ 4,609.59	$ 9,609.62
VEHICULES PARTS	$ 8,922.30	$ 941.64	$ 9,863.94
EQUIPMENT PARTS	$ 26,812.40	$ 7,200.97	$ 34,013.37
OILS	$ 3,446.40	$ (103.46)	$ 3,342.94
LABOTATORY EQUIPMENT MAINTENANCE	$ 5,708.16	$ 60.00	$ 5,768.16
VEHICULES MAINTENANCE	$ 65.00		$ 65.00
A/C MAINTENANCE	$ 51,845.47	$ 12,852.66	$ 64,698.13
ELEVATOR MAINTENANCE	$ -	$ 3,025.00	$ 3,025.00
BUILDING MAINTENANCE	$ -	$ 2,244.75	$ 2,244.75
OTHER EQUIPMENT MAINTENANCE	$ 28,974.71	$ 50,195.87	$ 79,170.58
CONSTRUCTION MATERIALS	$ 105,823.97	$ 13,284.47	$ 119,108.44
LEASE OFFICE CS	$ 30,600.00		$ 30,600.00
LEASE CONSTRUCTION EQUIPMENT		$ 3,900.00	$ 3,900.00
QUALITY WATER LEASE	$ 1,494.00	$ 3,278.00	$ 4,772.00
PHOTOCOPY MACHINE LEASE	$ 6,625.16		$ 6,625.16
TELECOMMUNICATIONS	$ 12,131.18	$ 1,812.85	$ 13,944.03
OTHERS EXPENSES	$ 2,597.11	$ 8,245.00	$ 10,842.11
VISITOR TRAVEL AGREEMENT (VTA)	$ 3,441.80		$ 3,441.80
ANNUAL ACREDITATION	$ 6,345.00		$ 6,345.00
OFFICE OF PLANIFICATION SERVICES	$ 8,198.00		$ 8,198.00
TRANSPORTATION EXPENSES	$ 7,140.81	$ (2,291.30)	$ 4,849.51
VEHICULE TAGS EXPENSES	$ 222.00		$ 222.00
GAS, GASOLINE & DIESEL	$ 19,537.62	$ 409.45	$ 19,947.07
WASTE DISPOSAL	$ 21,259.85	$ 6,749.90	$ 28,009.75
TRAVEL	$ 10,209.74	$ 368.00	$ 10,577.74
MINOR EQUIPMENT	$ 26,523.43	$ 27,437.11	$ 53,960.54
MAYOR EQUIPMENT	$ 77,840.00	$ 37,476.00	$ 115,316.00
	$ 1,185,561.32	**$ 215,411.30**	**$ 1,400,972.62**

RESEARCH & RELATED BUDGET - SECTION A & B

ORGANIZATIONAL DUNS*: 948108063

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: UNIVERSITY OF PUERTO RICO MED SCIENCES

Start Date*: 12-01-2018 **End Date*:** 11-30-2019

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	Melween		Martinez		PI	Institutional Base	%			36,999.00	11,159.00	48,158.00
2.	Redacted by agreement												
3.													
4.													
5.													

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

Additional Senior Key Persons: File Name:

Total Senior/Key Person **231,148.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
4	Secretarial/Clerical	27.28			95,879.00	40,893.00	136,772.00
20	Vets (2), Colony Mangers (2), Behaviorist/Research (2), AHT (3), LAb Aid(1), Lab Tech (1), Repairmen (4) Caretakers (4), Chief Operations (1)	215.05			514,867.00	268,094.00	782,961.00
24	**Total Number Other Personnel**					**Total Other Personnel**	**919,733.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**1,150,881.00**

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

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

ORGANIZATIONAL DUNS*: 948108063
Budget Type*: ● Project ❍ Subaward/Consortium
Enter name of Organization: UNIVERSITY OF PUERTO RICO MED SCIENCES

Start Date*: 12-01-2018 **End Date*:** 11-30-2019

C. Equipment Description

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

Equipment Item	Funds Requested ($)*
1. ATTUNE ACOUSTIC FOCUSING CYTOMETER	25,000.00
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**25,000.00**

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	2,817.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**2,817.00**

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*: 948108063

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F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	112,115.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	34,091.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. MONKEY CHOW	217,006.00
Total Other Direct Costs	**363,212.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**1,541,910.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1. Modified Total Direct Cost	50.0	1,482,819.00	741,410.00
		Total Indirect Costs	**741,410.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number): DHHS REGION II, DARYLL W MAYES,212-264-2069

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**2,283,320.00**

J. Fee	Funds Requested ($)*
	0.00

K. Budget Justification* File Name: Budget Justification UPR-2018.pdf (Only attach one file.)

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

Program Director/Principal Investigator (Last, First, Middle): Martinez, Melween

BUDGET JUSTIFICATION	GRANT NUMBER 5P40OD01227-32

Provide a detailed budget justification for those line items and amounts that represent a significant change from that previously recommended. Use continuation pages if necessary.

Personnel: Same as year 3. Personnel budget reflects requested personnel in the original application, which is critically needed to attain our grant objectives. Total Personnel: $1,150,881.00

Supplies: Veterinary and animal care supplies $43,252; Curation & maceration supplies : $2,495. Also, $2,000 is requested for diagnostic procedures for veterinary pathology, necropsies and histology supplies in order for the Veterinary Clinic to adequately function on a daily basis. $ 64,368 is requested for the supplies for the Model Oriented projects I,2,3,4 & Immunology Core. For a total of $112,115.

Equipment: $ 25,000 is requested for year 3 to cover the remaining amount of Attune® Acoustic Focusing Cytometer for the immunology core.

Travel: Same as year 2-$2,817

Subawards/Consortium/ Contractual Costs- (DC$18,629 +IC$15,462 = $34,091) with University of Texas @ Rio Grande Valley with Redacted by agreement

Other Expenses: $21,000 is requested to cover the costs of genotyping and paternity testing at VGL. $148,434 is requested (based on our current expenses) to purchase commercial high protein monkey diet to the conventional facility monkeys at Redacted by agreement In addition $15,000 is requested to balance the diet with fruits and vegetables. $ 32,572 is requested for the Model Oriented projects I, & 2. Total other Expenses: $217,006.00

Total Direct Cost Requested	$1,541,910
Total Direct Cost + Indirect Cost	$2,283,320

CURRENT BUDGET PERIOD	FROM	THROUGH

Explain any estimated unobligated balance (including prior year carryover) that is greater than 25% of the current year's total budget.

DETAILED PERSONNEL	NAME	ROLE IN PROJECT	Effort requested	Requested Salary	Requested Fringe	Total funds requested
	Melween Martinez	PI	EFFORT	$ 36,999.00	$ 11,159.00	$ 48,158.00
	Redacted by agreement					
Vet Pathologist Veterinary						
Total						
Colony Manager						
Total						
Behaviorist/Research						
Total						
Administrative/Clerical						
Other Personnel						
Total			**168.00**	**$ 309,960**	**$ 185,414**	**$ 495,374**
GRAND TOTAL			**271.58**	**$ 781,880**	**$ 369,001**	**$ 1,150,881**

ITEMS VETERINARY MATERIALS	TOTAL
Tuberculin	$ 4,299.00
Tetanus toxoid	$ 1,200.00
Rabies vaccine	$ 2,520.00
Protective clothing 1425 +4,876 (uniformes vet care)+ 3,025 (construction)+ 2,750 (Cayo)=9,076	$ 9,076.00
Medicines (900 animals +Cayo)= 4927	$ 4,927.00
Ketamine	$ 1,800.00
Clinical and samples processing supplies(syringes, bleeding vials,butterflies, alcohol,gauze,drapes, fluids,endotracheal tubes,capture equipment,sharp containers etc)	$ 12,446.00
Sanitation material	$ 6,984.00
	$ 43,252.00

Budget Applied Research Component

	SUPPLIES	OTHER	EQUPMENT	TOTAL
P1	$ 6,368.00	$ 14,672.00		$ 21,040.00
P2	$ 8,000.00	$ 17,900.00		$ 25,900.00
P3	$ 20,000.00	$ -		$ 20,000.00
P4	$ 20,000.00	$ -		$ 20,000.00
IC	$ 10,000.00		$ 25,000.00	$ 35,000.00
TOTAL	**$ 64,368.00**	**$ 32,572.00**	**$ 25,000.00**	**$ 121,940.00**

Project I	$ 2,000.00		
	$ 1,500.00		
	$ 1,668.00		
	$ 1,200.00	**$ 6,368.00**	
Project 2	$ 8,000.00	**$ 8,000.00**	
Project 3	$ 3,600.00		
	$ 2,400.00		
	$ 1,000.00		
	$ 800.00		
	$ 1,440.00		
	$ 1,160.00		
	$ 1,380.00		
	$ 2,000.00		
	$ 8,020.00	**$ 20,000.00**	The total for this project is $21,800; but we are requesting only $20,000.
Project 4	$ 10,000.00	**$ 20,000.00**	
	$ 2,000.00		
	$ 8,000.00		
Immunology Core	$ 10,000.00	**$ 10,000.00**	
	$ 66,168.00	$ 64,368.00	
Difference	$ 1,800.00		