Notice of Award

PRIMATE RESEARCH CENTER GRANT **Issue Date:** 04/28/2014

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

Grant Number: 5P51OD011104-53
FAIN: P51OD011104

Principal Investigator(s):
L. Lee HAMM, MD

Project Title: Tulane National Primate Research Center

Kathleen M. Kozar
Tulane University
Director, Sponsored Projects Admin
1430 TULANE AVENUE, EP-15
NEW ORLEANS, LA 701122632

Award e-mailed to: elecnotf@tulane.edu

Budget Period: 05/01/2014 – 04/30/2015
Project Period: 05/09/1997 – 04/30/2018

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $8,157,458 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to TULANE UNIVERSITY OF LOUISIANA 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 P51OD011104. 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 42 CFR Part 50 Subpart F. Subsequent to the compliance date of the 2011 revised FCOI regulation (i.e., on or before August 24, 2012), Awardees must be in compliance with all aspects of the 2011 revised regulation; until then, Awardees must comply with the 1995 regulation. 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 – 5P51OD011104-53

Award Calculation (U.S. Dollars)

Salaries and Wages	$2,728,458
Fringe Benefits	$727,656
Personnel Costs (Subtotal)	$3,456,114
Consultant Services	$8,377
Equipment	$600,000
Supplies	$1,170,604
Travel Costs	$22,010
Other Costs	$1,972,244
Federal Direct Costs	$7,229,349
Federal F&A Costs	$928,109
Approved Budget	$8,157,458
Federal Share	$8,157,458
TOTAL FEDERAL AWARD AMOUNT	$8,157,458
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$8,157,458

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
53	$8,157,458	$8,157,458
54	$10,071,913	$10,071,913
55	$10,071,913	$10,071,913
56	$10,071,913	$10,071,913

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

Fiscal Information:

CFDA Number:	93.351
EIN:	1720423889A5
Document Number:	POD011104J
PMS Account Type:	G (Pooled)
Fiscal Year:	2014

IC	CAN	2014	2015	2016	2017
OD	8014499	$8,086,802	$10,001,257	$10,001,257	$10,001,257
AG	8470701	$70,656	$70,656	$70,656	$70,656

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

NIH Administrative Data:
PCC: CMP01 / **OC:** 414E / **Released:** eRA Commons User Name 04/24/2014
Award Processed: 03/04/2014 08:59:52 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P51OD011104-53

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 – 5P51OD011104-53

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 74 or 45 CFR Part 92 as applicable.
d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. 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.)

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

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

This award has been assigned the Federal Award Identification Number (FAIN) P51OD011104. 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/.

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

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

Treatment of Program Income:
Additional Costs

SECTION IV – OD Special Terms and Conditions – 5P51OD011104-53

SUBJECT FOA:
This award is subject to the conditions set forth in PAR11-136, "Limited Competition: National Primate Research Center." which are hereby incorporated by reference as special terms and conditions of this award. Copies of this Funding Opportunity Announcement can be found at the following link: http://grants.nih.gov/grants/guide/pa-files/PAR-11-136.html

ORIP FUNDING PLAN FOR FY2014
This non-competing award reflects the NIH Fiscal Policy for Grant Awards for FY2014 (see NIH Guide Notice NOT-OD-14-055) and the implementation of the ORIP FY2014 grants funding policy: http://dpcpsi.nih.gov/orip/rf/fyg_fp2014.aspx

CO-FUNDING
This award reflects support from ORIP in the amount of $8,086,802 total costs and from the National Institute on Aging in the amount of $70,656 total costs.

KEY PERSONNEL:
In addition to the PI, the following individuals are named as key personnel (individuals who have

effort that ORIP staff is tracking):

Dr. Andrew Lackner

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

DIRECT CHARGES OF F&A-TYPE COSTS:
Funds requested for long distance, printing, postage, shipping, photocopier expenses, stationary, enveloped are included in the awarded budget. The allowability of charges to this project for this purpose is predicated on the grantee's compliance with the applicable cost principles.

PRIOR APPROVAL REQUEST:

Any prior approval request (e.g., changes to key personnel as noted on the award, changes in human and animal subjects requiring prior approval, carryover requests) must be submitted to the assigned Grants Management Specialist and Programmatic Official. Please refer to the NIH Grants Policy Statement for the activities and/or expenditures that require NIH approval at http://grants.nih.gov/grants/policy/nihgps_2013/nihgps_ch8.htm#prior_approval_requirements

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

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

STAFF CONTACTS

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

Grants Management Specialist: Judith Musgrave
Email: musgravj@mail.nih.gov **Phone:** (301) 435-0841 **Fax:** (301) 480-3777

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

SPREADSHEET SUMMARY
GRANT NUMBER: 5P51OD011104-53

INSTITUTION: TULANE UNIVERSITY OF LOUISIANA

Budget	Year 53	Year 54	Year 55	Year 56
Salaries and Wages	$2,728,458	$3,743,598	$3,743,598	$3,743,598
Fringe Benefits	$727,656	$1,016,467	$1,016,467	$1,016,467
Personnel Costs (Subtotal)	$3,456,114	$4,760,065	$4,760,065	$4,760,065
Consultant Services	$8,377	$7,500	$7,500	$7,500
Equipment	$600,000	$520,500	$600,000	$600,000
Supplies	$1,170,604	$1,368,159	$1,368,159	$1,368,159
Travel Costs	$22,010	$37,080	$37,080	$37,080
Alterations and Renovations		$79,500		
Other Costs	$1,972,244	$2,135,892	$2,135,892	$2,135,892
TOTAL FEDERAL DC	$7,229,349	$8,908,696	$8,908,696	$8,908,696
TOTAL FEDERAL F&A	$928,109	$1,163,217	$1,163,217	$1,163,217

TOTAL COST	$8,157,458	$10,071,913	$10,071,913	$10,071,913

Facilities and Administrative Costs	Year 53	Year 54	Year 55	Year 56
F&A Cost Rate 1	14%	14%	14%	14%
F&A Cost Base 1	$6,629,349	$8,308,696	$8,308,696	$8,308,696
F&A Costs 1	$928,109	$1,163,217	$1,163,217	$1,163,217

Progress Report Scanning Cover Sheet

5P51OD011104-53

PI Name:	**HAMM, L.**
Org:	**TULANE UNIVERSITY OF LOUISIANA**
Start Date:	**05/01/2014**
Snap:	**N/A** (NEEDS TO BE BOOKMARKED)
Appl ID:	**8685365**
Rec'd Date:	**03/26/2014**

OD 11104-53

Form Approved Through 08/31/2015 OMB No. 0925-0002

Department of Health and Human Services
Public Health Services

Grant Progress Report

Review Group	Type	Activity	Grant Number
	5	P51	OD01104-53

Total Project Period
From: 5/1/2013 Through: 4/30/2018

Requested Budget Period
From: 5/1/2014 Through: 4/30/2015

1. TITLE OF PROJECT
National Primate Research Center

2a. PROGRAM DIRECTOR / PRINCIPAL INVESTIGATOR (Name and address, street, city, state, zip code)
Lee Hamm, MD
Senior Vice President for Health Sciences
Tulane University Health Sciences Center
1430 Tulane Avenue
New Orleans, LA 70112

2b. E-MAIL ADDRESS
lhamm@tulane.edu

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Tulane National Primate Research Center

2d. MAJOR SUBDIVISION
Tulane National Primate Research Center

2e. Tel: 985-871-6201 Fax: 985-893-1352

3a. APPLICANT ORGANIZATION (Name and address, street, city, state, zip code)
Tulane University Health Sciences Center
1430 Tulane Avenue
New Orleans, LA 70112

3b. Tel: 504-988-5207 Fax: 504-988-1748

3c. DUNS: 053785812

4. ENTITY IDENTIFICATION NUMBER
1720423889A1

6. HUMAN SUBJECTS ☒ No ☐ Yes

6a. Research Exempt	If Exempt ("Yes" in 6a): Exemption No.	If Not Exempt ("No" in 6a): IRB approval date
☐ No ☐ Yes		

6b. Federal Wide Assurance No.

6c. NIH-Defined Phase III Clinical Trial ☐ No ☐ Yes

5. NAME, TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL
Kathleen Kozar, Director Sponsored Projects Administration

Tel: 504-988-5207 Fax: 504-988-1748

E-MAIL: elecnotf@tulane.edu

7. VERTEBRATE ANIMALS ☐ No ☒ Yes

7a. If "Yes," IACUC approval Date 09/05/2013

7b. Animal Welfare Assurance No. A4499-01

10. PROJECT/PERFORMANCE SITE(S)

Organizational Name: Tulane National Primate Research Ctr

DUNS: 053785812

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD

8a. DIRECT $7,120,823 8b. TOTAL $8,033,738

9. INVENTIONS AND PATENTS ☐ No ☒ Yes

If "Yes," ☒ Previously Reported ☐ Not Previously Reported

Street 1: 18703 Three Rivers Road

Street 2:

City: Covington County: St Tammany

State: LA Province:

Country: USA Zip/Postal Code: 70433

Congressional Districts: 02

11. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION *(Item 13)*
Kathleen Kozar

TEL: 504-988-5207 FAX: 504-988-1748 E-MAIL: kkozar@tulane.edu

12. Corrections to Page 1 Face Page

13. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 11 *(In Ink)* Kathleen M Kozar DATE 2-17-14

Program Director/Principal Investigator (Last, first, middle): Hamm, L/Lackner,A

GRANT NUMBER
OD01104-53

CHECKLIST

1. PROGRAM INCOME *(See Instructions.)*
All applications must indicate whether program income is anticipated during the period(s) for which grant support is requested. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)
	$0	

2. ASSURANCES/CERTIFICATIONS *(See Instructions.)*
In signing the application Face Page, the authorized organizational representative agrees to comply with the policies, assurances and/or certifications listed in the application instructions when applicable. Descriptions of individual assurances/certifications are provided in Part III of the PHS 398, and listed in Part I, 4.1 under Item 14. If unable to certify compliance, where applicable, provide an explanation and place it after the Progress Report (Form Page 5).

3. FACILITIES AND ADMINSTRATIVE (F&A) COSTS
Indicate the applicant organization's most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the appropriate PHS Agency Cost Advisory Office.

F&A costs will *not* be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, Small Business Innovation Research/Small Business Technology Transfer Grants, foreign grants, and specialized grant applications.

☒ DHHS Agreement dated: 05/14/2013 ☐ No Facilities and Administrative Costs Requested.

☐ NO DHHS Agreement, but rate established with _____ Date _____

CALCULATION*

Entire proposed budget period: Amount of base $ 6,520,823 x Rate applied 14.00 % = F&A costs $ 912,915

Add to total direct costs from Form Page 2 and enter new total on Face Page, Item 8b.

*Check appropriate box(es):

☐ Salary and wages base ☒ Modified total direct cost base ☐ Other base *(Explain)*

☐ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.)*:

ALL PERSONNEL REPORT

Place this form at the end of the signed original copy of the application. Do not duplicate.

GRANT NUMBER: OD01104-53

Always list the PD/PI(s). In addition, list all other personnel who participated in the project during the current budget period for at least one person month or more, regardless of the source of compensation (a person month equals approximately 160 hours or 8.3% of annualized effort). Use the following abbreviated categories for describing Role on Project:

- PD/PI
- Co-Investigator
- Faculty
- Postdoctoral (scholar, fellow, postdoctoral position)*
- Technician
- Staff Scientist (doctoral level)
- Statistician
- Graduate Student (research)
- Non-Student Research Assistant
- Undergraduate Student
- High School Student
- Consultant
- Other (please specify)

If personnel are supported by a Reentry or Diversity Supplement please indicate such after the Role on Project, using the following abbreviations: RS - Reentry Supplement; DS - Diversity Supplement.

*Commons ID required for any personnel holding this Role on Project and for all individuals supported by a Reentry or Diversity Supplement. The Commons ID will be required in the future for all individuals with a graduate student, or undergraduate role. The Commons ID is strongly encouraged, but not required, for all other Project Personnel.

Use Cal (calendar), Acad, or Summer to enter months devoted to project.

Commons ID*	Name	Degree(s)	SSN (last 4 digits)	Role on Project	DoB (MM/YY)	Cal	Acad	Summer
eRA Commons User Name	Excluded by Requester		SSN	Animal Care Technician II	DOB	% Effort		
				Operations Manager I				
				Medical Research Specialist				
				Custodial Worker				
		PhD,MBA		Chief Operating Officer				
				Secretary				
		PhD		Research Associate Professor				
				Animal Care Technician III				
				Animal Care Technician II				
				Clerk				
		DVM, PhD		Research Associate Professor				
				Grants Management Specialist				
				Accountant II				
				Animal Care Technician II				
				Animal Care Technician III				
		PhD		Primate Center Research Scientist I				
				Animal Care Trainee				
				Medical Research Specialist				
				Veterinary Technician III				
				Executive Secretary				
				Animal Research Supervisor				
				Equipment Technician III				
				Animal Research Supervisor				
				Animal Research Supervisor				
		DVM, PhD		Executive Director				
				General Maintenance Worker II				
		DVM, PhD		Associate Director				
		DVM, PhD		Associate Professor				
		PhD		Research Assistant Professor				
				Animal Care Technician III				
				Operating Engineer				
				Animal Research Supervisor				
				Animal Care Technician I				
				Animal Care Technician I				
				Lab Supervisor II				
				Animal Care Technician II				
				Animal Care Technician I				
		PhD		Professor				
				Animal Care Technician III				
				Animal Research Supervisor				
				Animal Research Supervisor				
				Animal Care Technician II				
				Animal Care Technician IV				
				Records Manager				
				Operating Engineer				
				Custodial Worker				
		CPA		Senior Accountant				
				Animal Care Technician III				
				Assistant Director				
				Animal Care Technician IV				
				Senior Program Coordinator				
				Environment Technician III				
				Maintenance Assistant Supervisor				
				Systems Specialist I				
				Lab Supervisor II				
				Animal Research Supervisor				
				Animal Care Technician III				
				Maintenance Assistant Supervisor				
				Veterinary Technician III				
				Veterinary Technician IV				
				Medical Research Specialist				
				Animal Care Technician II				
				Animal Care Technician III				
				Secretary				
				Grounds Attendant				
				Animal Research Supervisor				
		PhD		Professor				
		DVM, PhD		Adjunct Assistant Professor				
				Veterinary Technician III				
				Animal Care Technician II				
				Medical Research Specialist				
		DVM		Veterinarian				
		DVM		Veterinarian				
				Lab Supervisor II				
		PhD		Research Assistant Professor				

eRA Commons User Name	Excluded by Requester		% Effort		DOB	% Effort
				Secretary		
				Project Assistant		
				Manager		
				Database Administrator III		
				Epidemiologist		
				Veterinary Technician II		
				Grants Management Analyst		
				General Maintenance Worker II		
				Grants Management Specialist		
				Medical Research Specialist		
				General Maintenance Worker II		
				Veterinary Technician III		
				Animal Research Supervisor		
				Programmer I		
				Animal Care Trainee		
		VM		Veterinarian		
				Medical Research Technician		
				Lab Supervisor II		
				Operating Engineer		
		VM		Assistant Professor		
				Animal Care Technician II		
				Animal Care Technician II		
				Plumber		
				Animal Care Technician I		
				Medical Technologist		
				Lab Supervisor II		
				Executive Assistant		
				Grounds Attendant		
				Secretary		
				User Services Analyst III		
				Histotechnician		
				TNPRC Procurement Specialist		
				Financial Services Specialist		
				Lab Supervisor II		
				Postdoc Fellow		
				Animal Care Technician II		
				Primate Center Research Scientist II		
				Postdoc Fellow		
				Welder		
				Associate Professor		
				Project Assistant		
				Animal Care Technician II		
				Lab Supervisor II		
				Assistant Director		
				Executive Secretary		
				Electrician		
				Primate Center Research Scientist I		
				Research Associate Professor		
				Operating Engineer		
				Sales Specialist		
				Animal Care Technician II		
		VM, PhD		Director		
				Medical Research Specialist		
				Mail Technician		
				Applications Specialist I		
				Support Services Supervisor		
				Medical Technician		
				Animal Care Technician II		
				Research Assistant Professor		
				Database Administrator I		
				Enrichment Technician II		
		VM, PhD		Research Assistant Professor		
				Accountant I		
				Enrichment Technician II		
				Animal Care Technician II		
				Assistant Professor		
				Program Manager		
				Animal Care Technician II		
				Veterinary Technician II		
				Equipment Operator		
				Veterinary Technician II		
				Research Assistant Professor		
				Welder		
				Professor		
				Operations Manager I		
				Medical Research Specialist		
				Histotechnician		
				Animal Research Supervisor		
				Department Administrator I		
				Associate Professor		
				Courier		
				General Maintenance Worker II		
				Medical Research Specialist		
		VM, PhD		Assistant Professor		
				Medical Research Specialist		
				Enrichment Technician II		
				Veterinary Specialist		
				Medical Research Technician		
				Lab Technician		
				Executive Secretary		
				Biomedical Engineer		
				Animal Care Technician II		
				Financial Services Associate		
				Research Assistant Professor		
				Professor		
				Animal Care Trainee		
				Secretary		
				Medical Technologist		

eRA Commons User Name	Excluded by Requester		SSN		DOB	% Effort
				Grants Management Specialist		
				Medical Research Technician		
				Medical Technician		
				Medical Research Technician		
				Resource Manager		
		PhD		Professor		
				Veterinary Technician II		
				Medical Technologist		
				Animal Care Technician II		
				Animal Care Trainee		
				Accounting Analyst		
				Operations Manager I		
		DVM		Veterinarian		
		BBA, CPA		Assistant Controller		
				Lab Technician		
				Animal Care Technician IV		
				Media and Communications Specialist		
		BA		Executive Secretary		
		PhD		Associate Professor		
				Animal Care Technician III		
				Animal Care Technician I		
				Veterinarian		
				Animal Care Technician I		
		CIS		Technology Services Manager		
				Veterinary Technician IV		
				Medical Research Specialist		
		MBA, PHR		Consultant		
				Department Administrator I		
				Animal Care Technician I		
		DVM, PhD		Associate Professor		
				Custodial Worker		
				Veterinary Technician II		
				Medical Technologist		
				Animal Care Technician IV		
				Animal Care Technician II		
				Occupational Health Nurse		
				Animal Care Technician II		
				Manager		
				General Maintenance Worker III		
				Operating Engineer		
				Mechanic		
				Animal Care Technician II		
				Animal Care Technician II		
				User Services Analyst I		
				Manager		
				Animal Care Trainee		
				Grounds Attendant		
				Animal Care Technician II		
				Lab Technician		
				Veterinary Specialist		
				Animal Research Supervisor		
				Medical Research Technician		
		PhD		Postdoc Fellow		
				Biomedical Technician		
				Medical Research Specialist		
				Enrichment Technician I		
				Animal Care Technician III		
				Licensed Practical Nurse		
				Animal Care Technician II		
		PhD		Research Associate Professor		
				Lab Specialist		
				Animal Care Trainee		
		DVM, PhD		Professor		
				Systems Programmer		
				Animal Care Technician I		
				Animal Care Trainee		
		PhD		Asst Professor		
				Animal Care Technician II		
				General Maintenance Worker II		
				Enrichment Technician III		
				Animal Research Supervisor		
				Animal Research Supervisor		
				Animal Research Supervisor		
				Animal Care Technician I		
				Animal Care Trainee		
				Enrichment Technician II		
				Research Instructor		
		PhD		Postdoc Fellow		
				Facilities & Maintenance Assistant Manager		
				Chief Operating Engineer		
				Animal Care Technician II		

Composite Summary

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Administration					368,268	100,902	469,170
Operations					347,880	106,379	454,259
Outreach					12,662	2,838	15,500
Pilot Research					4,705	809	5,514
Veterinary Resources					920,509	255,449	1,183,385
Microbiology					313,296	70,560	383,856
Immunology					90,916	22,668	113,584
Bacteriology & Parasit					110,852	25,502	136,354
Comparative Pathology					425,428	102,153	527,581
Regenerative Medicine					89,276	21,057	110,333
Improvement & Modern					0	0	0
SUBTOTALS					2,683,792	708,317	3,399,536

CONSULTANT COSTS				
Administration	8,240			
Operations	0			8,240
EQUIPMENT (Itemize)				
Administration	0	Immunology	0	
Operations	0	Bacteriology & Parasitology	0	
Outreach	0	Comparative Pathology	0	
Pilot Research	0	Regenerative Medicine	0	
Veterinary Resources	0	Improvement & Modernization	600,000	
Microbiology	0			600,000
SUPPLIES (Itemize by category)				
Administration	33,090	Immunology	17,300	
Operations	235,400	Bacteriology & Parasitology	14,150	
Outreach	0	Comparative Pathology	10,300	
Pilot Research	0	Regenerative Medicine	15,000	
Veterinary Resources	695,200	Improvement & Modernization	0	
Microbiology	131,000			1,151,440
TRAVEL		Immunology	0	
Administration	12,150	Microbiology	0	
Operations	6,500	Bacteriology & Parasitology	0	
Outreach	0	Comparative Pathology	0	
Pilot Research	0	Regenerative Medicine	0	
Veterinary Resources	3,000			21,650
INPATIENT CARE COSTS				0
OUTPATIENT CARE COSTS				0
ALTERATIONS AND RENOVATIONS (Itemize by category)				
Improvement & Modernization	0			0
OTHER EXPENSES (Itemize by category)				
Administration	127,450	Immunology	0	
Operations	1,462,409	Bacteriology & Parasitology	13,310	
Outreach	35,000	Comparative Pathology	3,750	
Pilot Research	180,000	Regenerative Medicine	550	
Veterinary Resources	114,588	Improvement & Modernization	0	
Microbiology	2,900			1,939,957
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD			$	7,120,823
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS		
CONSORTIUM/CONTRACTUAL COSTS		FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)			$	7,120,823

ADMINISTRATION - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Director's Office					124,260	27,297	151,557
Business Office					108,079	33,396	141,475
Center Resources					43,522	11,655	55,177
Human Resources					37,070	11,455	48,525
Grants Administration					55,337	17,099	72,436
SUBTOTALS					368,268	100,902	469,170

CONSULTANT COSTS				
Director's Office	8,240			8,240
EQUIPMENT (Itemize)				0
SUPPLIES (Itemize by category)				
Director's Office	10,540			
Business Office	11,050			
Center Resources	9,950			
Human Resources	200			
Grants Administration	1,350			33,090
TRAVEL		Business Office	0	
Director's Office	12,000	Human Resources	150	
Grants Administration	0			12,150
INPATIENT CARE COSTS				0
OUTPATIENT CARE COSTS				0
ALTERATIONS AND RENOVATIONS (Itemize by category)				0
OTHER EXPENSES (Itemize by category)				
Director's Office	20,300	Grants Administration	100	
Business Office	200			
Center Resources	101,100			
Human Resources	5,750			127,450
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD				**650,100**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS			
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS			
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)				**650,100**

ADMINISTRATION - DIRECTOR'S OFFICE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Chief Operating Officer	% Effort			40,800	7,018	47,818
	Adm Sec				12,580	3,887	16,467
	Exec Asst to Dir				18,484	5,712	24,196
	Director				40,220	6,918	47,138
	Exec Secretary				12,176	3,762	15,938
SUBTOTALS					124,260	27,297	151,557

CONSULTANT COSTS					
Annual Sci. Advisory Meeting	8,240				8,240
EQUIPMENT (Itemize)					0
SUPPLIES (Itemize by category)					
Office Supplies	2,140				
Data Processing	3,800				
Miscellaneous Oper. Supplies	3,600				
Community Outreach Supplies	1,000				10,540
TRAVEL					
Domestic/International Travel	12,000				12,000
INPATIENT CARE COSTS					0
OUTPATIENT CARE COSTS					0
ALTERATIONS AND RENOVATIONS (Itemize by category)					0
OTHER EXPENSES (Itemize by category)					
Freight	1,000				
Cellular Phone/Radio Service	3,300	Printing/Illus Serv	2,000		
Long Distance	500	Recruitment Exp	7,500		
Visiting Professional Exps	5,000	Dues/Membership	1,000		20,300
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD				$	**202,637**
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS			
CONSORTIUM/CONTRACTUAL COSTS		FACILITIES AND ADMINISTRATIVE COSTS			
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)				$	**202,637**

ADMINISTRATION - BUSINESS OFFICE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	Senior Accountant				25,355	7,835	33,190
	Fin Serv Spec				11,988	3,704	15,692
	Billing Spec				10,658	3,293	13,951
	Fin Assoc				10,623	3,283	13,906
	Acct Analyst				11,807	3,648	15,455
	Asst. Controller				37,648	11,633	49,281
SUBTOTALS					108,079	33,396	141,475

CONSULTANT COSTS 0

EQUIPMENT (Itemize) 0

SUPPLIES (Itemize by category) 11,050
- Office/Operating Supplies 8,900
- Data Proc Supplies 2,150

TRAVEL 0

INPATIENT CARE COSTS 0

OUTPATIENT CARE COSTS 0

ALTERATIONS AND RENOVATIONS (Itemize by category) 0

OTHER EXPENSES (Itemize by category) 200
- Long Distance 100
- Freight 100

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD		$ 152,725
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)		$ 152,725

ADMINISTRATION - CENTER RESOURCES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Chief Operating Officer	% Effort			8,160	1,404	9,564
	Clerk				5,241	1,619	6,860
	Mail Tech				6,573	2,031	8,604
	Support Services Sup				12,176	3,762	15,938
	Courier				6,448	1,992	8,440
	Veterinarian				4,924	847	5,771
SUBTOTALS					43,522	11,655	55,177

CONSULTANT COSTS — 0

EQUIPMENT (Itemize) — 0

SUPPLIES (Itemize by category)

Misc. Operating Supplies	2,700
Office Supplies	250
Vehicle fuel/maintenance	2,000
Library Expense	5,000

9,950

TRAVEL — 0

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category)

Service Contracts	56,300	Printing	1,600
Cellular Phone/Radio Service	500	Long Distance	1,200
Freight	150	Postage	1,000
Digital Network Copier Maint	5,000	Tolls	350
Phone Service	13,000		
Repairs & Gen'l Maint.	22,000		

101,100

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	166,227
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS		
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	166,227

ADMINISTRATION - HUMAN RESOURCES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Operations Manager I	% Effort			15,650	4,836	20,486
	Consultant				21,420	6,619	28,039
SUBTOTALS					37,070	11,455	48,525

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Operating Supplies	200	
		200
TRAVEL		
Local Travel - to NO area	150	150
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Advertising	5,500	
Long Distance	250	
		5,750
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**54,625**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**54,625**

ADMINISTRATION - GRANTS ADMINISTRATION

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Grants Mgmt Specialist	% Effort			13,421	4,147	17,568
	Grants Mgmt Analyst				12,900	3,986	16,886
	Grants Mgmt Specialist				14,508	4,483	18,991
	Grants Mgmt Specialist				14,508	4,483	18,991
SUBTOTALS					55,337	17,099	72,436

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Office/Operating Supplies	1,350	
		1,350
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Freight	50	
Long Distance	50	
		100
~~SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD~~	$	~~73,886~~
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	**73,886**

OPERATIONS - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Information Technology					163,062	50,387	213,449
Facilities Services					122,208	37,763	159,971
Occupational Health					54,450	16,825	71,275
Security					8,160	1,404	9,564
SUBTOTALS					347,880	106,379	454,259

CONSULTANT COSTS				0
EQUIPMENT (Itemize)				0
SUPPLIES (Itemize by category)				
Information Technology	41,950			
Facilities Services	180,500			
Occupational Health	6,750			
Security	6,200			235,400
TRAVEL				
Information Technology	3,000	Occupational Health	2,000	
Facilities Services	1,500			6,500
INPATIENT CARE COSTS				0
OUTPATIENT CARE COSTS				0
ALTERATIONS AND RENOVATIONS (Itemize by category)				0
OTHER EXPENSES (Itemize by category)				
Information Technology	23,395			
Facilities Services	1,113,584			
Occupational Health	16,130			
Security	309,300			1,462,409
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD			$	2,158,568
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS		
CONSORTIUM/CONTRACTUAL COSTS		FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)			$	2,158,568

OPERATIONS - INFORMATION TECHNOLOGY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	Systems Spec I				16,617	5,135	21,752
	Database Admin III				26,065	8,054	34,119
	Programmer I				13,895	4,294	18,189
	User Services Analyst III				18,772	5,801	24,573
	App Spec				11,459	3,541	15,000
	Media/ Commun Spec				15,373	4,750	20,123
	Technology Services Manager				32,673	10,096	42,769
	App Spec				13,359	4,128	17,487
	System Prog				14,849	4,588	19,437
SUBTOTALS					163,062	50,387	213,449

CONSULTANT COSTS — 0

EQUIPMENT (Itemize) — 0

SUPPLIES (Itemize by category)

Database Software	3,300
Operating Supplies	1,100
Office Supplies	550
Data processing supplies	12,000
Desktop Comp upgrades	25,000

41,950

TRAVEL
Domestic 3,000 — 3,000

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category)

Desktop Software Licensing and Maintenance Contracts	8,200	Freight	150
Printing	1,645	Photocopier exp	7,500
Cellular Service	5,900		

23,395

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD		$ 281,794
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)		$ 281,794

OPERATIONS - FACILITIES SERVICES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
See Continuation Page							
SUBTOTALS					122,208	37,763	159,971

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Operating Supplies	180,500	
		180,500
TRAVEL		
Domestic travel	1,500	1,500
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Utilities	901,584	
Testing, Inspec & Certifications	25,000	
Other building repairs and maint	187,000	
		1,113,584
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	1,455,555
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	1,455,555

OPERATIONS - FACILITIES SERVICES - ITEMIZATION OF PERSONNEL

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Custodial Worker	% Effort			2,281	705	2,986
	Gen Maint Wkr II				3,177	982	4,159
	Opr Engr				4,168	1,288	5,456
	Opr Engr Shift				4,330	1,338	5,668
	Custodial Worker				2,512	776	3,288
	Asst Director				11,220	3,467	14,687
	Maint Asst Sup				3,548	1,096	4,644
	Maint Asst Sup				3,838	1,186	5,024
	Grounds Attendant				2,562	792	3,354
	Project Asst				2,932	906	3,838
	Gen Maint Wkr II				3,177	982	4,159
	Gen Maint Wkr II				3,556	1,099	4,655
	Opr Engr				3,346	1,034	4,380
	Plumber				3,994	1,234	5,228
	Grounds Attendant				2,154	666	2,820
	Welder				4,428	1,368	5,796
	Electrician				3,429	1,060	4,489
	Opr Engr				4,051	1,252	5,303
	Equip Opr				2,902	897	3,799
	Welder				3,992	1,234	5,226
	Oper Manager				4,231	1,307	5,538
	Gen Maint Wkr II				3,282	1,014	4,296
	Lab Tec				2,474	764	3,238
	Custodial Worker				2,281	705	2,986
	Gen Maint Wkr II				3,008	929	3,937
	Oper Engineer				3,605	1,114	4,719
	Mechanic				3,493	1,079	4,572
	Grounds Attendant				2,154	666	2,820
	Biomedical Tech				6,001	1,854	7,855
	Gen Maint Wkr II				3,161	977	4,138
	Facilities & Maintenance Asst Man				6,920	2,138	9,058
	Chief Opr Engr				6,001	1,854	7,855
	SUBTOTALS				122,208	37,763	159,971

OPERATIONS - OCCUPATIONAL HEALTH & SAFETY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	MD, Assoc Professor	% Effort			14,541	4,493	19,034
	Occupational Health Nurse				25,505	7,881	33,386
	Licensed Practical Nurse				14,404	4,451	18,855
	SUBTOTALS				54,450	16,825	71,275

CONSULTANT COSTS				0
EQUIPMENT (Itemize)				0
SUPPLIES (Itemize by category)				
Clinical Supplies	5,350			
Office Supplies	600			
Data Processing Supplies	800			
				6,750
TRAVEL				
Domestic	2,000			2,000
INPATIENT CARE COSTS				0
OUTPATIENT CARE COSTS				0
ALTERATIONS AND RENOVATIONS (Itemize by category)				0
OTHER EXPENSES (Itemize by category)				
Medical Examinations	12,000	Cellular Phone Service	630	
Freight	3,500			
				16,130
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD			$	96,155
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS		
CONSORTIUM/CONTRACTUAL COSTS		FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)			$	96,155

OPERATIONS - SECURITY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Chief Operating Officer	% Effort			8,160	1,404	9,564
	SUBTOTALS				8,160	1,404	9,564

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Operating Supplies	3,200	
Maint of Vehicles	3,000	
		6,200
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
University Security Services	300,000	
Cellular Service/Exp	5,000	
Uniforms	4,300	
		309,300
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**325,064**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**325,064**

OUTREACH - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Education & Training					12,662	2,838	15,500
SUBTOTALS					12,662	2,838	15,500

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Education & Training 35,000	35,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 50,500**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 50,500**

OUTREACH - EDUCATION AND TRAINING

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Mgr, Program	% Effort			4,823	1,490	6,313
	Professor				7,839	1,348	9,187
SUBTOTALS					12,662	2,838	15,500

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Summer Student Stipends 23,000 Vet Student Stipends 12,000	35,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 50,500**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 50,500**

PILOT RESEARCH - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Pilot Research Program					4,705	809	5,514
SUBTOTALS					4,705	809	5,514

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Pilot Research Program 180,000	180,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 185,514**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 185,514**

OUTREACH - PILOT RESEARCH PROGRAM

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	Res Assoc Prof				4,705	809	5,514
SUBTOTALS					4,705	809	5,514

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) 3 Research Projects @ $60,000 ea 180,000	180,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 185,514**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 185,514**

VETERINARY RESOURCES - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Office of the Chair					126,913	34,705	161,618
Clinical & Research Med					198,190	47,470	245,660
Research Resources					29,550	7,906	37,456
Animal Resources					229,449	73,199	310,075
Environmental Enrichment					113,439	32,456	145,895
Collaborative Research					45,381	11,446	56,827
Compliance and Training					54,740	16,915	71,655
Breeding Colonies					42,307	10,531	52,838
Aging					0	0	0
Genetics					44,917	9,814	54,731
Biomedical Engineering					35,623	11,007	46,630
SUBTOTALS					920,509	255,449	1,183,385

CONSULTANT COSTS				0
EQUIPMENT (Itemize)				0
SUPPLIES (Itemize by category)				
Research Resources	130,000			
Genetics	16,000			
Compliance and Training	700			
Biomedical Engineering	3,000			
Animal Resources	507,000			
Env Enrichment	34,000			
Collaborative Research	4,500			695,200
TRAVEL				
Office of the Chair	0	Collaborative Research	3,000	3,000
INPATIENT CARE COSTS				0
OUTPATIENT CARE COSTS				0
ALTERATIONS AND RENOVATIONS (Itemize by category)				0
OTHER EXPENSES (Itemize by category)		Collaborative Research	1,000	
Office of the Chair	0	Compliance and Training	2,000	
Biomedical Eng	0	Breeding Colonies	6,000	
Research Resources	10,000	Aging	63,088	
Animal Resources	27,500	Genetics	3,000	
Env Enrichment	2,000			114,588
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD			**$**	**1,996,173**
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS		
CONSORTIUM/CONTRACTUAL COSTS		FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)			**$**	**1,996,173**

VETERINARY RESOURCES - OFFICE OF THE CHAIR

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Operations Manager	% Effort			15,942	4,926	20,868
	Accountant 2				14,655	4,528	19,183
	Assoc Dir				18,150	3,122	21,272
	Records Mgr				5,674	1,753	7,427
	Secretary				11,110	3,433	14,543
	Epidemiologist				9,907	3,061	12,968
	Project Asst				10,463	3,233	13,696
	Exec Secretary				12,942	3,999	16,941
	Accountant 1				13,297	4,109	17,406
	Veterinarian				14,773	2,541	17,314
SUBTOTALS					126,913	34,705	161,618

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	
Domestic travel	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 161,618**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 161,618**

VETERINARY RESOURCES - CLINICAL & RESEARCH MEDICINE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
See Continuation Page							
SUBTOTALS					198,190	47,470	245,660

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 245,660**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 245,660**

VETERINARY RESOURCES - CLINICAL & RESEARCH MEDICINE - ITEMIZATION OF PERSONNEL

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Vet Tec 3	% Effort			11,681	3,609	15,290
	Assoc Dir				9,075	1,561	10,636
	Sr Prog Coord				8,160	2,521	10,681
	Anim Research Sup				16,076	4,967	21,043
	Veterinarian				17,339	2,982	20,321
	Veterinarian				17,211	2,960	20,171
	Vet Tec 2				11,361	3,511	14,872
	Veterinarian				18,036	3,102	21,138
	Asst Prof				17,314	2,978	20,292
	TNPRC Procurement Specialist				2,818	871	3,689
	Post Doc				14,017	3,420	17,437
	Vet Tec 2				11,069	3,420	14,489
	Veterinarian				12,024	2,068	14,092
	Vet Tec 4				14,655	4,528	19,183
	Vet Tec 2				11,347	3,506	14,853
	Post Doc				6,007	1,466	7,473
SUBTOTALS					198,190	47,470	245,660

VETERINARY RESOURCES - RESEARCH RESOURCES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Vet Tec 4	% Effort			12,742	3,937	16,679
	TNPRC Procurement Specialist				6,959	2,150	9,109
	Veterinarian				9,849	1,819	11,668
SUBTOTALS					29,550	7,906	37,456

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Surgical Instruments & Supplies	20,000	
Uniforms/PPE Scrubs	30,000	
Medical Supplies-Non-Pharm	30,000	
Blood Collection Supplies	15,000	
Pharmaceutical Supplies	35,000	130,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Shipping & Freight	10,000	10,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD		$ 177,456
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)		$ 177,456

VETERINARY RESOURCES - ANIMAL RESOURCES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
See Continuation Page							
SUBTOTALS					229,449	73,199	310,075

CONSULTANT COSTS — 0

EQUIPMENT (Itemize) — 0

SUPPLIES (Itemize by category)

Food	290,000	PPE Gowns/Gloves/Masks	75,000
Produce	45,000	Caging Supplies	3,000
Nursery Formula	15,000	Vehicle Supplies	25,000
Cleaning Supplies	4,000		
Husbandry Supplies	50,000		

507,000

TRAVEL — 0

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category)

Routine maintenance	20,500
Freight	7,000

27,500

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	844,575
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	844,575

VETERINARY RESOURCES - ANIMAL RESOURCES - ITEMIZATION OF PERSONNEL

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	ACT 2	% Effort			2,659	822	3,481
	ACT 3				2,626	811	3,437
	ACT 2				2,636	815	3,451
	ACT 2				2,466	762	3,228
	ACT 3				2,693	832	3,525
	Trainee				2,206	682	2,888
	Animal Research Sup				3,110	961	4,071
	Animal Research Sup				3,548	1,096	4,644
	Animal Research Sup				3,449	1,066	4,515
	ACT 3				2,767	855	3,622
	Animal Research Sup				3,361	1,039	4,400
	ACT 1				2,226	688	2,914
	ACT 1				2,164	669	2,833
	ACT 2				2,408	744	3,152
	ACT 1				2,171	671	2,842
	ACT 3				2,745	848	3,593
	Animal Research Sup				3,246	1,003	4,249
	ACT 2				2,468	763	3,231
	Animal Research Sup				3,998	1,235	5,233
	ACT 4				2,960	915	3,875
	Records Manager				5,674	1,753	7,427
	ACT 3				2,624	811	3,435
	ACT 4				3,089	955	4,044
	Animal Research Sup				3,445	1,065	4,510
	ACT 3				2,624	811	3,435
	Vet Tech III				8,091	2,500	10,591
	ACT 2				2,409	744	3,153
	ACT 3				2,743	848	3,591
	Vet Tech III				9,362	2,893	12,255
	ACT 2				2,468	763	3,231
	Vet Tech III				3,994	1,234	5,228
	Animal Research Sup				3,895	1,204	5,099
	Trainee				2,142	662	2,804

VETERINARY RESOURCES - ANIMAL RESOURCES - ITEMIZATION OF PERSONNEL

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	●D011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	ACT 2				2,408	744	3,152
	ACT 2				2,516	777	3,293
	ACT 1				2,549	788	3,337
	ACT 2				2,468	763	3,231
	ACT 2				2,590	800	3,390
	Asst Director				9,690	2,994	12,684
	ACT 2				2,580	797	3,377
	ACT 2				2,775	857	3,632
	ACT 2				2,516	777	3,293
	ACT 2				2,520	779	3,299
	Vet Tech 2				2,842	878	3,720
	Vet Tech 2				3,292	1,017	4,309
	Animal Research Sup				3,972	1,227	5,199
	ACT 3				2,588	800	3,388
	Trainee				2,196	679	2,875
	ACT 2				2,468	763	3,231
	Trainee				2,196	679	2,875
	ACT 4				3,825	1,182	5,007
	ACT 3				2,709	837	3,546
	ACT 1				2,158	667	2,825
	ACT 1				2,212	684	2,896
	ACT 1				2,268	701	2,969
	ACT 4				3,246	1,003	4,249
	ACT 2				2,580	797	3,377
	ACT 2				2,496	771	3,267
	ACT 2				2,484	768	3,252

VETERINARY RESOURCES - ANIMAL RESOURCES - ITEMIZATION OF PERSONNEL

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
(cont'd from previous pg)		% Effort					
Excluded by Requester	ACT 2				2,468	763	3,231
	Manager				5,901	1,823	7,724
	Trainee				2,196	679	2,875
	ACT 2				2,468	763	3,231
	Vet Specialist				4,076	1,259	5,335
	Animal Research Sup				3,377	1,043	4,420
	ACT 3				2,755	851	3,606
	ACT 2				2,584	798	3,382
	Trainee				2,151	665	2,816
	ACT 1				2,222	687	2,909
	Trainee				2,142	662	2,804
	ACT 2				2,468	763	3,231
	Animal Research Sup				4,058	1,254	5,312
	Animal Research Sup				3,214	993	4,207
	Animal Research Sup				3,186	984	4,170
	ACT 1				2,171	671	2,842
	Trainee				2,248	695	2,943
	ACT 2				2,580	797	3,377
	SUBTOTALS				229,449	73,199	310,075

VETERINARY RESOURCES - ENVIRONMENTAL ENRICHMENT

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Primate Center Research Scientist I	% Effort			18,951	3,260	22,211
	Enrich Tech III				6,139	1,897	8,036
	Enrich Tech III				13,380	4,134	17,514
	Enrich Tech II				12,649	3,909	16,558
	Enrich Tech II				12,258	3,788	16,046
	Enrich Tec II				14,139	4,369	18,508
	Enric Tech I				9,927	3,067	12,994
	Enrich Tech III				14,215	4,392	18,607
	Enrich Tech II				11,781	3,640	15,421
SUBTOTALS					113,439	32,456	145,895

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Feeding Enrichment	13,000	
Toys and Manipulanda	3,000	
Foraging and Grooming	2,000	
Other Supplies	16,000	
		34,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Fabrication of Enrich. Items	1,000	
General Maintenance	1,000	
		2,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	181,895
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	181,895

OUTREACH - COLLABORATIVE RESEARCH

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal. Acad. or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Res Assoc Prof	% Effort			94,095	18,819	3,237	22,056
	Med Res Spec				43,911	2,196	679	2,875
	Database Admin. I				44,277	15,497	4,789	20,286
	Med Res Spec				44,345	8,869	2,741	11,610
SUBTOTALS						45,381	11,446	56,827

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Supplies	4,500	
		4,500
TRAVEL		
Domestic Travel	3,000	3,000
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Long Distance	500	
Dues/Membership Fees	500	
		1,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	65,327
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	65,327

VETERINARY RESOURCES - COMPLIANCE AND TRAINING

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	Manager				17,275	5,338	22,613
	Vet Specialist				19,578	6,050	25,628
	Resource Mgr				17,887	5,527	23,414
	SUBTOTALS				54,740	16,915	71,655

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Training Materials	700	
		700
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Dues/Seminars	2,000	
		2,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**74,355**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**74,355**

VETERINARY RESOURCES - BREEDING COLONIES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Primate Center Research Scientist I	% Effort			9,476	1,630	11,106
	Assoc Director				9,075	1,561	10,636
	Epidemiologist				4,953	1,530	6,483
	Manager				18,803	5,810	24,613
SUBTOTALS					42,307	10,531	52,838

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) SPF Screening 6,000	6,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD $	58,838
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page) $	58,838

VETERINARY RESOURCES - AGING ANIMALS

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	5/1/2014	THROUGH 4/30/2015	GRANT NUMBER OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
							0
							0
SUBTOTALS					0	0	0

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Per Diem 63,088	63,088
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 63,088**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 63,088**

VETERINARY RESOURCES - GENETICS AND GENOME BANKING CORE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Epidemiologist	% Effort			2,477	765	3,242
	Med Res Tech				12,767	3,945	16,712
	Primate Res Scientist I				29,673	5,104	34,777
SUBTOTALS					44,917	9,814	54,731

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Paternity Test Supplies	14,000	
Genome Banking Supplies	1,000	
Minor Equipment	1,000	
		16,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Freight	500	
Maintenance	2,500	
		3,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**73,731**
~~CONSORTIUM/CONTRACTUAL COSTS~~	~~DIRECT COSTS~~	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**73,731**

VETERINARY RESOURCES - BIOMEDICAL ENGINEERING

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Biomedical Engineer	% Effort			20,474	6,326	26,800
	Engineering Lab Tech				15,149	4,681	19,830
	SUBTOTALS				35,623	11,007	46,630

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category) Lab Supplies 1,500 Operating Supplies 1,500	3,000
TRAVEL Domestic travel	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 49,630**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 49,630**

MICROBIOLOGY - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Office of the Chair					206,811	43,293	250,104
VCIP Core					7,532	1,296	8,828
Pathogen Detect/Quant					82,541	21,429	103,970
Aerobiology Core					16,412	4,542	20,954
SUBTOTALS					313,296	70,560	383,856

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Office of the Chair	0	
VCIP Core	5,000	
Pathogen Detect/Quant Core	120,000	
Aerobiology Core	6,000	
		131,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Office of the Chair	0	
Pathogen Detect/Quant Core	400	
Aerobiology Core	2,500	
		2,900
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**517,756**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**517,756**

MICROBIOLOGY - OFFICE OF THE CHAIR

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Med Res Spec	% Effort			3,764	1,163	4,927
	Secretary				11,159	3,448	14,607
	Med Res Spec				3,764	1,163	4,927
	Prof				10,580	1,820	12,400
	Secretary				12,600	3,893	16,493
	Post Doc				4,472	1,091	5,563
	Res Asst Prof				29,988	5,158	35,146
	Prof				18,150	3,122	21,272
	Prof				45,375	7,805	53,180
	Med Res Spec				3,764	1,163	4,927
	Dept Admin I				16,683	5,155	21,838
	Assoc Prof				24,957	4,293	29,250
	Res Assoc Prof				17,230	2,964	20,194
	Post Doc				4,325	1,055	5,380
	SUBTOTALS				206,811	43,293	250,104

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$ 250,104
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$ 250,104

MICROBIOLOGY - VIRUS CHARACTERIZATION, ISOLATION AND PRODUCTION CORE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Prof	% Effort			7,532	1,296	8,828
SUBTOTALS					7,532	1,296	8,828

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category) Lab supplies 5,000	5,000
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 13,828**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 13,828**

MICROBIOLOGY - PATHOGEN DETECTION AND QUANTIFICATION CORE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	Med Res Spec				13,283	4,104	17,387
	Prof				29,757	5,118	34,875
	Med Res Spec				15,497	4,789	20,286
	Med Res Tec				12,002	3,709	15,711
	Med Res Tech				12,002	3,709	15,711
	SUBTOTALS				82,541	21,429	103,970

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Lab Supplies	120,000	
		120,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Books, Subscriptions	200	
Shipping Costs	200	
		400
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	224,370
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	224,370

MICROBIOLOGY - AEROBIOLOGY CORE

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Lab Supervisor II	% Effort			5,100	1,576	6,676
	Eng Lab Tech				7,442	2,300	9,742
	Assoc Prof				3,870	666	4,536
SUBTOTALS					16,412	4,542	20,954

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Supplies	6,000	6,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Data Processing	2,500	2,500
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	29,454
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	29,454

IMMUNOLOGY - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Office of the Chair					39,597	6,811	46,408
Flow Cytometry					51,319	15,857	67,176
SUBTOTALS					90,916	22,668	113,584

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Office of the Chair	0	
Flow Cytometry	17,300	
		17,300
TRAVEL		
Office of the Chair	0	0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Office of the Chair	0	
Flow Cytometry	0	
		0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**130,884**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**130,884**

IMMUNOLOGY - OFFICE OF THE CHAIR

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Res Assoc Prof	% Effort			39,597	6,811	46,408
SUBTOTALS					39,597	6,811	46,408

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 46,408**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 46,408**

IMMUNOLOGY - FLOW CYTOMETRY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Lab Supv II	% Effort			15,259	4,715	19,974
	Lab Supr II				16,956	5,239	22,195
	Med Res Spec				16,304	5,038	21,342
	Med Tech				1,234	381	1,615
	Med Tech				1,566	484	2,050
SUBTOTALS					51,319	15,857	67,176

CONSULTANT COSTS — 0

EQUIPMENT (Itemize) — 0

SUPPLIES (Itemize by category)

Lab Supplies	14,900	Antibodies	1,300
Data Processing Supplies	350	FACS/Perm/Lyse Supplies	500
Operating Supplies	250		

17,300

TRAVEL — 0

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category) — 0

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	84,476
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS		
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	84,476

BACTERIOLOGY & PARASITOLOGY - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Office of the Chair					56,631	12,633	69,264
Diagnostic Parasitology					15,497	4,789	20,286
Vector-Borne Diseases					10,358	3,201	13,559
DNA Microarray & Expressi					28,366	4,879	33,245
SUBTOTALS					110,852	25,502	136,354

CONSULTANT COSTS — 0

EQUIPMENT (Itemize) — 0

SUPPLIES (Itemize by category)

Office of the Chair	0
Diagnostic Parasitology	1,250
Vector-Borne Diseases	7,900
DNA Microarray & Expression	5,000

14,150

TRAVEL
Office of the Chair 0 — 0

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category)

Office of the Chair	0	Vector-Borne Diseases	750
Diagnostic Parasitology	200		
DNA Microarray & Expression	12,360		

13,310

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	163,814
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	**163,814**

BACTERIOLOGY & PARASITOLOGY - OFFICE OF THE CHAIR

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Res. Asst Prof	% Effort			8,077	1,389	9,466
	Lab Supr II				9,063	2,800	11,863
	Prog Man				12,056	3,725	15,781
	Prof				27,435	4,719	32,154
SUBTOTALS					56,631	12,633	69,264

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$ 69,264
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$ 69,264

BACTERIOLOGY & PARASITOLOGY - DIAGNOSTIC PARASITOLOGY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Med Res Spec	% Effort			15,497	4,789	20,286
SUBTOTALS					15,497	4,789	20,286

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category) Disposable Lab Supplies 500 Molecular Reagents 750	1,250
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Books and subscriptions 100 Illustrations 100	200
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 21,736**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 21,736**

BACTERIOLOGY & PARASITOLOGY - VECTOR-BORNE DISEASES

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Lab Sup II	% Effort			10,358	3,201	13,559
SUBTOTALS					10,358	3,201	13,559

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category) Lab Supplies 7,900	7,900
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Storage 750	750
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 22,209**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 22,209**

BACTERIOLOGY & PARASITOLOGY - DNA MICROARRAY & EXPRESSION

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Assoc Prof	% Effort			28,366	4,879	33,245
SUBTOTALS					28,366	4,879	33,245

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category) Lab supplies 5,000	5,000
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category) Software 12,360	12,360
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 50,605**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 50,605**

COMPARATIVE PATHOLOGY - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Office of the Chair					117,730	24,820	142,550
Anatomic Pathology					194,755	46,319	241,074
Clinical Pathology					79,547	23,451	102,998
Confocal Microscopy					33,396	7,563	40,959
SUBTOTALS					425,428	102,153	527,581

CONSULTANT COSTS — 0

EQUIPMENT (Itemize) — 0

SUPPLIES (Itemize by category)

Office of the Chair	0		
Anatomic Pathology	4,800		
Clinical Pathology	1,000		
Confocal Microscopy	4,500		
			10,300

TRAVEL

Office of the Chair	0		0

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category)

Office of the Chair	0	Clinical Pathology	750
Anatomic Pathology	1,000		
Confocal Microscopy	2,000		3,750

~~SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD~~ $ ~~541,631~~

CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS

CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS

TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page) $ **541,631**

COMPARATIVE PATHOLOGY - OFFICE OF THE CHAIR

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Executive Sec	% Effort			7,542	1,297	8,839
	Executive Sec				13,735	4,244	17,979
	Rsch Asst Prof				12,860	2,212	15,072
	Asst Prof				32,256	5,548	37,804
	Dept Admin I				19,635	6,067	25,702
	Asst Prof				20,595	3,542	24,137
	Rsch Asst Prof				4,174	718	4,892
	Prof				6,933	1,192	8,125
SUBTOTALS					117,730	24,820	142,550

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$ 142,550
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$ 142,550

COMPARATIVE PATHOLOGY - ANATOMIC PATHOLOGY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort					
	Assoc Prof				39,758	6,838	46,596
	Histotechnician				17,850	5,516	23,366
	Asst Prof				27,473	4,725	32,198
	Med Res Spec				9,860	3,047	12,907
	Lab Supervisor				18,296	5,653	23,949
	Histotechnician				16,037	4,955	20,992
	Rsch Asst Prof				33,927	5,835	39,762
	Histotechnician				14,777	4,566	19,343
	Med Res Tech				10,287	3,179	13,466
	Secretary				6,490	2,005	8,495
	SUBTOTALS				194,755	46,319	241,074

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Histopathology Supplies	750	
Necropsy Supplies	4,050	4,800
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Freight	500	
Dues/Memberships	500	1,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD		$ 246,874
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)		$ 246,874

COMPARATIVE PATHOLOGY - CLINICAL PATHOLOGY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Asst Prof	% Effort			8,242	1,418	9,660
	Med Tech				16,695	5,159	21,854
	Med Tech				18,289	5,651	23,940
	Med Tech				20,174	6,234	26,408
	Med Tech				16,147	4,989	21,136
SUBTOTALS					79,547	23,451	102,998

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Chem/Hematology Supplies	500	
Microbiology Supplies	500	
		1,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Routine Maintenance	750	
		750
~~SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD~~	~~$~~	~~104,748~~
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	**104,748**

COMPARATIVE PATHOLOGY - CONFOCAL MICROSCOPY

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Res Assoc Prof	% Effort			20,113	3,459	23,572
	Med Res Spec				13,283	4,104	17,387
	SUBTOTALS				33,396	7,563	40,959

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Lab Supplies	4,500	4,500
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Books/Subscriptions	500	
Computer License	1,000	
Freight	400	
Uniforms	100	2,000
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	**47,459**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	**47,459**

REGENERATIVE MEDICINE - COMPOSITE BUDGET

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Office of the Chair					74,087	16,364	90,451
Stem Cell Production					15,189	4,693	19,882
SUBTOTALS					89,276	21,057	110,333

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Office of the Chair	0	
Stem Cell Production	15,000	
		15,000
TRAVEL		
Office of the Chair	0	0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Office of the Chair	0	
Stem Cell Production	550	
		550
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**125,883**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**125,883**

REGENERATIVE MEDICINE - OFFICE OF THE CHAIR

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester		% Effort						
	Res Asst Prof				90,017	15,753	2,710	18,463
	Prof				181,500	31,908	5,488	37,396
	Executive Sec				41,212	14,424	4,457	18,881
	Med Res Tec				34,290	12,002	3,709	15,711
SUBTOTALS						74,087	16,364	90,451

CONSULTANT COSTS	0
EQUIPMENT (Itemize)	0
SUPPLIES (Itemize by category)	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS (Itemize by category)	0
OTHER EXPENSES (Itemize by category)	0
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$ 90,451**
CONSORTIUM/CONTRACTUAL COSTS — DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS — FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$ 90,451**

REGENERATIVE MEDICINE - STEM CELL PRODUCTION

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omit cents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Excluded by Requester	Lab Spec	% Effort			15,189	4,693	19,882
SUBTOTALS					15,189	4,693	19,882

CONSULTANT COSTS		0
EQUIPMENT (Itemize)		0
SUPPLIES (Itemize by category)		
Supplies	15,000	
		15,000
TRAVEL		0
INPATIENT CARE COSTS		0
OUTPATIENT CARE COSTS		0
ALTERATIONS AND RENOVATIONS (Itemize by category)		0
OTHER EXPENSES (Itemize by category)		
Freight	250	
Printing	300	
		550
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	**$**	**35,432**
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	**$**	**35,432**

IMPROVEMENT AND MODERNIZATION

Program Director/Principal Investigator (last, first, middle): Hamm, L./Lackner, A.

DETAILED BUDGET FOR INITIAL BUDGET PERIOD - DIRECT COSTS ONLY	FROM	THROUGH	GRANT NUMBER
	5/1/2014	4/30/2015	OD011104-53

List PERSONNEL (Applicant organization only)
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested (omitcents) for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
SUBTOTALS					0	0	0

CONSULTANT COSTS — 0

EQUIPMENT (Itemize)

Water Heater System Replacement	181,000	Bobcat Front end Loader	29,998
BD FACSAria System Upgrade	75,000	Electric Van	17,189
VoIP Support/Install & Network Upgrade (Partial)	11,713		
Tissue Processor	52,783		
Social Interaction Primate Housing	202,584		
PICCOLO Analyzer	15,900		
Freezer Upgrade(1)	13,833		

600,000

SUPPLIES (Itemize by category) — 0

TRAVEL — 0

INPATIENT CARE COSTS — 0

OUTPATIENT CARE COSTS — 0

ALTERATIONS AND RENOVATIONS (Itemize by category) — 0

OTHER EXPENSES (Itemize by category) — 0

SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD	$	600,000
~~CONSORTIUM/CONTRACTUAL COSTS~~ ~~DIRECT COSTS~~		
CONSORTIUM/CONTRACTUAL COSTS FACILITIES AND ADMINISTRATIVE COSTS		
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 8a, Face Page)	$	600,000

Biographical Sketches (130 pages) removed – Excluded by Requester

Program Director/Principal Investigator (Last, First, Middle):	Hamm, Lee	
PROGRESS REPORT SUMMARY	GRANT NUMBER 2P51OD011104-52	
	PERIOD COVERED BY THIS REPORT	
PROGRAM DIRECTOR / PRINCIPAL INVESTIGATOR Lee Hamm	FROM 5/1/13	TO 4/30/14
APPLICANT ORGANIZATION Tulane University		
TITLE OF PROJECT (Repeat title shown in Item 1 on first page) Tulane National Primate Research Center		

A. Human Subjects (Complete Item 6 on the Face Page)		
Involvement of Human Subjects	☒ No Change Since Previous Submission	☐ Change
B. Vertebrate Animals (Complete Item 7 on the Face Page)		
Use of Vertebrate Animals	☒ No Change Since Previous Submission	☐ Change
C. Select Agent Research	☒ No Change Since Previous Submission	☐ Change
D. Multiple PI Leadership Plan	☒ No Change Since Previous Submission	☐ Change

SEE PHS 2590 INSTRUCTIONS.

WOMEN AND MINORITY INCLUSION: See PHS 398 Instructions. Use Inclusion Enrollment Report Format Page and, if necessary, Targeted/Planned Enrollment Format Page.

a. Specific Aims

The aims of the TNPRC are:

- Conduct basic and applied biomedical research on human health problems that require the use of nonhuman primates
- Investigate nonhuman primate biology and diseases particularly with regard to the study of human health problems
- Serve as a regional and national resource and center of excellence for biomedical research using nonhuman primates
- Provide training for graduate students, postdoctoral fellows, undergraduates and visiting scientists

There has been no change in these aims.

b. Studies and Results

The TNPRC has continued to show improvement and accomplishment in all areas. Since the last PHS 2590 progress report major achievements include: 1) renewal of our P51 base grant, 2) reorganization of administration and hiring of a chief operations officer, 3) conversion of our breeding colonies to specific pathogen free status, 4) successfully dealt with the challenges of sequestration of the NIH budget, 5) established a system of joint academic appointments with the LSU School of Veterinary Medicine, Proprietary Info

The utilization of the TNPRC as a national resource also continues at a high level. In the last year we supported over 400 investigators that had more than $240 million in PHS funded research that could not have been accomplished without the resources of the NPRC program.

During the last year we have continued to make progress in multiple scientific areas. Below are selected brief examples.

AIDS pathogenesis, transmission and prevention: Vaccination and the application of a vaginal microbicides have traditionally been considered independent methods to prevent the sexual transmission of HIV-1 to women. This year, we addressed whether vaccines and microbicides can be used together to provide reinforced protection to rhesus macaques. Four groups of macaques were vaccinated systemically with an Adenovirus vector-based vaccine, or not, and then given a vaginal microbicide (the fusion inhibitor T-1249 or the CCR5 inhibitor Maraviroc; MVC), or a placebo gel, shortly before vaginal challenge with SIVmac251 or SHIV-162P3. We demonstrated that a combination of a partially effective microbicide when combined with a vaccine showed better protection than when either were used alone demonstrating synergy between these two concepts Excluded by Requester Excluded by Requester. In other microbicide studies we are testing various microbicide ring and gel formulations that confer sustained protection against SHIV challenge Excluded by Excluded by Requester Excluded by Requester We are currently focusing on testing Proprietary Info

More recently we have been involved in novel approaches to preexposure prophylaxis. In the past preexposure prophylaxis involving daily doses of drugs or microbicides have met with variable success in large part due to problems with a lack of adherence to the prescribed regimen. To address this problem we have demonstrated the safety and efficacy of a long acting integrase inhibitor (GSK744) that protected macaques against repeated intrarectal challenges of SIV for months. The plasma levels of GSK744 achievable with quarterly injections in humans, protected all animals against repeated low-dose challenges. In a second experiment, macaques were given GSK744 1 week before virus administration and challenged repeatedly until infection occurred. Protection decreased over time and correlated with the plasma drug levels. With a quarterly dosing schedule in humans, our results suggest that long acting GSK744 could potentially decrease adherence problems associated with daily preexposure prophylaxis. This work was published in Science Excluded by Requester

Lyme disease: Although early treatment of Lyme disease with antibiotics is usually successful, in 10 to 20% of patients long-term disabilities persist. We discovered that human oligodendrocytes, which are glial cells that play a major role in neuronal homeostasis in the central nervous system (CNS), produce pro-inflammatory mediators not only when co-cultured with live *Borrelia burgdorferi* (the spirochete that causes Lyme disease) but also when these glial cells are exposed to non-viable spirochetes or spirochetal fragments. In addition, oligodendrocytes die by apoptosis in this context Excluded by Requester Excluded by Requester These results suggest that *B. burgdorferi* may continue to be pathogenic in the CNS even when rendered non-viable by a course of antibiotic treatment. Therefore, other therapies might be required in addition to the traditional antibiotic treatment regimen, to control symptoms of Lyme neuroborreliosis. We are also investigating the possible role of the Proprietary Info We had previously shown, using explants from the brain frontal cortex of rhesus macaques, that when *B. burgdorferi* was co-cultured with these brain sections it elicited the production of pro-inflammatory mediators by glial cells and neurons, as well as neuronal and oligodendrocyte apoptosis. We have now shown that Proprietary Info some of which have been used in clinical trials for other purposes, may be beneficial

The persistence of symptoms in Lyme disease patients following antibiotic therapy, and their causes, continue to be a matter of intense controversy. Previously, we demonstrated that Lyme disease spirochetes may persist following antibiotic treatment of an infection by needle inoculation of the spirochetes. In the last year, we published a revised method for feeding ticks on animals Excluded by

Excluded by Requester This has been used successfully for our project "Defining Persistence in Post-treatment Lyme disease," where we are testing Proprietary Info Proprietary Info We are also using Proprietary Info to determine if the Proprietary Info Proprietary Info We are also developing an improved diagnostic test for Proprietary Info and treatment response that uses Proprietary Info Proprietary Info We have optimized the assay using well-characterized Proprietary Info and demonstrated that the assay has a Proprietary Info Proprietary Info the assay is now being tested with Proprietary Info Proprietary Finally, we have successfully developed a nonhuman primate, model of Relapsing Fever with the spirochete *Borrelia turicatae* by tick bite. The animals had multiple spirochetemic and febrile episodes. The model development, including monitoring of body temperature, heart rate and respiration by telemetry, and pathology comprised a Submitted Submitted

Tuberculosis: The TB research program continued to make significant contributions. We identified spatially restricted intra-granulomatous expression of indoleamine 2, 3, dioxygenase (IDO), a potent T cell suppressant in the lungs of animals with active TB. These results indicate that the IFN-dependent IDO pathway may by hijacked by *M. tuberculosis* to potentiate its survival Excluded by Requester Excluded by Requester featured on Journal cover). In additional explorations of the correlates of control of mycobacterium tuberculosis and pulmonary pathology we have identified CXCR5+ T helper cells as playing a critical role in protection against TB Excluded by Requester We have also demonstrated that in human patients with active TB and in nonhuman primate models of M. tuberculosis infection that neutrophils producing S100 proteins are dominant within the inflammatory lung granulomas. Using the mouse model of TB, we demonstrated that the exacerbated lung inflammation seen as a result of neutrophilic accumulation is dependent on S100A8/A9 proteins. S100A8/A9 proteins promote neutrophil accumulation by inducing production of proinflammatory chemokines and cytokines, and influencing leukocyte trafficking. Importantly, serum levels of S100A8/A9 proteins along with neutrophil-associated chemokines, such as keratinocyte chemoattractant, can be used as potential surrogate biomarkers to assess lung inflammation and disease severity in human TB Excluded by Requester Additional studies, that complement the work on Tuberculosis but that are independent of it have identified and characterized the phenotype and biology of distinct populations of lung macrophages involved in diverse lung pathology Excluded by Requester

Chikungunya: Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that causes major epidemics of rash, fever, and debilitating arthritis. Presently, there is an outbreak of CHIKV in the carribean and significant concern of spread to the southern United States. No preventive vaccine or treatment for Chikungunya exists. As part of our biodefense program we have developed a nonhuman primate model of Chikungunya that recapitulates the hallmark signs, viremia, and physiological changes associated with clinical infection in humans. Subsequently, we used this model to assess the safety and efficacy of 2 live-attenuated vaccine candidates based on the insertion of a picornavirus internal ribosome entry site (IRES) sequence into the genome of CHIKV. Vaccination of cynomolgus macaques with a single dose of either vaccine produced no signs of illness but was highly immunogenic. After challenge with a subcutaneous inoculation of wild-type CHIKV, both vaccine candidates prevented the development of detectable viremia. Protected animals also exhibited no significant changes in core body temperature or cardiovascular rhythm, whereas sham-vaccinated animals showed hyperthermia, followed by sustained hypothermia, as well as significant changes in heart rate. These CHIKV/IRES vaccine candidates appear to be safe and efficacious, supporting their strong potential as human vaccines to protect against CHIKV infection and reduce transmission and further spread Excluded by Requester

C. Significance:

The TNPRC takes its mission as a national resource very seriously as illustrated by the large number of investigators supported and the dollar amount of NIH research supported. For every dollar in Base Grant support received from NCRR, the TNPRC supported ("leveraged") more than $20 in other PHS awards. This illustrates the importance and significance of the TNPRC to NIH supported biomedical research. In addition to the general impact of the TNPRC, the research programs continue to result in scientific advances (as illustrated above) that have a positive impact on human health and well-being.

The composite budget for the coming year is submitted in accordance with the peer reviewed P51 renewal approved in 2012. Elements in this budget are needed to sustain our mission, support research and provide necessary infrastructure. Justification for the detailed budget categories in each component was also previously peer reviewed and approved.

D. Plans:

Major goals for the next 12 months include: 1) Proprietary Info 2) Continue to compete aggressively for NIH research funding, 3) Recruit additional faculty members that complement our strengths, 4) Continue to perform world-class research that benefits human health, and 4) Foster collaborative efforts among the NPRCs.

TABLE OF CONTENTS

- Early Events in Vaginal SHIV and SIV Transmission
- Effects of HIV-1 in Male Rhesus Macaque Model
- Evaluating Mucosal Immune Responses in the Vagina
- Evaluation of Immune Mediators for Protection from SHIV
- Harnessing Antibody-mucus Interactions to Prevent HIV Transmission
- Intersubtype Recombinants for Polyvalent Anti-HIV Vaccine
- Modeling HIV-1 Primary Transmission
- Role of antibodies in Protection from HIV
- Standardization of Flow Cytometry of Intestinal Cells
- Testing Maraviroc as a Microbicide
- The Effects of Alcohol on SIV Pathogenesis
- Tissue Reservoirs in SIV-infected Macaques
- Vaccines to Prevent HSV-2 Transmission

Excluded by Requester

- Development of the Neonatal Mucosal Immune System in Nonhuman Primates

Excluded by Requester

- Development, Differentiation and Kinetics of Blood Monocytes and DCs in Macaques
- Flow Cytometry Core Laboratory
- Immunology Assay Core Laboratory
- Innate Immunity in Pediatric Macaques Infected with *Mycobacter*
- Lung Macrophages in Rhesus Macaques
- Neuropathogenesis of SIV in Macaques

Excluded by Requester

- Gastrointestinal Disease in Captive Rhesus Macaques Microsporidiosis Genome Analyses and Diagnostics
- Immune Responses to Microsporidia
- Pathogen Detection and Quantification Core

Excluded by Requester

- Antisense Epitopes as Novel Markers of Latently Infected Cells
- Functional Consequences of CTL Escape in SIV Nef

Excluded by Requester

- A New Chimeric SIVmac251/SIVmac239 Virus for Vaccines
- DNA Vaccine for Induction of Mucosal Immunity
- Efficacy and Toxicity of CSIC and Retrocyclin in the SIV Vaginal Challenge Model
- Highly Effective Control of AIDS Virus Challenge in Macaques
- Isolation of a New HIV-2 Group in the US
- Modeling the Molecular Evolution of SIV to HIV using Humanized Mice
- Pathogenesis of Natural SIV and STLV Infections in Humans
- Serial Passage of HIV-2F in Pigtail Macaques to Investigate
- Virus Characterization, Isolation, and Production Core

Excluded by Requester

- Prime-boost Vaccination against *Mycobacterium Tuberculosis*

Excluded by Requester

- Host-targeted Interventions of Category A, B and C Bunyaviruses

- Platform for Defining the Host Response to RNA Virus Infection

Excluded by Requester

- An Antibody Immunoprotectant for Category B Toxins
- Development of Ricin Antitoxin for Treatment
- Evaluation of Live Attenuated Brucella Vaccines in NHP
- Infectious Disease Aerobiology Core
- Monoclonal Immunoprotectants for Select Agent Toxins
- Therapeutic Human Monoclonal Antibodies against SEB
- Thermostable Vaccines for Biodefense
- Treatment for Pulmonary Anthrax
- Vaccine Development for Alphaviruses
- Vaccine Development for *Burkholderia pseudomallei*
- VLP Vaccine Development for Alphaviruses

Excluded by Requester

- Epidemiology of Rhesus Enteric Caliciviruses
- Functional Analysis of Phage-displayed Coronavirus Proteins
- Immunogenetics of Gluten Sensitivity in Rhesus Macaques
- Infection and Immunity Induced by Rhesus Enteric Caliciviruses
- Molecular ABO Phenotyping of Cynomolgus Macaques
- Role of Rhesus Rotavirus Gene 4 in Biliary Atresia
- The Rhesus Macaque Gut Microbiome in Health and Disease

Excluded by Requester

- Animal Models to Design and Evaluate Improved VZV Vaccines
- Identification and Preclinical Testing of Microbicides for HPV
- Molecular Pathogenesis of Varicella Zoster Virus Infection

Excluded by Requester

- Genetically Engineered CTL Against HIV Env
- Sustained Expression of Peptide Inhibitor in MSCs

Excluded by Requester

- Biology of Nonhuman Primate Marrow Stromal Cells
- Immunopathologic Alterations in Rhesus Macaques with Globoid Cell Leukodystrophy
- Nonhuman Primate Model for Krabbe's Disease
- Stem Cell Production Core

Excluded by Requester

- Behavioral Management Program
- Social Housing and SIV Disease

Excluded by Requester

- Blocking Virus Spread by DCs with Carrageenan-Based Compounds
- HIV-envelope-specific DARP In-based Microbicide Strategies
- Imaging
- Impact of ART on DC and Treg Responses in Oral Tissues
- Macaque Explant Model for Microbicide Testing
- Mucosal Dendritic Cell-T Cell Milieu and SIV Spread
- Phenotypic and Genotypic Determinants of SHIV Pathogenesis

- R5 SHIV/macaque Model for the Evaluation of T and B Cell-based HIV-1 Vaccine
- Surgery

Excluded by Requester

- Development of Therapies for Preexposure Prophylaxis (PreP) for Prevention of HIV Infection
- Establishment of SPF Rhesus Colony for Non AIDS
- *In vitro* HIV/SIV Assays Using Rhesus Macaque Blood
- NIA: Aging Colony Maintenance
- Optimal Dose of 7DW8-5 as an Adjuvant for AdPfCA, a Candidate Malaria Vaccine
- Special Trans through Red Cages on Circadian Met and Phys in Nude Rats
- Special Trans through Tint Cages on Circadian Met and Phys in Nude Rats
- Special Trans through Tinted Cages on Circadian Met and Phys in SD Rats
- SPF Rhesus Monkey Colony for AIDS Research
- Treatment with Vivitrol to Reduce Self-biting Behavior in Adult Rhesus Macaques
- Tulane Resource Allocation Committee
- Videotaped Behavior as a Predictor of Clinical Outcomes in Rhesus Macaques

Excluded by Requester

- *In vivo* Suppression of SIV-mediated Immune Activation
- Oral Vaccination for AIDS Prevention in Rhesus Macaques

Excluded by Requester

- Alcohol, SIV Infection and Host Defense

Excluded by Requester

- *Moraxella osloensis* Septic Arthritis in a Rhesus Macaque

Excluded by Requester

- Development and Pharmacology of Novel Lipidic rAHF
- dmLT Adjuvanted Sublingual Vaccination with IPV in NHPs
- Efficacy of Lipidic Formulations for Monoclonal Antibody Delivery
- Safety Assessments of Lipidic Formulations for Protein Delivery

Excluded by Requester

- Development of a SNP Assay for Determination of Ancestry of Rhesus Monkeys
- Empirical Comparison of STRs and SNPs
- Exome Sequencing of TNPRC Rhesus Monkeys
- Genetics and Genome Banking Core
- Parameters of Reproductive Efficiency and Longevity among Female Rhesus Macaques
- Reproductive Efficiency of Captive Rhesus Macaque Females
- Whole Genome Sequencing of Rhesus Macaques

Excluded by Requester

- A Macaque Model of Acute *Coxiella burneti* Infection
- Development of a Subunit Vaccine against Q Fever
- OMV Vaccine-Mediated Protection against Aerosolized *B. pseudomallei*

ADMINISTRATIVE PROJECTS

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Administrative Services/Business Office
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Director
Principal Core Scientist associated with the project
Excluded by Requester C Assistant Controller/Assistant Director for Finance
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

The Center Business Office serves as the central point of contact on behalf of Center faculty and staff for virtually all financial and administrative functions. All transactions submitted by the Primate Center are reviewed and approved by the Business Office to assure compliance with both Federal and University regulations and policies. Pre- and post-grant and contract award functions are executed by the Business Office. Other services provided by the Business Office include budgeting, invoicing, setting cost recovery rates, processing employee labor distributions and overseeing the employee effort reporting.

Project Progress (one paragraph)

During the past year we hae implemented a new timekeeping program for the Center which allows tracking of employee time for payroll, as well as accruals for time off. We also began using a new Human Capital Management System for hiring and terminating employees and labor distribution. We reduced the number of employees by 1.2 full-time positions in order to make more efficient use of center resources by realigning the duties and reporting structures.

Funding Sources (include name of the source and the grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Communications
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI, with Institutional affiliation
Excluded by Requester C Director
Principal Core Scientist associated with the project
Excluded by Requester C Chief Operations Officer
Other affiliate scientists with Institutional affiliation (doctoral level only)

Project Description

The mission of the Communications Unit (CU) is to manage internal and external communications for the faculty and staff of the Tulane National Primate Research Center. The CU collects, organizes and disseminates information (scientific and nonscientific) regarding Center-related activities to both internal and external audiences. The CU responds to information requests for the National Institutes of Health (NIH), the broader University, the public and other entities. This Unit serves as liaison with public information officers from the other seven National Primate Research Centers and the NIH to develop consistent and effective communications and tracking and reporting Center of related communications and community outreach activities. The CU also serves as a liaison with Tulane University Office of Public Relations in preparing public news releases and responding to issues relating to animal rights activities, biological safety and Freedom of Information requests. The CU is responsible for the development, organization and dissemination of internal information, newsletters and the Intranet to inform faculty and staff of Center current events. The CU is responsible for developing and overseeing the content of public relations-related publications and tools as needed, such as media kits, fact sheets and brochures. This Unit coordinates the TNPRC Community Advisory Board, which consists of local community members that meet regularly to advise TNPRC administration about issues that impact the community. The Unit coordinates or participates in all tours of the Center.

Project Progress (one paragraph)

Due to the budgetary constriction as a result of sequestration, the two employees who worked in the Communications Unit (CU) were laid off. The CU continues to function under the direction of the Chief Operations Officer (COO) and with the assistance of the Tulane University Public Relations and the Tulane University Governmental and Community Relations units. The COO is also filling in as liaison with the Outreach Consortium of the eight National Primate Research Centers to maintain consistent and effective communications and community outreach activities. The former Community Focus Group of local community leaders has been revitalized into the Community Advisory Board to advise Center leadership on community and business perspectives and to facilitate Center-community relations and collaborations.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Director's Office
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Director

Principal Core Scientist associated with the project

Excluded by Requester

C Chief Operations Officer/Associate Director
C Associate Director for Veterinary Resources
C Assistant Controller and Assistant Director for Finance

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

The Director's Office provides oversight and overall responsibility for the scientific, administrative and operational functions of the Center. The Director, with input from the Executive Committee, faculty and the Scientific Advisory Board, develops and implements the scientific direction and planning for the Center. This includes determining future funding opportunities, long range strategic planning, establishing collaborative agreements with other institutions and representing the Center's interests with our host institution, funding institutions and local community. The director's Office is also responsible for allocation of resources to the various units at the Center. Administrative and operational oversight is also provided from the director's Office with primary responsibility for supervision of Administrative Services, Facilities Services, Information Technology Services, Occupational Health and safety, Communications and Security. Each unit has a manager who reports to the Director's Office.

Project Progress (one paragraph)

The major achievements since the last progress report were: 1) renewal of our P51; 2) reorganization of administration and hiring a new Chief Operations Officer/Associate Director for Administration; 3) conversion of our breeding colonies to specific pathogen free status; 4) successfully dealt with the challenges of sequestration; 5) established a system of joint academic appointments with LSU/School of Veterinary Medicine; 6) renovated 1,500 sf of laboratory space; 7) created a freezer farm; and 8) upgraded the electrical distribution system at the Center for improved reliability and safety.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
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Project Title Facilities Services and Infrastructure Upgrades
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Director
Principal Core Scientist associated with the project
Excluded by Requester C Chief Operations Officer
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description

The Facilities Services Unit is responsible for the daily operations of all Center HVAC, utilities, maintenance, potable and waste water systems, hazardous waste disposal, janitorial, grounds keeping, glassware and laundry services. This division is responsible for cleaning and disinfecting all laboratory glassware, and laundering all uniforms for those individuals working in animal care. The Facilities Services Maintenance Subunit is responsible for the maintenance of Proprietary Info buildings with a total area of approximately Proprietary Info In addition, the Unit is responsible for the upkeep of Specific Animal Location outdoor animal housing corrals, maintenance of large equipment such as cage washers, autoclaves, and a motor pool of over Prop vehicles, tractors, heavy duty machinery, and lawn equipment. The hazardous waste disposal functions of the Facilities Services Unit include a combination of in-house efforts managing our on-site waste disposal equipment (tissue digesters and Chem-Clav) and in coordination with Tulane University's Office of Environmental Health and Safety and Safety any hazardous chemical and radioactive waste disposal. The Engineering Subunit is responsible for all building systems, maintaining the potable and wastewater treatment plan, water distillation systems, and all sterilization equipment for the Center. The engineering staff has a 24/7 presence at all times. The Facilities Services Unit has physical responsibility of all buildings, performs small renovations, and takes an active role in the overall management of larger scale projects with the support of the Tulane Capital Projects and Real Estate Division. The Facilities Services Unit additionally provides input to professional design teams, coordinates in the review and documentation of on-going projects, and ultimately provides oversight and quality control of all maintenance and construction related projects at the Center.

Project Progress (one paragraph)

Completed Construction Projects

~~Cafe: The TNPRC "break room" was converted to the full-service "Jazzman Café and Bakery" that provides breakfast,~~ lunch and snack items including fresh baked muffins, fruit, sandwiches, salads, soups, coffee, tea, etc. to the staff.

Proprietary Info

Proprietary Info

Funded/ongoing construction projects:

Proprietary Info

Funding Sources (include name of the source and the grant number)
Electrical Upgrade: Grant Number: 1G0RR032477-01, Amount: $499,558, PI:

Excluded by Requester

Surgery Facility: Grant Number 1C06RR032704-01, Amount: $1,459,013, PI:

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

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Project Title Information Technology Services
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Chief Operations Officer
Principal Core Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

The mission of **Information Technology (IT)** is to provide services in alignment with the mission and goals of the TNPRC in 4 primary areas: Database, Technology Support, Web & Media, and Infrastructure. Database supports the center's animal records and billing system that provides clinical veterinarians, clinical lab technicians, pathologists and research scientists the ability to retrieve data on research and breeding colony animals as well as financial management of the center's billing system. Technology Support provides traditional help desk services including diagnosis and repair of laptop and desktop computers, installation of site licensed and public domain software for all computers, and assists customers in maintenance and system upgrades. Support is provided for MacOS and Windows computers, printers, mobile computing and numerous other specialized devices. The Web & Media staff provide multimedia production support by assisting with the following: web development and design, intranet management, research slide presentations, research poster presentations, document and image scanning, color document and image creation and printing, newsletters, brochures, video production (including filming and editing), and video conferencing. Information Technology, communications, network services, media services, and desktop support are critical components of the research and business that the Center is chartered to offer to investigators, grants management, animal records, research database and the like. The IT component touches every aspect of the work that is performed at the TNPRC and facilitates the TNPRC mission to improve animal and human health through basic and applied biomedical research.

Project Progress (one paragraph)

Proprietary Info

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

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Project Title Office of Occupational Health and Safety
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Director
Principal Core Scientist associated with the project
Excluded by Requester C Chief Opertions Officer
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Tulane University School of Medicine

Project Description (one paragraph)

The Occupational Health and Safety Unit is staffed by a full time Occupational Health Nurse Specialist and a full time Licensed Practical Nurse. The 24-hour availability of the Occupational Health Nurse (OHN) allows for immediate evaluation/consultation and treatment of work related injuries and exposures. This service has provided a positive and dramatic impact on the employee's health and wellness. The OHN works closely with on-site representatives of the Tulane Office of Biosafety and the Tulane Office of Environmental Health and Safety (OEHS) as well as a Tulane infectious disease physician assigned to the TNPRC and other related physicians to provide case management of potentially biohazardous exposures and work related injuries. The current focus of occupational health is the occupational hazards related to Herpes B virus, Tuberculosis, SIV/SHIV and biodefense related research agents. TNPRC participates in a voluntary collaborative project with the CDC to test monkey retrovirus seroprevalence in employees with exposures to SIV. In addition to working closely with Tulane's Office of Biosafety and OEHS, the OHN serves as the liaison to outside healthcare providers, local, state, and government agencies on occupational health matters.

Project Progress (one paragraph)

The occupational health unit has implemented modifications to the program as it relates to federal regulatory changes made for select agents. These modifications were implemented in January of 2013. The unit also collaborates extensively with Tulane infectious disease physicians. Training has been provided for Tulane's infectious disease fellows who will be providing post exposure treatments and/or prophylaxis. This training will continue yearly for each new group of fellows and involves components from occupational health, biosafety and environmental health and safety. The occupational health program continues to be the liaison between injured employees and the Tulane Work Force Management Organization (WFMO) as is relates to submitting first reports of injury and injury follow up. The program monitors for compliance with TB skin testing as well as coordinating respiratory physicals and other health related needs for employees.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Scientific Advisory Board
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Director

Principal Core Scientist associated with the project

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A Emory University School of Medicine
A NIH/NIAID
A College of Veterinary Medicine, Univ. of Colorado
A LSU School of Veterinary Medicine
A Private Source
A TX A&M Health Sciences Center
A Tulane University School of Medicine

Project Description (one paragraph)

The TNPRC maintains an external scientific advisory board comprised of outstanding scientists from around the country with expertise in areas of research being conducted at the Primate Center. The term for committee members is 3 years. This Committee conducts regular reviews of all Center programs. Two complementary types of reviews are conducted – first a general overview of all components of the institution, which occurs every 18-24 months and a second focused on single research divisions, which are much more indepth. Two research divisions are reviewed each year. Together, these reviews provide a thorough oversight of all Center programs.

Project Progress (one paragraph)

Review of the Division of Comparative Pathology and the Division of Microbiology have occurred since the last progress report.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

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Project Title Security
Division/Unit Administrative
Type of Project Management
Percent P51 dollars - 0.830%
AIDS? No
PI. with institutional affiliation
Excluded by Requester C Director
Principal Core Scientist associated with the project
Excluded by Requester C Chief Operations Officer
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

The Tulane University Police Department (TUPD) provides security at the TNPRC. Officers are staffed on a 24/7 basis. Officers provide for on-site patrols, employee escorts, traffic control for events and construction, employee training (personal security, bicycle safety, CPR), Center access, and they act as the principle liaison with local law enforcement agencies for the purposes of criminal investigations and intelligence.

Facility Security

Project Progress (one paragraph)

The Tulane University Police Department (TUPD) continues to provide continuous on-site security to the TNPRC. As a result of a workload efficiency analysis the TUPD has adjusted staffing levels to provide peak staffing to coincide with peak call hours. Additionally the TUPD has added an additional off-road capable patrol vehicle to augment patrols and security response to undeveloped areas. Local law enforcement liaisons have been reinforced by TUPD working alongside local law enforcement at community events. TUPD officers have continued their commitment to providing the highest levels of police services by attending all Louisiana P.O.S.T. required training in addition to training in other areas such as crime prevention through environmental design.

Facility Security

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Training and Education
Division/Unit Administrative
Type of Project (Research, Management, Pilot or Other) Management
Percent P51 dollars - 0.830%
AIDS? No

PI, with institutional affiliation

Excluded by Requester

C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester

C Comparative Pathology
C Veterinary Medicine
C Regenerative Medicine
C Microbiology
C Comparative Pathology
C Bacteriology and Parasitology
C Bacteriology and Parasitology
C Immunology
C Director
C Comparative Pathology
C Comparative Pathology
C Microbiology
C Microbiology
C Microbiology
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A Physiology - LSU Health Sciences Center, LA
A Louisiana State University
A Microbiology/Immunology– TUHSC, LA
A Parasitology/Veterinary Science – LSU School of Veterinary Medicine, LA
A LSU School of Veterinary Medicine, LA
A LSU Health Sciences Center, LA

Project Description (one paragraph)

The educational mission of the TNPRC is to provide training for undergraduate, veterinary and graduate students, post-doctoral fellows, veterinarians, and visiting scientists. The TNPRC educational effort is further broadened by participation in a T35 training grant in conjunction with the Louisiana State University School of Veterinary Medicine (LSUSVM), a T32 training grant also held together with the LSUSVM, a Summer Fellowship Program, a Pathology Training Curriculum, and a Veterinary Preceptorship. The summer fellowships entail one-on-one participation in a research project with an end-of-summer seminar session by the students. An R25 training grant provides funding for residency training of veterinarians in clinical medicine of nonhuman primates. This program is run in collaboration with the LSUSVM. The basic objective of this program is to provide an understanding of the mission and functions of a National Primate Research Center. The Pathology Training Curriculum is directed toward furthering professional development of staff veterinary pathologists, staff veterinarians, and veterinarians involved in research. Lastly, three Center-wide colloquia address diverse educational interests of TNPRC scientists: 1) a seminar on infectious diseases, with invited

speakers, 2) a biweekly research lab meeting, and 3) quarterly pathology and medicine Grand Rounds. The Center also welcomes visiting scientists.

This year there were 13 invited speakers and 2 visiting scientists. The center hosted 13 graduate students and 11 post-doctoral fellows, 3 research scientists, one laboratory animal medicine resident, 4 T32 trainees, as well as 5 students in the Veterinary Preceptorship Program. The Summer Fellowship Program was subscribed by 7 undergraduate students. There were 13 participants in the Pathology Training Curriculum. We are pleased with the response of students and investigators to our educational efforts, and look forward to maintaining this trend in the future.

Project Progress (one paragraph)

Two trainees were added to the training program during this reporting period, both physically located at the LSU School of Veterinary Medicine.

Funding Sources (include name of the source and the grant number)

Excluded by Requester NIH 3R21AI055013-02S1, NIH 5R01EB006493-03
Excluded by NIH 5T35RR017504-05, NIH 5P20RR016456-06
Excluded by Requester NIH T32OD011124
Excluded by Requester P20 GM103458-09

TNPRC PILOT PROGRAM

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

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Project Title A Nonhuman Primate Model of Relapsing Fever Borreliosis
Division/Unit Bacteriology and Parasitology
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? No
PI, with institutional affiliation
Excluded by [redacted] A Mississippi State University
Principal Core Scientist associated with the project
Excluded by Requester C Bacteriology and Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

Relapsing fever (RF) spirochetes are blood-borne pathogens transmitted by soft ticks within the genus Ornithodoros or by the human body louse. This zoonotic infection occurs on five of seven continents, causing considerable morbidity and has a severe impact in developing countries primarily because of the nonspecific, malaria-like clinical manifestation of the disease. While mice are a natural and necessary host for preliminary studies, the murine model is suboptimal because mice do not generally exhibit the clinical manifestations of human disease, and persistent infection of mice requires those that lack essential arms of the immune system. Our central hypothesis was that *B. turicatae* infection in the rhesus macaque would recapitulate human disease with spirochete evasion and modulation of the host immune response.

Project Progress (one paragraph)

We infected four rhesus macaques with *B. turicatae* by tick bite. The infection was assessed by telemetric monitoring of body temperature, heart and respiratory rates, clinical pathology and quantification of spirochete densities in the blood. Histopathology and immune responses (antibody and immune cell subsets) will also be included in the analysis. The animals presented with multiple spirochetemic and febrile episodes. Disruption of cardiac physiology was also apparent. [redacted] Our results indicate that this will be a viable and appropriate animal model for future studies.

In Preparation;Submitted

Funding Sources (include name of the source and the grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Genetic Requirements for the Survival of *Mycobacterium tuberculosis* in Nonhuman Primates during Immune Deficiency

Division/Unit Bacteriology and Parasitology

Type of Project Pilot

Percent P51 dollars - 0.339%

AIDS? Yes

PI, with institutional affiliation

Excluded by Requester — A Howard Hughes Medical Institute

Principal Core Scientist associated with the project

Excluded by Requester — C Bacteriology and Parasitology
C Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester — C Howard Hughes Medical Institute

Project Description (one paragraph)

Our goal is to identify the factors that contribute to the increased susceptibility of HIV patients to tuberculosis (TB). To do this, we plan to identify bacterial factors that are differentially required during immune compromise. In this proposal, we will determine which factors are responsible for survival of *Mycobacterium tuberculosis* in nonhuman primates and lay the groundwork for comparing survival in SIV-infected animals.

Project Progress (one paragraph)

Proprietary Info

Funding Sources (include name of the source and the grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

2013-2014 Annual Progress Report
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Reporting Period: May 1, 2013 – April 30, 2014
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****

Project Title Role of B and CD8 Cells In Early West Nile Virus Infection In Macaques
Unit/Division Comparative Pathology
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A University of Texas Medical Branch

Project Description (limited to one paragraph)

West Nile virus (WNV) is a positive stranded RNA flavivirus that is naturally transmitted by mosquitoes, which can readily infect a wide variety of hosts including humans. Most people (~80%) infected with WNV have no symptoms; about 20% have clinical manifestations ranging from febrile illness to neurological syndromes and possible death. No specific antiviral therapy or vaccine currently exists for human WNV infection, treatment or prevention. A recent successful test of a live chimeric WNV vaccine in cynomolgus macaque (CMs) and an aging study in rhesus macaque (RMs) and CMs have demonstrated strong age-independent resistance to WNV and suggest that the roles of cellular and humoral immunity can be defined in non-human primates. However, healthy adult RMs exposed intradermally to WNV fail to develop clinical signs despite measurable viremia. Lack of classical clinical symptoms in macaques hampers our thorough understanding of viral pathogenesis, viral transmission, and vaccine development.

Project Progress (one paragraph)

Proprietary Info

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
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****

Project Title Mechanism of Follicular CD4+ T Cell Impairment in Rhesus Macaques
Unit/Division Comparative Pathology
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Comparative Pathology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Although HIV is characterized by failure of humoral antiviral immune responses, the mechanism remains unclear. The development and maturation of B cells, which are responsible for antibody responses, are predominantly initiated in germinal centers in secondary lymphoid tissues, such as lymph node, bone marrow, spleen and possibly in Peyer's patches. In the context of B-cell development and maturation, the CD4+ TFH cells are central to the regulation of T cell-dependent humoral immune responses. TFH cells are involved in the initiation and maintenance of GC responses that generate memory B cells and long-lived plasma cells. However, the existence of, and location of TFH cells in nonhuman primates is not well defined. In this study, we will define the TFH cells in rhesus macaques, determine their phenotype and function, and monitor their changes during SIV infection, and further investigate the effects of SIV infection on TFH cell function and their role in stimulating or promoting B-cell immunity. Insight into these mechanisms will provide new strategies for immune modulatory therapy for HIV patients and in vaccine design.

Project Progress (one paragraph)

Proprietary Info

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

2013-2014 Annual Progress Report
OD-011104-52
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Project Title NHP Model of Immunosenescence and Vaccination
Unit/Division Microbiology
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Microbiology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Veterinary Medicine
C Immunology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A George Washington University Medical Center
A Private Source

Project Description (limited to one paragraph)

Background: Questions remain about whether inflammation is a cause, consequence, or coincidence of aging. The purpose of this study was to define baseline immunological characteristics from blood to develop a model in rhesus macaques that could be used to address the relationship between inflammation and aging. Hematology, flow cytometry, clinical chemistry, and multiplex cytokine/chemokine analyses were performed on a group of 101 outdoor-housed rhesus macaques ranging from 2 to 24 years of age, approximately equivalent to 8 to 77 years of age in humans. Results: These results extend earlier reports correlating changes in lymphocyte subpopulations and cytokines/chemokines with increasing age. There were significant declines in numbers of white blood cells (WBC) overall, as well as lymphocytes, monocytes, and polymorphonuclear cells with increasing age. Among lymphocytes, there were no significant declines in NK cells and T cells, whereas B cell numbers exhibited significant declines with age. Within the T cell populations, there were significant declines in numbers of CD4+ naïve T cells and CD8+ naïve T cells. Conversely, numbers of CD4+CD8+ effector memory and CD8+effector memory T cells increased with age. New multiplex analyses revealed that concentrations of a panel of ten circulating cytokines/chemokines, IFNγ, IL1b, IL6, IL12, IL15, TNFα, MCP1, MIP1α, IL1ra, and IL4, each significantly correlated with age and also exhibited concordant pairwise correlations with every other factor within this group. To also control for outlier values, mean rank values of each of these cytokine concentrations in relation to age of each animal and these also correlated with age.

Project Progress (one paragraph)

A panel of ten cytokines/chemokines was identified that correlated with aging and also with each other. This will permit selection of animals exhibiting relatively higher and lower inflammation status as a model to test mechanisms inflammation status in aging with susceptibility to infections and vaccine efficacy.

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104 and NIH AI071778 Excluded by AI097059 Excluded by AI087302 Excluded by AI091501 Excluded by Requester

Publications Resulting from this Project *(only include publications with a PMCID number)*

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

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****

Unit/Division Microbiology
Project Title Novel SIV proteins
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) Scientist associated with the project

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A University of Alabama School of Medicine
A Wisconsin National Primate Research Center

Project Description (limited to one paragraph)

Simian immunodeficiency virus encodes two small proteins in alternate reading frames of the env gene. We previously verified these ORFs are translated as they are targeted by T cells in many infected individuals. We hypothesized that these proteins are indeed functional and perform tasks enabling viral replication *in vivo*. We have begun a series of experiments, *in vivo* and *in vitro*, to determine if these proteins are functional and if so, to begin to understand their function.

Project Progress (one paragraph)

Proprietary Info

Funding Sources (include name of the source, PI and the FULL grant number)

This work was funded in part by a grant from the Private Source to Excluded Private Source Exclu ed, PI: Excluded by Requester and by the TNPRC Pilot Program under NIH P51 OD011104

Publications Resulting from this Project (only include publications with a PMCID number)

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2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title NHP Model for Hantavirus Infection
Unit/Division Microbiology
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? No
PI, with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Immunology
	C	Director
	C	Microbiology
	C	Microbiology
	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Hantaviruses are, zoonotic, rodent-borne, RNA viruses and members of the *Bunyaviridae* virus family. These viruses persistently infect their rodent hosts without causing apparent disease but upon transmission to humans via aerosols cause hantavirus pulmonary syndrome (HPS), which has a high mortality rate. The virus infects pulmonary endothelial cells resulting in capillary leak syndrome. The loss of plasma from blood results in profound hypotension and cardiogenic shock. The prototype North and South American hantaviruses are Sin nombre (SNV) and Andes virus (ANDV), respectively. These viruses, along with other key members of the family, epitomize emerging RNA viruses that threaten human populations due to changing geographic and environmental interaction between human and natural reservoirs harboring these viruses. The goal of this study is to identify host response hallmarks elicited by ANDV infection of Rhesus macaques (*Macaca mulatta*), and to define the host gene expression response to infection using transcriptome and microarray analysis. Our project will involve aerosol delivery of ANDV, as this is a biologically relevant mode of transmission. We will obtain RNA samples from pertinent tissues from infected animals including liver, lung and kidney. The effect of virus infection on host gene expression will be determined using microarray and transcriptome analysis. Since this project is a collaborative effort to define the hallmarks of ANDV infection, additional methodology includes aerosol delivery of virus particles, telemetry, blood chemistry, basic cellular response to infection, determination of virus titer, temporal effects of infection on liver and lung tissue, and complete necropsy.

Project Progress (one paragraph)

We plan to carry out initial animal studies this spring. As a prelude, we have examined the effect of hantavirus infection on human primary endothelial cells and are refining our approaches to define the response of the innate and adaptive immune responses, and core biological processes that are affected by hantavirus infection. Using microarray analysis in a combination with Partek®, Ingenuity IPA® and Cytoscape® analysis, we find that pathways including interferon signaling, antigen presentation, innate and adaptive immune cell, apoptosis, and protein ubiquitination are markedly stimulated following hantavirus infection. We will use parallel analysis of RNA samples from infected animals to examine the *in vivo* host response to infection, and to provocatively compare the genomic response in human and Rhesus macaque cells. Starting with virus from a human patient (provided by our collaborators in Chile), we are attempting to expand virus in culture and by in vivo expansion. Expanded virus will then be used to infect five or six

animals. Multiple complementary analyses will be carried out to examine hallmarks of virus-induced pathogenesis parallel to hantavirus cardiopulmonary syndrome (HCPS), and to examine the innate immune response to infection based, on lung interstitial and alveolar macrophages. Additionally, we will investigate the early adaptive immune response to infection by using Mamu-A1 animals and examining CTL response.

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title AAV/GALC Treatment of Krabbe Disease in Rhesus
Unit/Division Regenerative Medicine
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? No

PI, with institutional affiliation

Excluded by Requester	A	University of North Carolina

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Regenerative Medicine
	C	Regenerative Medicine
	C	Veterinary Medicine
	C	Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Neurology, LSU Health Sciences Center

Project Description (limited to one paragraph)

Krabbe Disease (OMIM #245200), also called globoid cell leukodystrophy (GLD or GCL), is a rare lysosomal storage disease (LSD) caused by mutations in the galactosylceramidase (GALC) gene. In human patients, lack of GALC activity causes a white matter disorder in the central and peripheral nervous system, which presents as neurological symptoms by 6 months of age and leads to death by approximately 18 months. Krabbe disease, as well as many other LSD, is an attractive candidate for gene therapy because a portion of the expressed enzyme is secreted and taken up by neighboring cells via the mannose-6-phosphate pathway. In previous studies, intrathecal (lumbar) administration of AAV9 vectors into the CSF can achieve widespread distribution of the transgene to neurons and glia throughout the spinal cord and brain at translationally relevant doses. If this treatment approach is successful, it not only provides preliminary data to support a human gene therapy trial for Krabbe, but also provides the proof-of-concept to generally apply this approach to multiple other LSDs. The Krabbe NHP model offers a unique resource to test the efficacy of intrathecal gene replacement therapy.

Project Progress (one paragraph)

We injected an AAV9 vector, expressing GALC and GFP, into rhesus macaques affected with Krabbe Disease when 1 month old. The treated animals lived for 6 months (3 months longer than historic controls) but disease progressed as assessed by clinical symptoms (hypotonia, incoordination, mobility, and tremors) and nerve function (nerve conduction velocities). We collected tissues samples at necropsy for analysis of vector biodistribution by qPCR, GFP expression, GALC enzyme distribution and activity, and effects on the disease pathology (size/frequency of globoid cells, extent of myelination/demyelination and activation of immuno-modulatory cytokines). In two infant animals, GFP was not detected in brain/CNS. Vector sequences (GFP, GALC) were near background as assessed by qPCR. Globoid cells were still present in brain and peripheral nerves were enlarged. Low gene transfer, late delivery, or immune responses may have limited therapeutic efficacy.

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

2013-2014 Annual Progress Report
OD-011104-52
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****

Project Title DC-based AIDS Vaccine
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.339%
AIDS? Yes
PI. with institutional affiliation

Excluded by Requester C Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Immunology, Tulane University
A VP of R&D, VIRxSYS Corp, MD, USA
A Biochemistry, Tulane University
A Surgery, Private Source USA

Project Description (limited to one paragraph)

Twenty five years after the HIV epidemic began, an effective AIDS vaccine remains elusive. Multiple vaccine strategies (ie, viral-like particles i.v. or DNA-prime/vector boost i.m.) have been developed to generate immune responses, but none have protected from eventual disease progression. The focus of this project is to amend AIDS vaccine strategies with gene transfer technologies such as using replication defective lentiviral vectors, co-expressing immuno-modulatory cytokine genes, transducing target cells *ex vivo*. The SIV-based lentiviral vectors will efficiently transduce CD34+ hematopoietic stem/progenitor cells (HSC) *ex vivo*, which will be expanded *in vitro*, induced to differentiate into professional antigen presenting cells (dendritic cells) for expression of viral antigens, and then used for vaccination of the autologous host. Therefore, we have developed a new series of SIV-based lentiviral vectors to express SIV Gag/Pol or SIV Env. Animals are currently being vaccinated and evaluated for immunological parameters and for protection from challenged with SIVmac.

Project Progress (one paragraph)

Proprietary Info

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title TDP-43 Gene Transfer Model of Amyotrophic Lateral Sclerosis
Unit/Division Regenerative Medicine
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? NO
PI, with Institutional affiliation

Excluded by Requester A LSU Health Sciences Center

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Regenerative Medicine
C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

The treatment options for amyotrophic lateral sclerosis (ALS) are limited and overall not efficacious. An improved animal model for this disease could be important to develop and validate new compounds. Research on ALS has been historically focused on gene mutations in superoxide dismutase-one which has provided a vast wealth of information. However, it is now known that the most prevalent neuropathology in ALS involves a protein called transactive response DNA binding protein of 43 kDa (TDP-43). Under normal conditions, TDP is found mainly in the nucleus, but in ALS and several other neurodegenerative diseases, aberrant TDP pathology in the cytoplasm is found post-mortem, so TDP dysfunction and mislocalization appear to be key steps in ALS pathogenesis. After these relatively recent discoveries, many new TDP transgenic mouse models have been generated. Taking advantage of a novel peripheral gene delivery method which yields extensive expression in the spinal cord, we have successfully generated a rat model of ALS based on TDP. Our vector method has several clear advantages to germ-line transgenic models related to cost-effectiveness and ability to rapidly screen variants of the TDP protein, but for this project, the biggest advantage relative to transgenics is that the vector method is applicable to nonhuman primates (NHP). The motor system in rodents and the motor tasks that can be studied have limited the relevance of the rodent models of ALS; the motor system and fine motor tasks in NHP has greater relevance to humans. We aim to translate and improve our model in NHP where we expect TDP, but not a control reporter gene, to induce relevant recapitulation of ALS symptomotology, i.e., limb weakness and dysfunction, motor neuron loss, and muscle atrophy. We will also test the hypothesis that there are functional and regional differences of TDP induced neurodegeneration in the spinal cord. Three major innovations coalesce in this project: research on TDP, peripheral gene delivery to affect the CNS, and application to NHP.

Project Progress (one paragraph)

The objective is to develop a non-human primate (NHP) test system, which may be more sensitive and more predictive for therapeutic efficacy than rodents, owing to the similar anatomy and the appropriate neurological testing that can be done in primates. One of the main pathological proteins in ALS is transactive response DNA binding protein 43 kDa (TDP-43). Rhesus macaques received a gene transfer vector, adeno-associated virus (AAV9) encoding TDP-43, by an intravenous route of administration. A control green fluorescent protein (GFP) vector was used in a separate subject. Motor function and electromyography (EMG) were assessed over time to detect disease relevant changes. The TDP-43 subjects did not manifest severe paralysis and atrophy, as observed previously in rodents. However, we did clearly observe recombinant TDP-43 or GFP expression respectively, and there were trends of a partial disease state in the TDP-43 subjects relative to the control including body mass, impaired forelimb use during comprehensive motor testing, spontaneous EMG activity, and increased cytoplasmic deposition of TDP-43 immunoreactivity in neurons. These data

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

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****

Project Title CNS White Matter Tracts as a Novel Avenue for Gene Therapy for Krabbe Disease
Unit/Division Regenerative Medicine
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? NO
PI, with institutional affiliation

Excluded by Requester	C	Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Regenerative Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source

Project Description (limited to one paragraph)

Gene therapy (GT) represents a promising approach for the treatment of the CNS pathology in Lysosomal Storage Disorders (LSD), as it has the potential to provide a permanent source of the deficient enzyme. Our group has been developing a lentiviral (LV)-mediated intracerebral GT to treat Globoid Cell Leukodystrophy (GLD) that could achieve maximal transgene dispersal in the CNS from a limited number of injection sites. Published data from our group (in Preliminary Data section in this proposal) clearly demonstrate that a single lentiviral vector (LV) injection into a highly interconnected white matter region (external/internal capsule; EC/IC) resulted in rapid and robust expression of functional galactocerebrosidase (GALC) throughout the entire brain and spinal cord in the Twitcher mouse (murine model of Krabbe disease), resulting in global rescue of enzymatic activity, and marked decrease of activated microglia. The stable production and widespread distribution of the GALC enzyme achieved following EC/IC injection in affected neonatal mice suggests that this approach effectively produces physiological levels of the missing enzyme. The logical scientific progression in the maturation of this gene delivery technology is to assess this strategy in large animals models, including nonhuman primates (NHPs). Hypothesis: Administration of lentiviral vector expressing GALC to the EC/IC region of the Krabbe-affected primate brain will result in transduction and robust expression throughout the CNS.

This hypothesis will be tested through two Specific Aims. #1. Determine if LV-mediated delivery of the GALC gene in to the EC/IC improves the behavioral and neuromotor deficits of Krabbe-affected rhesus macaques. #2. To assess gene transfer efficiency, diffusion, distribution and long-term expression of the GALC enzyme in CNS tissues of injected NHP (Krabbe-affected and normal animals), histopathologic outcomes and immune response associated with the white matter-directed gene delivery strategy.

Project Progress (one paragraph)

All of the proposed animals have been injected with the lentiviral vectors expressing GALC. The behavioral testing has been completed on both animals and is currently being analyzed. All of the animals associated with this study have been necropsied and samples are currently being analyzed for gene transfer efficiency, diffusion, distribution and long-term expression of the GALC enzyme. Analysis of tissue sections demonstrated successful transduction within the brain as evidenced by expression of EGFP. Histopathologic assessments indicate that no overt problems resulted form the lentivirus transduction. We are currently working on shipping samples to Excluded by Request lab for analysis of enzyme levels and distribution.

Funding Sources (Include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

2013-2014 Annual Progress Report
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FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Universal Adult Stem Cell Vaccine Platform
Unit/Division Regenerative Medicine
Type of Project Pilot
Percent P51 dollars - 0.339%
AIDS? NO
PI, with institutional affiliation

Excluded by Requester	A	Microbiology and Immunology, TU SoM

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Regenerative Medicine
	C	Bacteriology and Parasitology
	C	Director

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Traditional vaccine approaches have thus far failed to provide protection against devastating diseases such as tuberculosis, AIDS, malaria, dengue, and many others. The reasons why vaccines have failed for these diseases are complex and varied. For example, *Mycobacterium tuberculosis* (Mtb) evades host responses by persisting in an intracellular niche, while HIV integrates functional proviral genomes into the DNA of host cells, thereby establishing latency or persistence. We will test the hypothesis that Adult mesenchymal stem cells can be developed as a safe and effective universal vaccine platform that can induce protective immunity to multiple pathogens simultaneously. Recent advances allow MSC to be derived by simple techniques from bone marrow or adipose tissue of adults and expanded to large numbers. In principle, MSC can be genetically modified to express virtually any protein from any human pathogen using non-replicating vectors. Bacterial, viral, fungal, or parasite proteins or toxoids expressed by MSC will induce both humoral and cellular immune responses. Preliminary Data in mice demonstrated robust expression of HIV-1 Env (gp120) from a CMV promoter. MSC expressing HIV-1 Env induced significantly higher levels of Env antibodies than injection of purified Env or MSC transfected with the vector minus env. The two specific aims of this proposal will extend these successful studies in mice and are designed to: 1. determine whether MSCs can be engineered to successfully express multiple pathogen antigens that elicit robust immune responses, and 2. evaluate efficacy of a multipathogen MSC vaccine candidate. Antigens that have shown promise in prior vaccine studies, Mtb strain CDC1551 antigen 85B-ESAT6 fusion protein and SIVmac251 Env and Gag-Pol, will be cloned and expressed in rhesus MSC. Rhesus macaques will be challenged with Mtb and SIVmac239 after immunization with MSC expressing Ag85B-ESAT6, Env and Gag-Pol. We will quantify Mtb and SIV loads in the immunized animals and compare pathological and immunological responses to well-characterized SIV and MTb infected singly- and dually-infected rhesus macaques from prior studies, leveraging the recent successful establishment of a NHP model to investigate co-morbidity of tuberculosis and AIDS. Although the MSC vaccine platform is a highly unconventional approach, it has the potential to transform the way that vaccines are developed, produced and delivered. The platform will be robust, versatile, and capable of expressing multiple variants of proteins from an array of complex pathogens simultaneously. Results obtained from these experiments will be key for future NIH grant applications.

Project Progress (one paragraph)

The vectors expressing the required SIV and TB antigens have been constructed and are currently being tested for the successful expression of the antigens *in vitro*. Once this is completed the *in vivo* studies will commence.

Funding Sources (include name of the source, PI and the FULL grant number)

This project was funded by the TNPRC Pilot Program under NIH P51 OD011104

RESEARCH PROJECTS

DIVISION OF BACTERIOLOGY AND PARASITOLOGY

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

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Project Title Defining "Persistence" in Post-treatment Lyme Disease
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

With over 300,000 new cases reported annually, Lyme disease is the most common tick-borne infection in North America. The causative agent, *Borrelia burgdorferi*, can chronically infect humans, causing rash, arthritis, carditis, and neurological dysfunction. A proportion of Lyme disease patients experience symptoms even after antibiotic treatment and the efficacy of antibiotic regimens for this disease is a very contentious issue. Our prior results have demonstrated that *B. burgdorferi* spirochetes persist in nonhuman primates (NHP) after antibiotic therapy. Importantly, the question of whether these antibiotic-tolerant organisms remain infectious and cause signs of disease has not been answered. Aim 1 is to confirm post-therapy persistence with tick-mediated infection, and consists of two subaims. The first (completed) was to perform pharmacokinetic analyses of doxycycline to determine an efficacious dose. The second was to examine tick-infected animals for persistent spirochetes post-treatment by multiple methods, including xenodiagnosis. Aim 2 is to determine if antibiotic-tolerant *B. burgdorferi* are infectious by attempting to transmit them to naïve animals. Aim 3 is to ascribe a phenotype to antibiotic-tolerant spirochetes wherein a molecular genetic approach will be employed to identify genetic markers specifically attributable to persistent spirochetes.

Project Progress (one paragraph)

To date, we have completed Aim 1 and are mid-way through the analysis of tissues for infection. In doing so, we optimized the tick-feeding process for improved yields. The experimental protocol for Aim 2 is nearing completion, and we have performed next-generation sequencing (Aim 3) on *B. burgdorferi* grown *in vitro* in the presence or absence of doxycycline to determine the phenotype of persisters. The project, upon completion, stands to generate data that has significant implications for Lyme disease treatment in particular, and for the understanding of bacterial tolerance to antimicrobials in general.

Funding Sources (include name of the source and the grant number)

P20 GM103458-09

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title A Multiplex Platform for Lyme Disease Diagnosis and Treatment Response
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

Because the nonhuman primate recapitulates the hallmark signs and disease course of human Lyme disease, we examined the specific antibody responses to multiple antigens of *B. burgdorferi* following infection of macaques with the Lyme disease spirochete. In doing so, we identified five antigens to which all animals responded; these also fluctuated with disease phase and antibiotic treatment. The five antigens will be incorporated into a diagnostic test, based on Luminex technology, and include OspC, DbpA, OspA, OppA-2 and the C6 peptide. While the C6 peptide will be synthesized; the four recombinant proteins have been expressed as glutathione S-transferase (GST) proteins in *E. coli* and purified over glutathione-sepharose beads.

Project Progress (one paragraph)

These proteins and peptide have been conjugated to fluorometric beads, tested singly, and in combination with immune serum and monoclonal antibodies to optimize the assay for detection and quantification of specific antibodies. We have determined the optimal ratios of the bead sets and compared the results obtained with that of standard ELISA. This showed that the range of detection using the multiplex test is much broader. The assay will next be tested with well-characterized Lyme patient sera and controls. The detection and quantification of *B. burgdorferi*-specific antibodies by our unique multiplex bead-based platform is expected to aid in more reliable diagnoses and in the monitoring of disease progression and treatment efficacy.

Funding Sources (include name of the source and the grant number)

1R21AI100166-01 (Embers, M) $243,271

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title DNA Microarray and Expression Core
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester	C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester	C Regenerative Medicine
	C Microbiology
	C Bacteriology and Parasitology
	C Immunology
	C Director
	C Comparative Pathology
	C Microbiology
	C Comparative Pathology
	C Microbiology
	C Bacteriology and Parasitology
	C Microbiology
	C Microbiology
	C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A Tulane University
	A Tulane University
	A Tulane University
	A Tulane University
	A Louisiana State Univ School of Veterinary Medicine
	A Private Source
	A Tulane University
	A Private Source
	A

Project Description (one paragraph)

The DNA Microarray and Expression Core (Microarray Core) at TNPRC currently provides the following services:

A. **DNA Microarrays:**
1) Microarray experimental design:
2) Spotted or 2-color microarray experiments:
3) Microarray Data Analysis
4) Small Sample Amplification
6) RNA Isolation
7) miRNA arrays

Project Progress (one paragraph)

During the year 2013, the core continued to perform numerous microarray hybridizations for various investigators. We performed several mouse and human array experiments this year in addition to the usual rhesus macaque array experiments. Some of this data has already been published, while much more is currently being analyzed. The core is fabricating custom arrays as well. A strong suite of the core remains the analysis of microarray data in a fashion that is easy for the investigators to publish.

Funding Sources (include name of the source and the grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Genetic Requirements for the Survival of Tubercle Bacilli in Nonhuman Primates
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Excluded by Requester C Microbiology
C Director
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

New drugs and vaccines are urgently needed to effectively control TB. This requires a better understanding of how *Mtb* adapts to a wide-variety of environmental conditions, inevitably faced by it during the various stages of infection. Nonhuman Primates (NHPs), arguably, best model critical aspects of TB. We have previously established this model and continue to either refine it or use it towards investigations of mechanisms of *Mtb* virulence.

Project Progress (one paragraph)

In the past we have studied the role of SigH, the major stress response transcription factor of *Mtb*. Our results suggest that the primate immune system is able to generate a higher degree and breadth of immune pressure on *Mtb* than the murine immune system. The mechanism of attenuation of this mutant is its inability to scavenge redox stress. We have further studied the immune response generated by infection with the Δ-sigH mutant. *In-vivo*, as well as *in-vitro*, the mutant appears to generate a higher degree of pro-inflammatory response relative to wild-type *Mtb*. We studied this in detail using controlled infection of macrophages *in-vitro* followed by silencing of the pro-inflammatory cytokine IL-6. Our results show that *Mtb* regulates IL-6 production in a sigH dependent manner to inhibit type-1 interferon signaling. ClgR is one of the transcription factors induced by SigH and it induces the expression of proteolytic genes in response to a wide-variety of protein damaging stress conditions. We have generated an isogenic mutant *Mtb*:Δ-*clg*R and shown that the mutant has a growth defect phenotype in both relevant stress conditions as well as *In-vivo* in the mouse model. Surprisingly however, in response to oxidative stress, ClgR appears to be involved in providing a transcriptional boost to the SigH regulon in the absence of any induction of Clp proteases.

Funding Sources (include name of the source and the grant number)

1R01AI089323-01A1 - Excluded by Requester – 06/01/10-05/31/15

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title A Multi-dimensional Approach to Understanding TB Latency and Reactivation
Division/Unit Bacteriology and *Parasitology*
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Excluded by Requester C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Johns Hopkins School of Medicine
A Johns Hopkins School of Medicine

Project Description (one paragraph)

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*), is a global infectious disease emergency. A major hurdle in combating TB is the fact *Mtb* is able to persist for long periods of time in host tissues, in a quiescent state. These bacilli are able to reactivate and cause pulmonary TB, when the immune system is compromised. Hence, a complete understanding of TB latency and reactivation is required for the effective control of TB. NHLBI has funded Excluded by Excluded by and colleagues at the Johns Hopkins School of Medicine to study tuberculosis latency and reactivation from the perspective of the pathogen in a number of experimental animal models. In a subcontract to the Tulane Primate Center, we have been entrusted with the task of performing these experiments in nonhuman primates.

Project Progress (one paragraph)

We have begun the phase I of the infection of NHPs with *Mtb* with the aim of generating latent TB Prop rieta animals were infected. After the verification of the onset of the latent phase of the disease, Proprie tar Inf were put on a weekly dose of 4 mg/Kg Adalimumab (TNF blocking antibody). Modest reactivation of latent TB after TNF blockage was observed. A second experiment has now begun where specified mutants which were computationally predicted to be involved in latency and/or reactivation by Excluded by group have been included in a pool and macaques infected with these. We will block TNF in Propr ietar y Inf of these animals and study reactivation of specific mutants in this experiment over the next few months.

Funding Sources (include name of the source and the grant number)

1R01HL106790-01 - Excluded by Requester – 09/17/10-08/31/14

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Transcriptomics of tuberculosis latency and reactivation
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester C Microbiology
C Director

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester C Tulane University

Project Description (one paragraph)

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*), is a global infectious disease emergency. A major hurdle in combating TB is the fact *Mtb* is able to persist for long periods of time in host tissues. These bacilli are able to reactivate and cause pulmonary TB, when the immune system is compromised. Hence, a complete understanding of TB latency and reactivation is required for the effective control of TB. Nonhuman Primates (NHPs) are excellent models of TB, especially to study the progression of experimental infection to latency, and to study the pathology and biology of granulomatous lesions - the hallmarks of TB infections. We have previously established a model of human TB, by exposing NHPs to true *Mtb* aerosols. This model continues to be refined. The central hypothesis of our proposal is that host granuloma responses can be used to predict latent and reactivation TB.

Project Progress (one paragraph)

We have performed a systematic study of the "transcriptome" and the "miRNAome" of NHP lung lesions during latent to chronic *Mtb* infection, during reactivation TB and during protection from BCG vaccination. We have thus identified correlates of protection from acute TB. We were able to identify specific differences in the innate immune response during the co-infection, which correlated with reactivation, and could be confirmed by immune response measurement at the protein level. Our results show signatures for neutrophil and macrophage turnover as well as inducible bronchus associated lymphoid tissue (iBALT) activation.

Funding Sources (include name of the source and the grant number)

1R01HL106790-01 Excluded by Requester - 09/17/10-08/31/14

Publications Resulting from this Project

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Diagnostic Parasitology Core
Division/Unit Bacteriology & Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No

PI. with institutional affiliation

Excluded by Requester C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester
C Director
C Veterinary Medicine
C Veterinary Medicine
C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Tulane University

Project Description (one paragraph)

The Diagnostic Parasitology Core Lab is the first line of defense against parasitic diseases in the animal colony and provides diagnostic services to clinical veterinarians and researchers when parasitic infections are suspected.

Project Progress (one paragraph)

From 1/1/13 – 1/1/14, the core lab examined the following: 2392 stool samples (98 quarantine, 2011 clinical, 52 research, and 231 from the outside rodent colony), 53 blood samples (49 quarantine, 4 research), 1 skin scrape (clinical), and 273 perianal/pelage samples from the outside rodent colony, yielding a total of 2719 samples presented to the lab for processing resulting in 5095 individual test charges (direct smears, flotations, blood films, tape tests, QBC, serodiagnosis, and Knott's blood examinations). The record-keeping system for parasitology results has now become completely paperless, with information on laboratory results forwarded to clinical veterinarians through the computerized animal records system. The laboratory now bills for all services rendered and sends a statement every month to projects for which parasitology diagnostic work was performed.

Funding Sources (include name of the source and the grant number)

Excluded by Requester NIH 3R21AI055013-02S1, NIH 5R01EB006493-03
Excluded by NIH 5T35RR017504-05, NIH 5P20RR016456-06
Excluded by Requester NIH T32OD011124
Excluded by Requester P20 GM103458-09

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Lyme Disease: Identification of Virulence Determinants Important in Infectivity
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A University of Texas @ Houston

Project Description (one paragraph)

The identification of genes important in the pathogenesis of Lyme disease has been hampered by exceedingly low transformation rates in low-passage, infectious organisms. Using the infectious, moderately transformable *B. burgdorferi* derivative 5A18NP1 and signature-tagged versions of the Himar1 transposon vector pGKT, we have constructed a defined transposon library for the efficient genome-wide investigation of genes required for wild-type pathogenesis, *in vitro* growth, physiology, morphology, and plasmid replication. To facilitate analysis, the insertion sites of 4,479 transposon mutants were determined by sequencing. The transposon insertions were widely distributed across the entire *B. burgdorferi* genome, with an average of 2.68 unique insertion sites per kb DNA. The 10 linear plasmids and 9 circular plasmids had insertions in 33 to 100 percent of their predicted genes. In contrast, only 35% of genes in the 910 kb linear chromosome had incapacitating insertions; therefore, the remaining 601 chromosomal genes may represent essential gene candidates. In initial signature-tagged mutagenesis (STM) analyses, 434 mutants were examined at multiple tissue sites for infectivity in mice using a semi-quantitative, Luminex-based DNA detection method. Examples of genes found to be important in mouse infectivity, both by needle and by tick inoculation, included those involved in motility, chemotaxis, the phosphoenolpyruvate phosphotransferase system, and other transporters, as well as putative plasmid maintenance genes. Availability of this ordered STM library and a high-throughput screening method is expected to lead to efficient assessment of the roles of *B. burgdorferi* genes in the infectious cycle and pathogenesis of Lyme disease.

Project Progress (one paragraph)

Genome sequence and NCBI blast search analysis showed that adenylate cyclase (AC) IV (encoded by BB0723, cyaB) is well conserved in different species of Borrelia. A conserved motif EXEXK, initially detected in class IV AC from other bacteria, was also found in the active site of borrelia AC. However, functional roles of AC in infectious cycle of Borrelia are largely unknown. Two mutants of cyaB; one has transposon insertion in the N-terminal (T11TC373) and the other has insertion in the C-terminal (T08TC498) were generated in the STM library. Both mutants were fully infectious in mice when injected by needle inoculation. Both cyaB mutants survived normally in unfed as well as fed ticks and were able to cause infection to naïve mice after transmission from ticks indicating that cyaB is dispensable in the maintenance of mouse-tick cycle of Borrelia.

Funding Sources (include name of the source and the grant number)

RO1-AI059048 Excluded by Requester 07/01/04 – 06/30/13 NIH/NIAID
Title: "Virulence determinants of *Borrelia burgdorferi*"

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Non-viable *B. Burgdorferi* Induce Inflammation and Apoptosis in Oligodendrocytes
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Excluded by Requester C Bacteriology and Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

In previous studies, exposure to live *Borrelia burgdorferi* was shown to induce inflammation and apoptosis of human oligodendrocytes. In this study we assessed the ability of non-viable bacteria (heat killed or sonicated) to induce inflammatory mediators and cell death.

Project Progress (one paragraph)

Both heat-killed and sonicated bacteria induced release of CCL2, IL-6, and CXCL8 from oligodendrocytes in a dose dependent manner. In addition, non-viable *B. burgdorferi* also induced cell death as evaluated by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) and another cell viability assay. These results suggest that spirochetal residues left after bacterial demise, due to treatment or otherwise, may continue to be pathogenic to the central nervous system.)

Funding Sources (Include name of the source and the grant number)

RO1-NS048952 Excluded by 07/01/04 – 01/31/15 NIH/NINDS
Title: "Lyme neuroborreliosis pathogenesis in the rhesus monkey"

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Pathogenesis of Lyme Neuroborreliosis: Studies *ex vivo* & *in vivo*
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester

C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester

C Bacteriology and Parasitology
C Veterinary Medicine
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A Louisiana State University
A Louisiana State University

Project Description (one paragraph)

Lyme neuroborreliosis (LNB) may present as meningitis, cranial neuropathy, acute radiculoneuropathy or, rarely, as encephalomyelitis. We hypothesized that glia, upon exposure to *B. burgdorferi*, the Lyme disease agent, produce inflammatory mediators that promote the acute cellular infiltration of early LNB. This inflammatory context could potentiate glial and neuronal apoptosis both in the central and peripheral nervous systems (CNS, PNS). We inoculated live *B. burgdorferi* into the cisterna magna of rhesus macaques Proprietar hesus macaques were given an intrathecal inoculation with 10^8 live spirochetes Propr ietary control animals received medium alone. Animals were followed for either 8 wks (n = 7) or 14 wks (n = 7) Propri etary I of the animals inoculated with *B. burgdorferi* were given a standard veterinary treatment with dexamethasone (2 mg/Kg once a day for 1 week and then 1 mg/kg q.d. for the remainder of the study), four were given a standard veterinary treatment with the non-steroidal anti-inflammatory drug meloxicam (0.18 mg/kg on the first day, then 0.09 mg/Kg q.d. until the end of the study). Both drugs were given orally. The remaining Proprietar animals were left untreated. Cerebrospinal fluid (CSF) was collected weekly and cultured in search of *B. burgdorferi*. In the CSF leukocytes (pleocytosis) were counted, and inflammatory mediators were quantified by Multiplex ELISA. Histology and immunohistochemistry of brain, spinal cord and DRG tissues were performed post-necropsy, in search of inflammatory lesions and apoptotic cells.

Project Progress (one paragraph)

CSF yielded positive cultures in all of the animals that had received *B. burgdorferi*. Pleocytosis was caused by *B. burgdorferi* and inhibited in animals treated with dexamethasone but not meloxicam. Pro-inflammatory mediators were elicited in the CSF by the infection and controlled by dexamethasone but not meloxicam. Meloxicam-treated and untreated animals that were infected with *B. burgdorferi* showed signs of meningitis, radiculoneuritis, as well as inflammatory lesions in dorsal root ganglia (DRG). Animals treated with dexamethasone showed no inflammatory lesions. In addition to inflammatory lesions, results show a) that infection with *B. burgdorferi* led to neuronal and glial apoptosis in DRG; b) as per our hypothesis, the anti-inflammatory drug dexamethasone mitigated the apoptosis; c) the NSAID meloxicam had no effect. No lesions were found in the negative control that received only carrier medium, RPMI.

Funding Sources (include name of the source and the grant number)

RO1-NS048952 Excluded by Requester 07/01/04 – 01/31/15 NIH/NINDS

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Pathogenesis of Lyme Neuroborreliosis: Studies *in vitro*
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Excluded by Requester C Bacteriology and Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

Inflammation caused by the Lyme disease spirochete *B. burgdorferi* is an important factor in the pathogenesis of Lyme neuroborreliosis. Our central hypothesis is that *B. burgdorferi* can cause disease via the induction of inflammatory mediators such as cytokines and chemokines in glial and neuronal cells. Earlier we demonstrated that interaction of *B. burgdorferi* with brain parenchyma induces inflammatory mediators in glial cells as well as glial (oligodendrocyte) and neuronal apoptosis using *ex vivo* and *in vivo* models of experimentation. In this study we evaluated the ability of live *B. burgdorferi* to elicit inflammation *in vitro* in differentiated human MO3.13 oligodendrocytes and in differentiated primary human oligodendrocytes, by measuring the concentration of immune mediators in culture supernatants using Multiplex ELISA assays. Concomitant apoptosis was quantified in these cultures by the *in situ* terminal deoxynucleotidyl transferase mediated UTP nick end-labeling (TUNEL) assay and by quantifying active caspase-three by flow cytometry. The above phenomena were also evaluated after 48 hours of stimulation with *B. burgdorferi* in the presence and absence of various concentrations of the anti-inflammatory drug dexamethasone.

Project Progress (one paragraph)

B. burgdorferi induced enhanced levels of the cytokine IL-6 and the chemokines IL-8 and CCL2 in MO3.13 cells as compared to basal levels, and IL-8 and CCL2 in primary human oligodendrocytes, in a dose-dependent manner. These cultures also showed significantly elevated levels of apoptosis when compared with medium controls. Dexamethasone reduced both the levels of immune mediators and apoptosis, also in a manner that was dose dependent. This finding supports our hypothesis that the inflammatory response elicited by the Lyme disease spirochete in glial cells contributes to neural cell damage. As oligodendrocytes are vital for the functioning and survival of neurons, the inflammation and subsequent apoptosis of oligodendrocytes induced by *B. burgdorferi* could contribute to the pathogenesis of Lyme neuroborreliosis.

Funding Sources (include name of the source and the grant number)

RO1-NS048952 Excluded by Requester 07/01/04 – 01/31/15 NIH/NINDS

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Pathogenesis of Lyme Neuroborreliosis: Studies in Dorsal Root Ganglia Cells
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI. with institutional affiliation

Excluded by Requester C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester C Bacteriology and Parasitology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Tulane University
A Louisiana State University
A Louisiana State University

Project Description (one paragraph)

Lyme neuroborreliosis (LNB), caused by the spirochete *Borrelia burgdorferi*, affects both the peripheral and the central nervous systems. Radiculitis or nerve root inflammation, which can cause pain, sensory loss, and weakness, is the most common manifestation of peripheral LNB in humans. We previously reported that rhesus monkeys infected with *B. burgdorferi* develop radiculitis as well as inflammation in the dorsal root ganglia (DRG), with elevated levels of neuronal and satellite glial cell apoptosis in the DRG. We hypothesized that *B. burgdorferi* induces inflammatory mediators in glial and neuronal cells and that this inflammatory milieu precipitates glial and neuronal apoptosis. To model peripheral neuropathy in LNB we incubated normal rhesus DRG tissue explants with live *B. burgdorferi ex vivo* and identified immune mediators, producer cells, and verified the presence of *B. burgdorferi* in tissue sections by immunofluorescence staining and confocal microscopy. We also set up primary cultures of DRG cells from normal adult rhesus macaques and incubated the cultures with live *B. burgdorferi*. Culture supernatants were subjected to multiplex ELISA to detect immune mediators, while the cells were evaluated for apoptosis by the *in situ* TUNEL assay. A role for inflammation in mediating apoptosis was assessed by evaluating the above phenomena in the presence and absence of various concentrations of the anti-inflammatory drug dexamethasone. As Schwann cells ensheath the dorsal roots of the DRG, we evaluated the potential of live *B. burgdorferi* to induce inflammatory mediators in human Schwann cell (HSC) cultures.

Project Progress (one paragraph)

Rhesus DRG tissue explants exposed to live *B. burgdorferi* showed localization of CCL2 and IL-6 in sensory neurons, satellite glial cells and Schwann cells while IL-8 was seen in satellite glial cells and Schwann cells. Live *B. burgdorferi* induced elevated levels of IL-6, IL-8 and CCL2 in HSC and DRG cultures and apoptosis of sensory neurons. Dexamethasone reduced the levels of immune mediators and neuronal apoptosis in a dose dependent manner. In this model, *B. burgdorferi* induced an inflammatory response and neuronal apoptosis of DRG. These pathophysiological processes could contribute to peripheral neuropathy in LNB.

Funding Sources (include name of the source and the grant number)

RO1-NS048952 Excluded by Requester 07/01/04 – 01/31/15 NIH/NINDS

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Substance P Exacerbation of CNS Inflammation
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Excluded by Requester C Bacteriology and Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A University of North Carolina @ Charlotte

Project Description (one paragraph)

The tachykinin, substance P (SP) mediates a variety of biological effects via high affinity neurokinin-1 receptors (NK-1R). NK-1R antagonists have been extensively studied for use in the treatment of a variety of disease conditions. We have begun a comprehensive preclinical evaluation of the ability of SP to augment classical inflammation in isolated nervous system tissues of rhesus macaques and in a rhesus model of bacterial meningitis. We are testing the hypothesis that inhibition of SP/NK-1R interactions attenuates pro-inflammatory responses of nervous system cells to clinically relevant bacterial pathogens, thereby limiting damage. As such, these studies will provide essential information in resolving the cellular mechanisms that precipitate classical inflammation within the brain during disease states. Furthermore, these studies represent a substantial and possibly final preclinical and translational phase to evaluate the therapeutic potential of NK-1 receptor antagonists in the treatment of classical nervous system inflammation prior to human trials.

Project Progress (one paragraph)

We began the assessment of the effect of endogenous Substance P on brain tissues obtained from rhesus macaques *ex vivo*. The experimental design consisted in exposing frontal cortex tissue sections for 6 hours to medium alone or to *B. burgdorferi* ($1x10^7$ bacteria/mL) in the presence and absence of 10 mM NK-1R antagonist. The antagonist we chose for this experiment, namely, L-703,606, had been used before to inhibit the enhancing effect of exogenous Substance P on the production of IL-6 by murine microglia and astrocytes *in vitro* Excluded by Requester Supernatants from treated brain slices were collected and the tissues were then homogenized to obtain a total protein lysate. Cytokine and chemokine levels in supernatants and in tissue lysates were quantified separately with a MILLIPLEX Non-Human Primate Cytokine 23-Plex Panel. Results obtained fo[Propr]ietary different animals consistently showed that the interaction of *B. burgdorferi* with rhesus monkey brain parenchyma *ex vivo* elicited primarily IL-6, IL-8, and CCL2/MCP-1 production in both lysate and supernatant. The addition of the NK-1R antagonist reduced the concentration of these inflammatory mediators to background levels. This change was statistically significant.

Funding Sources (include name of the source and the grant number)

RO1-NS050325 Excluded by Requester 12/01/04 – 05/31/15 NIH/NINDS

2013-2014 Annual Progress Report
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Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title TLR and other Pathways in the Response of Oligodendrocytes to *B. BURGDORFERI*
Division/Unit Bacteriology and Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Bacteriology and Parasitology

Principal Core Scientist associated with the project

Excluded by Requester C Bacteriology and Parasitology

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (one paragraph)

Lyme neuroborreliosis (LNB) affects both the central and peripheral nervous systems. In a rhesus macaque model of LNB we had previously shown that brains of rhesus macaques inoculated with *Borrelia burgdorferi* release inflammatory mediators, and undergo oligodendrocyte and neuronal cell death. In vitro analysis of this phenomenon indicated that while *B. burgdorferi* can induce inflammation and apoptosis of oligodendrocytes per se, microglia are required for neuronal apoptosis. We hypothesized that the inflammatory milieu elicited by the bacterium in microglia or oligodendrocytes contributes to the apoptosis of neurons and glial cells, respectively, and that downstream signaling events in NFkB and/or MAPK pathways play a role in these phenotypes. To test these hypotheses in oligodendrocytes, several pathway inhibitors were used to determine their effect on inflammation and apoptosis, as induced by *B. burgdorferi*.

Project Progress (one paragraph)

In a human oligodendrocyte cell line (MO3.13), inhibition of the ERK pathway in the presence of *B. burgdorferi* markedly reduced inflammation, followed by the JNK, p38 and NFkB pathway inhibition. In addition to eliciting inflammation, *B. burgdorferi* also increased total p53 protein levels, and suppression of the ERK pathway mitigated this effect. While inhibition of p53 had a minimal effect in reducing inflammation, suppression of the ERK pathway or p53 reduced apoptosis as measured by active caspase-3 activity and the TUNEL assay. A similar result was seen in primary human oligodendrocytes wherein suppression of ERK or p53 reduced apoptosis. It is possible that inflammation and apoptosis in oligodendrocytes are divergent arms of MAPK pathways, particularly the MEK/ERK pathway. A paper on this subject was recently published.

Funding Sources (include name of the source and the grant number)

RO1-NS048952 Excluded by Requester 07/01/04 – 01/31/15 NIH/NINDS

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Vector-Borne Diseases Core
Division/Unit Bacteriology & Parasitology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI. with institutional affiliation
Excluded by Requester C Bacteriology and Parasitology
Principal Core Scientist associated with the project
Excluded by Requester C Bacteriology and Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A University of Texas at Houston
A Louisiana State University

Project Description (one paragraph)

The tick colony has continued to be instrumental in enabling our division to do research in Lyme borreliosis using the natural mode of infection. The technique of capillary feeding of nymphal ticks, which we have available, allows us to infect ticks with spirochetal clonal isolates. This is often essential to ensure defined host responses to infection. We also are able to infect larval ticks by immersion in culture fluid that contains spirochetes. We have currently available numerous specimens of all of the developmental stages of *Ixodes scapularis*. Larvae, nymphs, and adults are stored at 4ºC in a staggered fashion. Therefore, we usually have all of the stages available at most times throughout the year. This includes Proprietary of larvae (with about Propri etary larvae each) and Proprietary Info uninfected nymphs for experimental needs as they arise. We have continued our collaboration with the University of Texas Health Sciences Center, Houston, TX, on the identification of virulence determinants of *B. burgdorferi* that affect infectivity of spirochetes to ticks, and to mice via ticks. We have been providing nymphs for Excluded by for the study of transmission of infection of non-human primates and xenodiagnosis post-infection, which includes use of uninfected nymphs on SCID mice which were previously injected with tick midguts. For the 2013 adult tick season Propr females and Prop males were collected. Of these, Prop adult female ticks were blood fed Proprietary for colony propagation. A total of Pr of those fed successfully, Propri etary of those laid eggs Pr were used by Excluded by Requester for saliva studies and Pro remain in 4°C storage. In addition, the remaining adults collected were available to Excluded by for more ticks saliva experiments. The number of larvae from colony propagation that fed and were collected were Propri and Propri of those successfully molted into nymphs to be used in future experiments. A total of Prop nymphs were capillary-fed successfully and used in an experiment for Exclude Excluded by Requester used Prop uninfected nymphs for her xenodiagnosis experiments using non-human primates.

Funding Source

NIH/NCRR Grant 8 P20 GM103458-09 Excluded by Requester
RO1-AI059048 Excluded by Requester

Publications Resulting from this Project
Excluded by Requester

Excluded by Requester

DIVISION OF COMPARATIVE PATHOLOGY

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Confocal Microscopy and Image Analysis Core
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI. with institutional affiliation

Excluded by Requester	C	Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Regenerative Med
	C	Comparative Pathology
	C	Bacteriology & Parasitology
	C	Bacteriology & Parasitology
	C	Immunology
	C	Director
	C	Comparative Pathology
	C	Comparative Pathology
	C	Microbiology
	C	Comparative Pathology
	C	Microbiology
	C	Comparative Pathology
	C	Bacteriology & Parasitology
	C	Microbiology
	C	Microbiology
	C	Microbiology
	C	Comparative Pathology
	C	Comparative Pathology
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	Tulane University SoM
	A	Frederick National Laboratory
	A	University of Wisconsin
	A	Private Source
	A	
	A	Eastern Virginia SoM
	A	LSUVM
	A	Tulane SoM
	A	Private Source
	A	YNPRC
	A	YNPRC
	A	Private Source
	A	Tulane University SoM

Project Description (limited to one paragraph)

The Confocal Microscopy and Image Analysis Core provides state-of-the-art confocal microscopy, multi-label fluorescent labeling and detection, and image analysis for TNPRC, and to numerous affiliate research scientists. Excluded by Requester has managed the Core since 2001. The Core has a Leica TCS SP2 laser scanning confocal microscope system equipped with 3 lasers, with 6 laser lines available, capable of simultaneously collecting information in four channels (3 fluorescent and one for differential interference contrast). The system is attached to two microscopes an upright (DMRE) and an inverted (DMIRE2) that allows for confocal microscopy of fixed preparations and also living cells. A separate workstation is available for data analysis. The Core also utilizes Volocity Software for the rendition of the data in 3 dimensions. There is also a Nuance spectral camera and CRI Multispectral Imaging System, and corresponding Inform software for image analysis. The equipment has been used for a variety of purposes including co-localization of green fluorescent protein (GFP) expressing SIV and T cell markers, localization of SIV-specific $CD8^+$, $tetramer^+$ T cells in tissues, co-localization of GFP and brain cell markers, co-localization of malaria parasites and cytokine producing cells, co-localization of *Borrelia burgdorferi* (causitve agent of Lyme disease), brain cell markers and cytokines, co-localization of SIV by *in situ* hybridization and dendritic cell markers, identification of pluripotent stem cells in tissues, and co-localization of *Mycobacterium tuberculosis*, SIV, and cell markers. The core also provides a significant amount of consulting regarding labeling by molecular techniques, molecular probes and antibodies to Core and Affiliate investigators. The Core also provides essential training in fluorescent microscopy, confocal microscopy and image analysis for investigators, graduate students, postdoctoral fellows, and technicians. We train an average of 8 persons per year. The training consists on at least 12 contact hours with the manager including theory and practice.

Project Progress (one paragraph)

In the last year, the confocal microscope was utilized by Pro prie investigators for a total usage of Propr ietary hrs used (average Pro prie hrs/wk). A total of Prop rietar slides were imaged and analyzed, generating Propriet ary Info of data in 2013. The CRI Multispectral Imaging System was used by Pro pri investigators for a total of Pro priet hours of assisted or solo camera time. Since the submission of the last report, Pro pri papers were published (below), and Pending Support

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Anatomic Pathology Core
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	C	Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Comparative Pathology
	C	Veterinary Medicine
	C	VETERINARY MEDICINE
	C	REGENERATIVE MEDICINE
	C	VETERINARY MEDICINE
	C	VETERINARY MEDICINE
	C	VETERINARY MEDICINE
	C	VETERINARY MEDICINE
	C	Bacteriology & Parasitology
	C	IMMUNOLOGY
	C	DIRECTOR
	C	Comparative Pathology
	C	VETERINARY MEDICINE
	C	Comparative Pathology
	C	MICROBIOLOGY
	C	Comparative Pathology
	C	Bacteriology & Parasitology
	C	VETERINARY MEDICINE
	C	MICROBIOLOGY
	C	VETERINARY MEDICINE
	C	MICROBIOLOGY
	C	MICROBIOLOGY
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	LSU HEALTH SCIENCES CENTER
	A	Excluded by Requester,Private Source
	A	

Project Description (limited to one paragraph)
The Anatomic Pathology Core consists of the Necropsy, Histology, and Tissue Collection and Distribution Units and is responsible for post-mortem examinations, tissue collection and distribution, fixation, processing, slide preparation, routine and special staining. It is a center policy that a cause of death is determined, if possible, for all animals that die at the center, whether of natural or experimental causes. This allows us to monitor and document all infectious agents and disease processes that occur within the colony and provides an opportunity to discover new diseases, which may be useful models. In addition, most major research areas at the center depend heavily on anatomic pathology support as an integral part of the research The Anatomic Pathology Core consists of the Necropsy, Histology, and Tissue Collection.

Project Progress (one paragraph)

In 2012 and 2013 respectively, a total of Proprietary Info necropsies, Proprietary Info biopsies were performed by the Core. The Anatomic Pathology Core Laboratory instrumentation includes 3 Microm HM325 microtomes and one automated Leica RM2145 microtome for preparing thin and thick tissue sections for routine H&E and special staining; sections for confocal microscopy, labeling studies with antibodies and molecular probes.. We also utilize a Leica ASP 300 tissue processor, a Tissue-Tek embedding station, Leica Autostainer XL automated slide stainer and cover slipper, and assorted water baths, ovens, microscopes, computer work station, Leica autostainer (automated slide stainer and cover slipper). A TBS Shur/Mark automated cassette labeler was added to the lab in 2012 and a Thermo Scientific slide labeler was purchased in 2013. In 2012 and 2013, the Core produced Proprietary Info units respectively, which includes stained and unstained slides, uncut blocks, and frozen sections. Research projects account for 75.6% and 79.6% respectively of the glass slides and all of the unsectioned blocks and frozen sections. Currently we employ three full time, and one part-time histologist, with a combined 51 years' laboratory experience. The AIDS research program is a major user of core services.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Clinical Pathology Core
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with Institutional affiliation

Excluded by Requester C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A UNIV OF PITTSBURGH
A LSUHSC, LA
A Private Source
A
A UNIVERSITY OF ARKANSAS
A Louisiana State University
A Private Source
A LSUHSC, LA
A Private Source
A UNIV OF NEW MEXICO
A Private Source
A

Project Description (limited to one paragraph)

The Clinical Pathology Core is staffed by P ro ASCP registered medical technologists and provides bacteriology, hematology, and clinical chemistry analyses for the clinical veterinarians and core and affiliate scientists.

Project Progress (one paragraph)

The Clinical Laboratory has an Proprietary Info chemistry analyzer and replaced the Proprietary Info hematology analyzer with an updated Proprietary Info n 2014. The Proprie tary Inf system will be upgraded this year. A Laboratory Information System (LIS) provides an interface for both the hematology and chemistry analyzer with the current TNPRC animal records database. The LIS also provides an interface for emailing Hematology, Chemistry and Microbiology reports to the veterinarians. In addition, we have a Proprietary Info and two Proprietary Info with separate LIS to allow data collection from animals infected with Select Agents when samples cannot be transported to the central lab. In 2012 and 2013 the Clinical Pathology Core performed Proprietary Info CBC's, Proprietary Info reticulocyte counts, manually reviewed Proprietary Info blood smears, performed Proprietary Info chemistry analyses panels Proprietar y Info and Proprieta ry Info analytes total) Proprietary CSF cell counts, Proprietary urinalyses, and Proprietary Info bacterial/fungal cultures, respectively. Environmental and clinical cultures increased 37 and 30%, respectively over year 2011.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Primate Pathology Database Collaborative
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester	C	Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Director
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	University of California
	A	Oregon National Primate Research Center
	A	Washington National Primate Research Center
	A	California National Primate Research Center
	A	Private Source
	A	California National Primate Research Center
	A	NIAID
	A	California National Primate Research Center
	A	Private Source
	A	Oregon National Primate Research Center
	A	Yerkes National Primate Research Center
	A	University of Arizona
	A	Southwest National Primate Research Center
	A	Oregon National Primate Research Center
	A	Wisconsin National Primate Research Center
	A	Yerkes National Primate Research Center
	A	Private Source
	A	California National Primate Research Center
	A	Yerkes National Primate Research Center
	A	Washington National Primate Research Center
	A	California National Primate Research Center
	A	Oregon National Primate Research Center
	A	Private Source
	A	Oregon National Primate Research Center
	A	New England Primate Research Center
	A	Private Source
	A	
	A	Oregon National Primate Research Center
	A	Wisconsin National Primate Research Center
	A	New England Primate ResearchCenter
	A	Private Source
	A	Washington National Primate Research Center
	A	Wisconsin National Primate Research Center
	A	California National Primate Research Center

Excluded by Requester

A Southwest National Primate Research Center
A NIAID
A California National Primate Research Center
A California National Primate Research Center
A Wisconsin National Primate Research Center
A Wisconsin National Primate Research Center
A Yerkes National Primate Research Center
A Wisconsin National Primate Research Center
A California National Primate Research Center
A Washington National Primate Research Center
A Private Source
A Yerkes National Primate Research Center
A Private Source
A New England Primate Research Center
A Private Source

Project Description (limited to one paragraph)

A consortium composed of pathologists, NPRC directors. IT and informatics personnel from each of the eight National Primate Research Centers (NPRCs) is establishing a database of images of nonhuman primate (NHP) pathology. The primate pathology image database (PPID) incorporates gross and histologic images and is derived from archival and ongoing contributions from each of the primate centers. Images will be organized for easy and rapid retrieval via the Web. The creation of this shared resource will facilitate collaborations among the primate centers, enhance the productivity of the pathologists and provide an invaluable resource to the veterinary and research communities. The database will facilitate collaboration among scientists working with simian immunodeficiency virus-related pathology by enabling archiving of cases, providing ready means of consultation with other pathologists, and comparison of related lesions across institutions. A monthly online seminar continues to generate cases for this collection.

Project Progress (one paragraph)

We contributed one seminar to this collection in 2012 and one in 2013. Excluded by Reques attended the NHPRC Consortium Pathology Working Group Annual Meeting held in Oregon in 2012, and Excluded by attended the 2013 meeting in Atlanta, GA. Tulane National Primate Research Center will host the 2014 meeting.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Monocyte/macrophages and their Role in NeuroAIDS
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES
PI, with institutional affiliation
Excluded by Requester A Private Source
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Director
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Private Source

Project Description (limited to one paragraph)

Neurological sequelae of human immunodeficiency virus (HIV) infection have been and remain a significant problem. Monocytes and macrophages in humans and monkeys are susceptible to infection by HIV and simian immunodeficiency virus (SIV), and are considered to be a main mechanism by which the central nervous system (CNS) is infected. Within the infected CNS, perivascular macrophages and, in some cases, parenchymal microglia are infected as are multinucleated giant cells when present. While neurons are not themselves directly infected, neuronal damage occurs within the infected CNS. Despite the success of antiretroviral therapy (ART) in limiting virus in plasma to non-detectable levels, neurological deficits persist. This review discusses the continued neurological dysfunctions that persist in the era of ART, focusing on the roles of monocyte and macrophage as targets of continued viral infection and as agents of pathogenesis in what appears to be emergent macrophage-mediated disease resulting from long-term HIV infection of the host. Data discussed include the biology of monocyte/macrophage activation with HIV and SIV infection, traffic of cells into and out of the CNS with infection, macrophage-associated biomarkers of CNS and cardiac disease, the role of antiretroviral therapy on these cells and CNS disease, as well as the need for effective adjunctive therapies targeting monocytes and macrophages.

Project Progress (one paragraph)

Funding Sources (include name of the source, PI and the FULL grant number)

This work was partially supported by National Institute of Health grants, NS082116 Excluded by Request NS040237 Excluded by Request RR000164 and RR021309 Excluded by R

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Loss of Tyrosine-Dependent Trafficking Motif In SIV
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES
PI, with institutional affiliation

Excluded by Requester	A	University of Pennsylvania

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Director

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	C	Comparative Pathology
	A	University of Texas Medical Branch
	A	NIH/Vaccine Research Center
	C	Immunology
	C	Comparative Pathology
	A	Private Source
	A	
	A	
	C	Comparative Pathology

Project Description (limited to one paragraph)

A hallmark of pathogenic SIV and HIV infection is the rapid and near complete depletion of mucosal CD4+ T-lymphocytes from the gastrointestinal tract. Loss of these cells and disruption of epithelial barrier function are associated with microbial translocation, which has been proposed to drive chronic systemic immune activation and disease progression. Here we evaluate in rhesus macaques, a novel attenuated variant of pathogenic SIVmac239, termed ΔGY, which contains a deletion of a Tyr and a proximal Gly from a highly conserved YxxØ trafficking motif in the envelope cytoplasmic tail. Compared to SIVmac239, ΔGY established a comparable acute peak of viremia, but only transiently infected lamina propria and caused little or no acute depletion of mucosal CD4+ T-cells and no detectable microbial translocation. Nonetheless, these animals developed T-cell activation, declining peripheral blood CD4+ T-cells and ultimately progressed with clinical or pathological features of AIDS. ΔGY-infected animals also showed no infection of macrophages or CNS tissues even in late stage disease. Although the ΔGY mutation persisted, novel mutations evolved including the formation of new YxxØ motifs in [Proprietary Info] animals. These findings indicate that disruption of this trafficking motif by the ΔGY mutation leads to a striking alteration in anatomic distribution of virus with sparing of lamina propria and a lack of microbial translocation. Because these animals exhibited wildtype levels of acute viremia and immune activation, our findings indicate that these pathological events are dissociable, and that immune activation unrelated to gut damage can be sufficient for the development of AIDS.

Project Progress (one paragraph)

Funding Sources (include name of the source, PI and the FULL grant number)

This work was supported by National Institutes of Health Grants RR000164 (TNPRC), RO1 AI074362 [Excluded by] AI045008 (UPenn CFAR [Excluded by Re] and T32-RR021309/OD011124 (TNPRC, [Excluded b] and with federal funds from the National Cancer Institute under contract HHSN266200400088C (AAL).

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Effect of cART on Chronic SIV Infection of Chinese Macaques
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with Institutional affiliation

Excluded by Requester C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A
A Private Source

Project Description (limited to one paragraph)

The aim of the project is to use SIV-infected Chinese-origin rhesus macaques as a model to study gut tissue SIV reservoirs in SIV-infected animals receiving suppressive combination antiretroviral therapy in the chronic phase of infection.

Project Progress (one paragraph)

Definitive treatment of HIV infection remains a critical but elusive goal, with persistence of residual virus even in the face of prolonged administration of suppressive combination antiretroviral treatment (cART) providing a source for recrudescent infection if treatment is stopped. Characterization of the residual virus and devising strategies to target it for eradication are key goals in HIV treatment research. Indian rhesus macaques (In-RM) infected with SIVmac have been widely used in such research. However, it has proven challenging to achieve and sustain clinically relevant levels of suppression (<30 vRNA copies/ml plasma) with cART in such models. As ease of viral suppression by cART is related to pretreatment levels of viral replication, and levels of replication of SIVmac239/251 are lower in Chinese rhesus macaques (Ch-RM) than in In-RM, we evaluated cART administration to SIVmac-infected Ch-RM as a potential model for studies of residual virus and eradication strategies. Propri etary I SIVmac239-infected Ch-RM received cART including reverse transcriptase inhibitors PMPA/FTC and integrase inhibitor L-870812 daily for 8 weeks. Plasma viral loads were promptly reduced to <30 copies/ml upon initiation of cART. Cell-associated SIV DNA levels in lymphocytes from the gut were also significantly reduced. Jejunal and colonic CCR5(+)CD4(+) mucosal memory T cells increased significantly; restoration of these cells was associated with reductions in immune activation. In conclusion, cART effectively suppressed viral replication to <30 vRNA copies/ml in SIVmac239-infected Ch-RM, reducing immune activation and restoring mucosal immune cell populations. SIVmac239-infected Ch-RM may be a useful model for studying responses to cART and persistent tissue reservoirs and evaluating candidate eradication strategies to cure HIV infection.

Funding Sources (include name of the source, PI and the FULL grant number)

Research was supported by NIAID R01 AI093307-01A1 Excl uded R01 AI084793 Exclu ded by a Tulane Research Enhancement grant (BL), and the National Center for Research Resources, and the Office of Research Infrastructure Programs (ORIP) of the National Institutes of Health through grant OD011104-51 and in part with federal funds from NCI/NIH contract HHSN261200800001E

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title The Role of Genistein in Actin Dynamics and HIV-infected Resting CD4+ T Cells
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Gorge Manson University
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Gorge Manson University

Project Description (limited to one paragraph)

Binding of HIV to the chemokine coreceptor CXCR4 mediates viral fusion and signal transduction that promotes actin dynamics critical for HIV infection of blood resting CD4 T cells. It has been suggested that this gp120-mediated actin activity resembles the chemotactic actin dynamics mediated by chemokines such as SDF-1. This project is to determine whether inhibiting SDF-1-mediated chemotactic activity can also inhibit HIV infection and to screen inhibitors known to reduce SDF-1-mediated chemotaxis of T cells such as Genistein.

Project Progress (one paragraph)

Genistein, a tyrosine kinase inhibitor, can inhibit both SDF-1-mediated chemotaxis and HIV infection of resting CD4 T cells. Genistein can also interfere with SDF-1- and HIV-mediated actin dynamics in CD4 T cells. This reduction in actin activity correlates with genistein-mediated inhibition of viral DNA accumulation in resting CD4 T cells. The safety of genistein was tested in Pro pri hinese rhesus macaques and each animal was given a monotherapy of genistein at 10 mg/kg orally for 12 weeks. No adverse drug effects were observed in these animals. These results suggest that novel therapeutic strategies can be developed based on targeting cellular proteins involved in HIV-dependent signaling. This approach can interfere with HIV-mediated actin dynamics and inhibit HIV infection.

Funding Sources (include name of the source, PI and the FULL grant number)

This work was supported by NIH Public Health Service Grant grants 1R01AI081568 from NIAID to Excl uded R01 AI093307-01A1from NIAID to Exc the National Center for Research Resources, and the Office of Research Infrastructure Programs (ORIP) of NIH (through grant OD011104-51). The study was supported in part by the Private Source organized by Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Dynamics of Endothelial Cell Signaling
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Comparative Pathology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Director
C Bacteriology & Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Productively infected macrophages in the encephalitic brain express numerous cytokines, including TNF. TNF-alpha receptors are present in the nonencephalitic brain, such that normal brains are primed to respond quickly to low levels of TNF. TNF induces increased chemokine production and secretion by astrocytes, and these chemokines induce monocyte migration preferentially over lymphocytes. Vascular endothelial growth factor (VEGF) promotes proliferation of BMEC, resulting in reorganization of the cytoskeleton and tight junction proteins. This induces a decrease in blood-brain barrier (BBB) integrity, creating a permissive environment for monocyte migration, and also bidirectional leakage of proteins across the BBB. A possible mechanism for the VEGF pathway could be as follows: HIV *tat* binds to the VEGF receptor, followed by the binding of the VEGF receptor to focal adhesion kinase, increases of which have been implicated in BBB disruption. . Other proinflammatory cytokines, including IFN-gamma and IL-6, are upregulated in the encephalitic brain, with far reaching effects on neuroinflammation. The complement pathway is also known to be induced through IFN-gama and IL-6 signaling, resulting in propagation of inflammation in the area surrounding lesions. There are well-characterized neurotoxicity manifestations associated with viral (including HIV) infection, including increased secretion of the neurotoxic IL-6 by glia in response to gp120. Therefore, rapid secretion of high levels of IL-6 by microglia would be anticipated to be a detrimental effect of SIV-infected macrophage infiltration into the brain.

Project Progress (one paragraph)

The blood-brain barrier is disrupted in numerous pathological conditions, oftentimes mediated by cytokines and chemokines.

Funding Sources (include name of the source, PI and the FULL grant number)

R01-MH077544, NIH. PI: Excluded by Requester Focal adhesion kinase in disruption of the blood-brain barrier in encephalitis.
R01-NS048952, NIH. PI: Excluded Lyme Neuroborreliosis Pathogenesis in the Rhesus Monkey

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Intermediate Filament Expression in Astrocytes
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester — C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
- C Regenerative Medicine
- C Veterinary Medicine
- C Director
- C Microbiology
- C Bacteriology & Parasitology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
- A Tulane University
- A Texas A&M

Project Description (limited to one paragraph)

The foot processes of astrocytes cover over 60% of the surface of brain microvascular endothelial cells and play a role in regulating blood brain barrier integrity. Movement of astrocytes in response to a proinflammatory cytokine or even limited retraction of processes could result in leaky junctions between endothelial cells. We are using an in vitro model system to investigate the activation of astrocytes derived from adult macaques to the cytokine TNF-α by four parameters: morphology, intermediate filament expression, adhesion, and cytokine secretion. Astrocytes were stellated following transient acidification; resulting in increased expression of GFAP and vimentin. Stellation was accompanied by decreased adhesion that could be recovered with proinflammatory cytokine treatment. Surprisingly, there was decreased secretion of proinflammatory cytokines by stellated astrocytes compared with polygonal cells. These results suggest that astrocytes are capable of multiple phenotypes depending on the stimulus and the order stimuli are applied.

Project Progress (one paragraph)

We have noted that astrocytes are activated with unique profiles depending on the disease: to date we have published on altered astrocyte morphology in depression, Krabbe disease, Brucellosis and SIV.

Funding Sources (include name of the source, PI and the FULL grant number)

R01-MH077544, NIH. PI: Excluded by Request. Focal adhesion kinase in disruption of the blood-brain barrier in encephalitis.
T32 RR021309/ T32OD011124, NIH. PI: Excluded by Reques Research Training in Experimental Medicine and Pathology.
U54 AI057156, NIH, and (WRCE) Western Regional Center of Excellence for Biodefense and Emerging Infectious Disease Research: Recombinant Antigen-based Assays for Flavivirus Serodiagnosis and Surveillance.

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Cannabinoid Epigenomic and miRNA Mechanisms Impact HIV/SIV Disease Progression
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI with institutional affiliation
Excluded by Requester
C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester
C Director
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A NIH
A LSUHSC, LA

Project Description (limited to one paragraph)

9-THC is the major psychoactive cannabinoid in marijuana. Advanced understanding of its pharmacology and the major cannabinoid receptor subtypes (CB1 and CB2) as well as their localization (CB2 predominantly on B lymphocytes and natural killer cells) has resulted in identification of multisystemic biomedical effects. Particularly important is the potential of 9-THC modulation of immune function in human immunodeficiency virus (HIV) infected individuals. Our studies indicate that chronic 9-THCtreatment attenuates viral load and tissue inflammation in simian immunodeficiency virus (SIV) infected non-human primates, significantly decreasing morbidity and mortality from SIV infection. In addition, 9-THC decreased viral replication *in vitro*. While the ability of cannabinoids to suppress inflammation and viral replication has been reported by others and confirmed by our ongoing studies, the mechanisms involved are not known. Preliminary data revealed increased expression of a distinct miRNA profile associated with decreased immune activation and anti-inflammatory properties (based on predicted targets) in CD4 T lymphocytes, intestinal mucosa, and brain of THC-treated SIV infected animals. Our overall hypothesis is that chronic 9-THC treatment decreases proinflammatory gene expression and viral replication through epigenomic (non-coding RNAs and DNA methylation) mechanisms. To study the effect of chronic THC administration on acute SIV infection, Prop rietar animals were assigned to the following 4 treatment groups: THC only, Vehicle only, THC/SIV and SIV only. Proximal duodenal pinch biopsies, CD4 T cells, monocytes, CSF have been collected before THC administration and at 2, 4 and 8 weeks post SIV infection. miRNA profiling will be performed on duodenal pinch biopsies.

Project Progress (one paragraph)

miRNA profiling on duodenal pinch biopsies collected during acute SIV infection has been completed

Excluded by Requester

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIDA, R01 DA030053-01, PI- Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Molecular Pathology of HIV/SIV Enteropathy
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI. with institutional affiliation

Excluded by Requester — C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C Director
C Comparative Pathology
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

The gastrointestinal (GI) tract is a major target of HIV/SIV infection and CD4+ T cell depletion. The damage to the mucosal immune system is associated with a variety of GI manifestations collectively called AIDS enteropathy; generally characterized by chronic diarrhea, and wasting. Although our understanding of HIV/SIV enteropathy has greatly improved, the recent discovery of microRNAs (miRNAs) has added yet another novel and complex regulator of gene expression with potential roles in the molecular pathogenesis of this disorder. miRNAs are ~21-23 nucleotide noncoding RNAs, highly conserved and suppress gene expression by targeting mRNAs for translational repression or degradation. While miRNA studies are being reported extensively in various types of cancer, and at increasing rates in cardiac, neurological, metabolic and skin diseases, their role in idiopathic GI disorders such as HIV/SIV enteropathy is unknown and yet to be addressed. To better understand the molecular mechanisms underlying GI disease we will analyze global miRNA expression profiles sequentially in the intestine of the same animals prior to and at 21 days, 3, 6 months and necropsy following SIV infection (PI). More importantly we will examine miRNA expression profiles in distinct mucosal components [intraepithelial lymphocytes (IEL), lamina propria lymphocytes, epithelium and fibrovascular stroma] separately to better understand the pathogenesis of HIV/SIV induced GI disease/dysfunction. A total of animals have been assigned to the project and study is currently in progress. Jejunal resections (10 cm long), PBMCs and CSF have been collected before and at 21 and 90 day post SIV infection. Intact jejunal segments were separated into epithelium, lamina propria lymphocytes, IELS and fibrovascular stroma. Total RNA has been extracted from all mucosal compartments and miRNA profiling studies are in progress.

Project Progress (one paragraph)

Submitted

Manuscripts submitted for publication:

Submitted

Funding Sources (Include name of the source, PI and the FULL grant number)

NIH/NIDDK, 1R01DK083929-01A4 , PI-Mohan Mahesh

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development of Glycoprotein K (gK)-deleted HSV-1 Vaccine Protects Mice
Unit/Division Comparative Pathology
Type of Project Research
Percent PS1 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Comparative Pathology
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A Louisiana State University
A Louisiana State University School of Vet. Medicine
A Louisiana State University
A Louisiana State University

Project Description (limited to one paragraph)

Herpes simplex virus type-1(HSV-1) and HSV-2 are important human pathogens that cause significant ocular and urogenital complications, respectively. We have previously shown that HSV-1 virions lacking glycoprotein K (gK) are unable to enter into neurons via synaptic axonal membranes and be transported in either retrograde or anterograde manner. Here, we tested the ability of HSV-1 (F) gK-null to protect against lethal challenge with either highly virulent ocular HSV-1 (McKrae strain), or genital HSV-2 (G strain).

Project Progress (one paragraph)

The gK-null virus vaccine efficiently protected mice against lethal vaginal infection with either HSV-1(McKrae) or HSV-2 (G). Female mice were immunized via a single intramuscular injection with 10^6 PFU of the gK-null virus. Immunized mice were treated with Depo-Provera fourteen days after vaccination and were challenged via the vaginal route one week later. Proprietary Info of mice vaccinated with the gK-null virus survived HSV-1 (McKrae) challenge, while Propr ietary of these mice survived after HSV-2 (G) challenge. Moreover, all vaccinated mice exhibited substantially reduced disease symptoms irrespective of HSV-1 or HSV-2 challenge as compared to the mock vaccinated challenge group. T-cell memory immune responses to specificglycoprotein B (gB) and glycoprotein D (gD) peptide epitopes were detectable at 7 months post vaccination. These results suggest that the highly attenuated, non-neurotropic gK-null virus may be used as an effective vaccine to protect against both virulent HSV-1 and HSV-2 genital infections and induce lasting immune responses.

Funding Sources (include name of the source, PI and the FULL grant number)

COBRE: Center for Experimental Infectious Disease Research – NIH:NIGMS P20GM103458
NIH NIAID AI43000 to Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Dynamics of Cytokine/Chemokine Responses During SIV Infection
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester

C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester

C Director
C Comparative Pathology;
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Understanding cytokine/chemokine networks during acute HIV/SIV infection is important for developing effective vaccines and therapeutics.

Project Progress (one paragraph)

Loss of intestinal CD4+ T-cells was associated with decreased production of several T-helper 1 (TH1) and TH2 cytokines, and increased production of interleukin 17 (IL-17), gamma interferon (IFN-γ), CCL4 and granulocyte-macrophage colony - stimulating factor (GM-CSF) by CD8+ T-cells at 21 days post SIV infection in rhesus macaques. Shifting of mucosal TH1 to TH2 or T-cytotoxic (TC1) to TC2 cytokine profiles was not evident. Additionally, both CD4+ and CD8+ T-cells showed up-regulation of macrophage migration inhibition factor (MIF) and basic fibroblast growth factor (FGF-Basic) cytokines that have been linked to HIV disease progression.

Funding Sources (include name of the source, PI and the FULL grant number)

COBRE: Center for Experimental Infectious Disease Research – NIH:NIGMS P20GM103458
NIH NIAID AI43000 to Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

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2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Anti-HIV Microbicidal Peptides
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A The Scripps Research Institute
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Over 90% of new HIV-1 infections occur as the result of unprotected sex, and women are biologically more vulnerable to HIV-1 infection. This project examines the feasibility and efficacy of new anti-microbial peptides that have been demonstrated to block HIV-1 infection in vitro. In the past few years, we have tested the efficacy of 4 different peptides/compounds for protection from vaginal SHIV transmission, most of which showed no significant level of protection. However, peptide C5a, an amphipathic alpha-helical peptide derived from the hepatitis C virus NS5A anchor domain, has been shown to be virocidal for the hepatitis C virus (HCV) and also shown to have potent antiviral activity against HIV. In macaque challenge models we previously showed that C5a also protects against vaginal SHIV transmission, as 4/5 animals treated with topical vaginal C5a were protected compared to 4/5 controls infected in the same experiment.

Project Progress (one paragraph)

More recently (last year), we tested the ability of C5a to protect against repeated vaginal challenge using a combination of CXCR4 (SHIV-Ku) and a CCR5 (SHIVsf162P3) using viruses simultaneously. Although only Proprie animals completely resisted challenges, there was a significant delay in acquisition of animals pre-treated vaginally with C5a. By week (challenge) 3, only Pro animals treated with C5a was infected compared to 3 placebo controls, and by week 4, only Propri etary I treated animals were infected compared to 4 of 5 controls. We will continue these studies by performing additional challenge studies, and also a safety assessment to see if repeated dosing of C5A alone results in vaginal inflammation.

Funding Sources (include name of the source, PI and the FULL grant number)

R21/R33 AI079782-04 Excluded by Requester Anti-HIV Microbicidal Peptides

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Early Events in Mucosal SIV Pathogenesis
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C Comparative Pathology
C Comparative Pathology
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A NCI Frederick

Project Description (limited to one paragraph)

The early cellular and molecular events, particularly in mucosal tissues of HIV infected patients are poorly understood. We have thus been examining the early immunologic events that occur in SIV infected macaques. Although increased lymphocyte turnover in chronic human immunodeficiency virus and simian immunodeficiency virus (SIV) infection has been reported in blood, there is little information on cell turnover in tissues, particularly in primary SIV infection.

Project Progress (one paragraph)

Here we examined the levels of proliferating T cell subsets in mucosal and peripheral lymphoid tissues of adult macaques throughout SIV infection. To specifically label cells in S-phase division, all animals were inoculated with bromodeoxyuridine 24 hours prior to sampling. In healthy macaques, the highest levels of proliferating CD4(+) and CD8(+) T cells were in blood and, to a lesser extent, in spleen. Substantial percentages of proliferating cells were also found in intestinal tissues, including the jejunum, ileum, and colon, but very few proliferating cells were detected in lymph nodes (axillary and mesenteric). Moreover, essentially all proliferating T cells in uninfected animals coexpressed CD95 and many coexpressed CCR5 in the tissues examined. Confocal microscopy also demonstrated that proliferating cells were substantial viral target cells for SIV infection and viral replication. After acute SIV infection, percentages of proliferating CD4(+) and CD8(+) T cells were significantly higher in tissues of chronically infected macaques and macaques with AIDS than in those of the controls. Surprisingly, however, we found that proliferating CD4(+) T cells were selectively decreased in very early infection (8 to 10 days postinoculation [dpi]). In contrast, levels of proliferating CD8(+) T cells rapidly increased after SIV infection, peaked by 13 to 21 dpi, and thereafter remained significantly higher than those in the controls. Taken together, these findings suggest that SIV selectively infects and destroys dividing, nonspecific CD4(+) T cells in acute infection, resulting in homeostatic changes and perhaps continuing loss of replication capacity to respond to nonspecific and, later, SIV-specific antigens.

Funding Sources (include name of the source, PI and the FULL grant number)

AI084793/AI/NIAID NIH Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Early Events in Vaginal SHIV and SIV Transmission
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation
Excluded by Requester — A Northwestern University

Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester — C Comparative pathology

Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A Duke University
A Northwestern University
A Private Source

Project Description (limited to one paragraph)

Worldwide, the vast majority of HIV-1 cases occur through heterosexual transmission. However, the earliest initial events involved in vaginal transmission are uncertain. In studies originally funded by CHAVI, and using photo-activateable HIV, we found that CD4+ T Cells in the vaginal epithelium were the earliest cells infected, at least by 3 days after mucosal challenge. Now, we are using new single-cycle replication deficient SIVmac viruses with reporter genes that can be detected within hours of exposure.

Project Progress (one paragraph)

In the last year we vaginal exposed over Pro prie animals to photoactivateable viruses and euthanized them 48-72 hours after exposure to track the initial target cells infected. We found that the vaginal mucosa was the major target tissue for first infection, but surprisingly, we also found that the virus reaches and infects ovarian tissue within 2-3 days as well. The vast majority of first cells infected are CD4+ T cells, and infected macrophages cannot be detected at this stage.

Funding Sources (include name of the source, PI and the FULL grant number)

R01 AI094595 Excluded by Reques CHAVI grant U01 AI067854 Excluded by Requester Excluded by Requester,Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Effects of HIV-1 in Male Rhesus Macaque Model
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI with institutional affiliation
Excluded by Requester C Comparative Pathology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Northwestern University, Chicago, IL
A Northwesern University, Chicago, IL
A California National Primate Research Center

Project Description (limited to one paragraph)

The model of HIV sexual transmission in the male genital tract has not been well developed and this has hindered our understanding of how male circumcision protects against HIV infection. Thus, tissues from circumcised and uncircumcised macaques were examined to compare tight junctions and other morphologic and structural components that could explain the protection that seems to be afforded to circumcised men against HIV acquisition. We are also comparing mucosal tissues of female macaques and tissues obtained from surgeries of humans to assess anatomical and molecular similarities between sexes, and primate species.

Project Progress (one paragraph)

Men and women differ in their susceptibility to sexually transmittable infections (STIs) such as human immunodeficiency virus (HIV). However, a paucity of published information regarding the tissue structure of the human genital tract has limited our understanding of these gender differences. We collected cervical, vaginal, and penile tissues from human adult donors. Tissues were prepared with hematoxylin and eosin stains or immunofluorescence labeling of epithelial cell proteins and were analyzed for structural characteristics. Rhesus macaque genital tissues were evaluated to assess the use of this model for HIV/simian immunodeficiency virus transmission events. We found the stratified squamous epithelia of the male and female genital tract shared many similarities and important distinctions. Expression of E-cadherins, desmogleins 1/2, and involucrin was seen in all squamous epithelia, though expression patterns were heterogeneous. Filaggrin and a true cornified layer were markedly absent in female tissues but were clearly seen in all male epithelia. Desmogleins 1/2 were more consistent in the outermost strata of female squamous genital epithelia. Macaque tissues were similar to their respective human tissues. These initial observations highlight how male and female genital epithelia resemble and differ from one another. Further information regarding tissue structural characteristics will help to understand how STIs traverse these barriers to cause infection. This knowledge will be essential in future HIV pathogenesis, transmission, and prevention studies.

Funding Sources (include name of the source, PI and the FULL grant number)

K08HD060451-02/HD/NICHD NIH HHS

R33AI076968/AI/NIAID NIH HHS/

U19 AI076981/AI/NIAID NIH HHS/

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Evaluating Mucosal Immune Responses in the Vagina
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	A	Case Western Reserve University

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	

Project Description (limited to one paragraph)

We are continuing to perform comparative gynecology studies in macaques and women. These studies are comparing the anatomy and immunology of the vaginal tract of humans, rhesus, and pigtail macaques using identical methodology. The data analysis of biopsies from 387 women has now been completed to compare vaginal anatomy including vaginal thickness and keratinization, pH, hormone levels, and by immunohistochemistry for relevant HIV target cells in normal women and different macaque species.

Project Progress (one paragraph)

Here we compared differences in hormone levels and vaginal mucosal thickness and anatomy of RM and PT through different stages of the menstrual cycle. Concentrations of plasma estradiol (E2) and progesterone (P4) were determined weekly, and vaginal biopsies examined at day 0 and 14 of the menstrual cycle. Consistent changes in vaginal epithelial thickness occurred at different stages of the menstrual cycle. In both species, the vaginal epithelium was significantly thicker in the follicular than in luteal phase. Keratinized epithelium was strikingly much more prominent in RM, especially during the luteal phase. Further, the vaginal epithelium was significantly thinner and the P4:E2 ratio was higher in PT during luteal phase than RM. Striking anatomical differences in the vaginal epithelium between rhesus and pigtail macaques combined with differences in P4:E2 ratio support the hypothesis that thinning and less keratinization of the vaginal epithelium may be involved in the greater susceptibility of pigtail macaques to vaginal transmission of SIV or other STD.

ACCEPTED

Funding Sources (include name of the source, PI and the FULL grant number)

NIH U19AI076981 Excluded by Requester PI of U19, Excluded by Requester of Res. Proj. 2)
R01 AI 084793 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Evaluation of Immune Mediators for Protection from SHIV
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester — A Case Western Reserve University

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester — C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Private Source
A
A Case Western Reserve University
A Private Source

Project Description (limited to one paragraph)

These experiments are designed to utilize the rhesus vaginal challenge model to explore the plausibility of two distinct hypotheses regarding the determinants of protection from HIV infection among persons exposed to HIV infection but who have remained uninfected. The first objective is to examine the role of immune quiescence in protection against HIV acquisition. It is plausible to propose that activation state could be a factor that determines relative risk or protection from HIV acquisition. We will therefore attempt to model quiescence using the rhesus vaginal challenge model by pre-treating animals with the cell cycle inhibitor hydroxyurea before vaginal challenge. The second objective is to test the hypothesis that mucosal expression or induction of type 1 interferons may provide protection against HIV acquisition. In these experiments we will test the plausibility of the hypothesis that type 1 interferons may block mucosal transmission of SHIV. Alternatively, it is possible that exposure to type 1 interferons induces a local inflammatory response that might enhance HIV transmission; thus dose ranging experiments are necessary to ascertain if there is an exposure to interferon that will induce antiviral elements without induction of inflammation that will increase infection risks.

Project Progress (one paragraph)

In a series of experiments we have shown that topical bIFN when applied to the vagina repeatedly before SHIV challenge, protects females from vaginal transmission of a CCR5 using SHIV (SHIVsf162P3). Macaques were treated vaginally with bIFN and 4 hrs later, challenged with RT-SHIVsf162Pr. One and 2 days after challenge, bIFN treatments were repeated and this regimen was repeated weekly for 5 weeks to determine if bIFN could protect macaques from infection after repeated challenges. In all [Proprieta] animals pre-treated with bIFN were completely protected from repeated vaginal viral challenge, whereas [Proprietar] animals treated with placebo were infected. These results showed a significant level of protection from challenge ($P<0.02$).

Funding Sources (include name of the source, PI and the FULL grant number)

NIH U19AI076981 [Excluded by Requester] PI of U19, [Excluded by Re] PI of Res. Proj. 2)
R01 AI 084793 [Excluded by Requester]

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Harnessing Antibody-mucus Interactions to Prevent HIV Transmission
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Northwestern University
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A University of Texas Medical Branch

Project Description (limited to one paragraph)

This study is to determine whether antibodies in vaginal secretions can interact with mucus and whether we can harness mucus/antibody interactions to delay the transit of HIV at mucosal sites and possibly prevent vaginal HIV transmission. This interaction could increase the dwell time of virus in mucus and decrease the chances of HIV reaching potential target cells to initiate HIV transmission. We have identified a specific interaction of an IgG glycotype and a vaginal mucus antibody called MUC16, and now will determine if this interaction can facilitate vaccine function. To this end we propose passive transfer experiments in rhesus macaques. These studies will determine the ability of antibodies targeted to MUC16 to provide protection from a vaginal challenge using a multiple low dose model.

Project Progress (one paragraph)

We are currently collecting vaginal mucus and female reproductive tissues of macaques and have confirmed that the MUC16 antibody discovered in humans has a counterpart in macaques, and that macaque mucus antibodies bind anti-HIV antibodies. In the coming year, we will generate purified MUC16 antibodies for passive infusion experiments in macaques to show that these are secreted in vaginal tissues and protect against pathogenic vaginal SHIV challenge.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester Private Source

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Intersubtype Recombinants for Polyvalent Anti-HIV vaccine
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Case Western Reserve University
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Case Western Reserve University, Cleveland, OH
A Case Western Reserve University, Cleveland, OH

Project Description (limited to one paragraph)

Producing an effective HIV vaccine remains difficult, largely due to the tremendous diversity of HIV strains in the population. Further, it is now known that essentially all strains of HIV-1 that are transmitted sexually (across mucosal surfaces such as vagina, rectum, or orally) use CCR5 to enter cells and infect hosts. Only very late in the course of disease do patients begin to harbor viruses that use CXCR4 or other co-receptors. In addition, worldwide (especially Africa and Asia), the vast majority of HIV-1 sexual transmissions occur due to infection with clade C viruses, whereas in the USA clade B viruses predominate. However there are few CCR5 using SHIVs and only one known clade C SHIV available to test vaccine candidates in nonhuman primate research. Therefore the objective of this work is to test new clade C, CCR5 using SHIVs that will be created by Excluded by Requester at Case Western Reserve in rhesus macaques here at the TNPRC for mucosal transmissibility and their ability to replicate in macaques.

Project Progress (one paragraph)

In the last year, we have tested over 100 different SHIVs in macaques, and only a few clade B derived env SHIVs showed sustained replication in plasma. However, we have found that these viruses induce immune responses and are currently testing the immunogenicity of a combined env antigen approach for a vaccine strategy. Propriet Info animals have been currently vaccinated with various clade A-E envelope SHIV strains and we are preparing for a challenge study this year to see if these viruses conferred protection.

Funding Sources (include name of the source, PI and the FULL grant number)

R01 AI084816 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Modeling HIV-1 Primary Transmission
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Comparative Pathology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A The Scripps Research Institute, LaJolla, CA
A Private Source

Project Description (limited to one paragraph)

We are working to determine why only certain HIV strains are selectively transmitted across mucosal barriers. Transmission of HIV-1 is a rare event that involves extreme, non-random selection of as few as one founder genotype out of as many as 100 million genotypes in the infected donor. The goal of this research proposal is to understand why transmission is so selective, and what biological properties define the rare, highly transmissible virus. The research proposal has two specific aims. The first is to model HIV transmission *in vitro* using transwell cultures where virus must cross an intact epithelial barrier to reach target cells. The hypothesis is that a highly transmissible virus must be able to both cross the epithelial cell barrier efficiently and infect the first available target cell efficiently, and that these two properties can be modeled *in vitro* to distinguish readily transmissible viruses from poorly transmissible viruses.

Project Progress (one paragraph)

To date, we have made substantial progress in refining SHIV mucosal challenges in macaques, and have completed a series of challenge experiments using new RT-SHIVs, and have worked out protocols for successful mucosal challenges with these viruses. We have also completed a series of studies with other investigators at Case Western who have attempted to generate infectious clade C and D SHIVs, and have tested several prototype SHIVs that replicate in cell culture, but to date, these have not proven to be infectious in macaques. Only the clade B viruses have been able to replicate in macaques, so the current proposal remains timely, and of the highest significance for developing clinically relevant SHIVs in places where the epidemic is spreading the fastest. In the coming year, we plan to test mucosal transmissibility of clade C SHIVs in macaques as provided by the Excluded by Reque lab. We will perform complete clinical, immunologic, and virologic assessments of these viruses in macaques for direct comparison with other clade B SHIVs currently in use in our lab.

Funding Sources (include name of the source, PI and the FULL grant number)

R01 AI094561 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Role of Antibodies In Protection from SHIV
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI with institutional affiliation
Excluded by Requester C Comparative Pathology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A Excluded by Requester
A
A
A Duke University School of Medicine
A Excluded by Requester
A

Project Description (limited to one paragraph)

Neutralizing antibodies may have critical importance in immunity against human immunodeficiency virus type 1 (HIV-1) infection. However, the amount of protective antibody needed at mucosal surfaces has not been fully established. We have worked with the mucosal immunology team of CHAVI since its inception, and here, we evaluated systemic and mucosal pharmacokinetics (PK) and pharmacodynamics (PD) of 2F5 IgG and 2F5 Fab fragments with respect to protection against vaginal challenge with simian-human immunodeficiency virus-BaL in macaques.

Project Progress (one paragraph)

Macaques were intravenously administered varying doses of 2F5 mAb and challenged with SHIV 12 hrs later. Antibody assessment demonstrated that 2F5 IgG was more potent than polymeric forms (IgM and IgA) across a range of cellular and tissue models. Vaginal challenge studies demonstrated a dose-dependent protection for 2F5 IgG and no protection with 2F5 Fab despite higher vaginal Fab levels at the time of challenge. Animals receiving 50 or 25 mg/kg of body weight 2F5 IgG were completely protected, while Propr ietar animals receiving 5 mg/kg were protected. In the control animals, infection was established by a minimum of 1 to 4 transmitted/founder (T/F) variants, similar to natural human infection by this mucosal route; in the Propri letary I nfected animals that had received 5 mg 2F5 IgG, infection was established by a single T/F variant. Serum levels of 2F5 IgG were more predictive of sterilizing protection than measured vaginal levels. Fc-mediated antiviral activity did not appear to influence infection of primary target cells in cervical explants. However, PK studies highlighted the importance of the Fc portion in tissue biodistribution. Data presented in this study may be important in modeling serum levels of neutralizing antibodies that need to be achieved by either vaccination or passive infusion to prevent mucosal acquisition of HIV-1 infection in humans.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH U01 AI067854 Excluded by Requester
R01 AI094595 Excluded

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Standardization of Flow Cytometry for Intestinal Cells
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI. with institutional affiliation

Excluded by Requester C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A New England Primate Research Center
A NIH/NIAID
A UCLA, Los Angeles, CA
A University of Pittsburgh
A Fred Hutchinson Cancer Research Center

Project Description (limited to one paragraph)

Gut associated lymphoid tissue (GALT) plays a critical role in both the acquisition and pathogenesis of human HIV-1 infection and SIV/SHIV infections in non-human primates (NHP). Characterization and quantification of GALT in both humans and NHP has provided important insights into both the early and late immunological manifestations of these infections. Increasingly, analysis of GALT will be important in the characterization of virological reservoirs, eradication strategies, and the response to preventive and therapeutic HIV/SIV vaccines. Flow cytometry provides a powerful and versatile tool to characterize cell phenotype within GALT. To maximize the impact of these technologies, it will be important to develop standardized approaches for the collection, processing, staining, and analysis of GALT to facilitate multicentre study site processing as well as comparing data between trial sites.

Project Progress (one paragraph)

We are currently performing characterizations of human and NHP GALT flow cytometric data to determine the similarities and/or significant biological differences in health as well as following HIV/SIV infection in humans and macaques. The purpose of this project is to compare GALT T cell phenotypes in both species, and between labs, under the auspices of the HVTN Mucosal Immunology (MIG) Program. To date we have collected tissues from 10 macaques at the TNPRC and viably froze intestinal and blood cells for high speed cell sorting and analysis. We are also comparatively analyzing the data in 3 nonhuman primate and two human labs. Excluded by Requester,Private is simultaneously assessing CD4+ T cell subsets, and Excluded by Requester (NIH) is assessing B cell subsets, which we will compare with data from human clinical trials conducted by Excluded by Requester

Funding Sources (include name of the source, PI and the FULL grant number)

U01 A 1068618 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Testing Maraviroc as a Microbicide
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester — A Cornell University

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester — C Comparative Pathology
C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester — A Cornell University
A Private Source
A

Project Description (limited to one paragraph)

The development of topically applied microbicide formulations able to reduce the incidence of sexually acquired HIV-1 infection remains a priority within the prevention science field. This study measured and compared the pharmacokinetics of CMPD167, a small molecule antiretroviral CCR5 inhibitor with potential as an HIV microbicide, following vaginal, rectal and oral administration in rhesus macaques.

Project Progress (one paragraph)

A vaginal hydroxyethylcellulose (HEC) gel, a rectal HEC gel, a silicone elastomer matrix-type vaginal ring and an oral solution, each containing CMPD167, were prepared and administered to rhesus macaques pretreated with Depo-Provera. CMPD167 concentrations in vaginal fluid, vaginal tissue (ring only), rectal fluid and blood plasma were quantified by HPLC–mass spectrometry. CMPD167 concentrations measured in rectal fluid, vaginal fluid and blood plasma were highly dependent on both the route of administration and the formulation type. Although rectal and vaginal fluid concentrations were highest when CMPD167 was administered locally (via either gel or ring), lower concentrations of the drug were also measured in these compartments following administration at the remote mucosal site or orally. CMPD167 levels in the vaginal and rectal fluid following oral administration were relatively low compared with local administration.

Funding Sources (include name of the source, PI and the FULL grant number)

R01 AI041420 (Moore, PI)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
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Project Title The Effects of Alcohol on SIV Pathogenesis
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Louisiana State University Health Sciences Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Louisiana State University Health Sciences Center
A Louisiana State University Health Sciences Center

Project Description (limited to one paragraph)

There is clearly an association between HIV infection and alcohol use. However, determining whether alcohol intake results in physiologic or immunologic conditions that increase the risk or susceptibility to infection rather than simply resulting in persons engaging in riskier behavior cannot be easily deciphered in humans. Thus, we are using the rhesus macaque model of alcohol use to assess the effects of alcohol on the systemic and mucosal immune system. We previously showed that viral loads and progression to disease were higher in SIV-infected macaques receiving alcohol. We have initiated a series of anti-retroviral therapy (ART) studies to see if alcohol affects the efficacy of ART or the rate of CD4+ T cell restoration.

Project Progress (one paragraph)

Animals receiving alcohol have significantly higher rates of intestinal CD4+ T cell turnover, suggesting that the reason animals have higher viremia is that their viral target cells (memory CD4+ T cells) are turning over at an accelerated rate. We now hypothesize alcohol use results in increased basal levels of CD4+ T cell turnover specifically in the intestine, resulting in increased numbers of viral target cells in the gut, as well as an accelerated rate of new CD4+ T cell production for continual viral infection, resulting in higher peak, and sustained viral loads in SIV infected animals. Since CD4+ T cells are turning over at an accelerated rate, and the numbers of times CD4+ memory cells can divide is finite, such a sustained, increased rate of turnover results in more rapid exhaustion of the CD4+ T cell precursor pool, leading to accelerated progression and AIDS. This unifying theory may open the door to new treatment strategies for patients who drink alcohol.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAAA P50 AA09803 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
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Project Title Immunologic Events in the Liver in SIV Infection
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C Bacteriology and Parasitology
C Comparative Pathology
C Comparative Pathology
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Case Western Reserve University
A NCI Fredrick

Project Description (limited to one paragraph)

The early cellular and molecular events, particularly in mucosal tissues of HIV infected patients are poorly understood. We have thus been examining the early immunologic events that occur in SIV infected macaques. Since the liver drains antigens from the intestinal tract, and since the intestinal tract is a major site of viral replication, we examined the dynamics of liver macrophages (Kupffer cells) throughout SIV infection including animals in acute and chronic infection to assess target cells in liver tissues.

Project Progress (one paragraph)

Absolute numbers of Kupffer cells increased in the livers in acute infection, and in animals with AIDS. Significantly higher percentages of proliferating (BrdU+) Kupffer cells were detected in acute infection and in AIDS with similar trends in blood monocytes. Significantly higher percentages of apoptotic (AC3+) Kupffer cells were also found in acute and AIDS stages. However, productively infected cells were not detected in liver of Propriet animals examined, despite abundant infected cells in gut and lymph nodes of all animals. Increased rates of Kupffer cell proliferation resulting in an increase in Kupffer cells without productive infection indicate SIV infection affects Kupffer cells, but the liver does not appear to be a major site of productive viral replication.

Funding Sources (include name of the source, PI and the FULL grant number)

R01 AI084793/AI/NIAID NIH Excluded by Requester U19 AI076981/AI/NIAID NIH Excluded by Requester T32-RR021309/OD011124 Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Vaccines to Prevent HSV-2 Transmission
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester — C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester — A Private Source
A
A Louisiana State University School of Vet. Medicine

Project Description (limited to one paragraph)

Human herpes simplex viruses types 1 and 2 (HSV-1 and HSV-2) are serious mucosal diseases, affecting the oro-facial and genital areas, respectively. HSV-1 is the leading cause of infectious blindness in the United States, and HSV-2 (genital herpes) is increasingly recognized as a major predisposing factor to acquiring HIV infection. The major objective of these studies are to determine whether infection with an attenuated, non-pathogenic, yet replication competent HSV-1 mutant (in collaboration with Excluded by Requester and/or vaccination with HSV-1 peptides (in collaboration with Dr. Excluded by Requester can confer protection against vaginal challenge and infection with virulent HSV-2, in a highly relevant nonhuman primate model.

Project Progress (one paragraph)

We have two pilot projects to test new vaccines for their efficacy in protecting against vaginal HSV-2 transmission. Dr. Friedman has supplied novel peptide subunit vaccines containing three purified HSV-2 envelop glycoproteins; glycoprotein D, glycoprotein C and glycoprotein E. These proteins were created by baculo-virus expression systems and were delivered to Prop rieta animals mixed with the adjuvants Alum and CpG. The Propr ietary control animals received only the adjuvants Alum and CpG alone. Pro priet animals were bled for cellular and humoral immune responses after each vaccine, and showed good levels of anti-HSV antibodies. We are currently assessing the binding levels of these antibodies and which will determine whether we vaccinate again or vaginally challenge them with HSV-2.

Funding Sources (include name of the source, PI and the FULL grant number)

U Penn CFAR Pilot grant 5P30 AI045008-15
LSU COBRE Pilot grant 8P20 GM 103458-10

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development of the Neonatal Mucosal Immune System in Nonhuman Primates
Unit/Division Comparative Pathology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI. with institutional affiliation

Excluded by Requester — C Comparative Pathology
C Comparative Pathology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester — C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Neonates are more susceptible than adults to a variety of infectious diseases including bacterial, viral, and fungal infections. Further, neonates have inferior responses to vaccination compared to older children and adults. Although this has been attributed to "immaturity" of the immune system, our prior studies in neonatal macaques suggest that the primate mucosal immune system may be much more competent than the systemic immune system at birth. However, little is known regarding the development of cellular and humoral immune responses in humans or nonhuman primates. Moreover, the innate immune system, a critical component of defense in neonates, is largely unexplored. This study will track and compare the development, function, and responses of the systemic and mucosal immune systems in the developing nonhuman primate, and it will be helpful to determine if mucosal routes of vaccination may result in improved vaccine responses of children, particularly newborns, which could have profound significance for human pediatric vaccination.

Project Progress (one paragraph)

We collected a complete set of tissues from a total [Proprietary] infants neonates, which were; 1) preserved in formalin for routine histology, immunohistochemistry and morphometric analysis; 2) snap frozen in liquid nitrogen for immunohistochemistry and archival use, and; 3) segments of jejunum, ileum, colon and portions of thymus, spleen, axillary, inguinal, and mesenteric lymph nodes were collected in media and immediately transported to the lab for processing of cell suspensions and flow cytometry. We are currently comparing the composition of B cells and Tregs from various tissues and their changes with age.

Funding Sources (include name of the source, PI and the FULL grant number)

NIAID/NIH, Excluded by Requester 1R01AI099795

DIVISION OF IMMUNOLOGY

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Development, Differentiation and Kinetics of Blood Monocytes and DCs in Macaques
Unit/Division Immunology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES
PI, with institutional affiliation

Excluded by Requester

C Immunology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester

C MICROBIOLOGY
C DIRECTOR

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

IH
A University of Oklahoma Health Sciences Center

Private Source

Project Description (limited to one paragraph)

Rhesus macaques are used to study immune responses to human infections, so it is important to fully characterize the similarities and differences between cells of the immune system in nonhuman primates and humans. The purpose of this study was to compare the immunophenotype of monocytes and dendritic cells (DC) between rhesus macaques and humans based on the nomenclature of human monocytes and DC. In addition, *in vivo* BrdU pulse/chase experiments were used to determine the turnover rate and development of each of the monocyte and DC subsets identified in macaques.

Project Progress (one paragraph)

We confirmed that the three subsets of monocytes, CD14+CD16-, CD14+CD16+, and CD14-CD16+ corresponding to classical, intermediate, and nonclassical monocytes, respectively, and the two subsets of DC, CD1c+ mDC and CD123+ pDC identified in humans, also exist in rhesus blood. A macaque-equivalent CD141+ mDC, however, was not identified because the anti-human CD141 antibody did not cross-react to rhesus cells. Our data suggest that the CD14, CD16, CD1c and CD123 negative cell fraction may include the CD141+ mDC. Although CD11c is widely used as an mDC marker for NHP, it was also expressed on intermediate and nonclassical monocytes in the NHP analyzed here. *In vivo* BrdU labeling indicated that the CD14-CD16+ fraction (previously identified as CD11c+ mDC in macaques) was derived as a monocyte subset clearly distinct from mDCs (CD1c+ DC). BrdU uptake first appeared in the CD14+CD16- monocytes, then in CD14+CD16+ cells, and finally in CD14-CD16+ cells indicating that this population reflects monocytes at different stages of maturation. The kinetics of CD1c+ mDC and CD123+ pDC were distinct from monocyte subsets. ***Conclusions:*** These results indicate that non-classical monocytes differentiate from CD14+CD16- (classical monocytes) by gradually expressing CD16+ to become CD16+CD14+ cells (intermediate monocytes) that subsequently mature in to the non-classical CD14-CD16+ cell subset through a gradual decrease in CD14 expression while circulating in blood. The kinetics of CD1c+ mDC and CD123+ pDC differentiation are distinct from that of the monocyte subsets indicating differences in their myeloid cell origins. This study sets the foundation to study the role of each subset of myeloid cells in AIDS disease pathogenesis using the NHP model.

Funding Sources (include name of the source, PI and the FULL grant number)

NIAID-AI097059 (Excluded by Requester) NIAID-AI087302 (PI: Excluded by Re) and NIAID-AI091501 (Excluded by Requester)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Flow Cytometry Core Laboratory
Unit/Division Immunology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES

PI, with institutional affiliation

Excluded by Requester — C Immunology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester

C COMPARATIVE PATHOLOGY
C VETERINARY MEDICINE
C VETERINARY MEDICINE
C REGENERATIVE MEDICINE
C BACTERIOLOGY & PARASITOLOGY
C BACTERIOLOGY & PARASITOLOGY
C DIRECTOR
C COMPARATIVE PATHOLOGY
C MICROBIOLOGY
C MICROBIOLOGY
C BACTERIOLOGY & PARASITOLOGY
C COMPARATIVE PATHOLOGY
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C COMPARATIVE PATHOLOGY
C COMPARATIVE PATHOLOGY

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A STATE UNIVERSITY OF NY, NY USA
A Priority Score
A
A A
A
A
A
A Mississippi State University
A UNIVERSITY OF COLORADO HSC, CO USA
A Private Source
A UNIVERSITY OF ALABAMA, AL USA
A Private Source
A
A UNIVERSITY OF TEXAS MEDICAL BRANCH, TX USA
A UNIVERSITY OF TEXAS MEDICAL BRANCH, TX USA

Project Description (limited to one paragraph)

The Flow Cytometry Core Laboratory instrumentation includes Proprietary Info Proprietary Info is a 4-laser platform capable of 15 parameter analysis (13 colors plus forward and side scatter). The Proprietary is a 3 laser cytometer that is capable of 10 parameter analysis (8 colors plus forward and side scatter). It is equipped with a flow sensor that allows for volumetric cell counting and an automated sample loader. The Proprietary is a cell sorter that is also used for 12-color analysis. The sorter can sort 4 subpopulations simultaneously into tubes. Plate sorting is also done. Most of the samples processed are multicolor stains (6 or more colors per tube). The Flow Cytometry Laboratory is responsible for sample acquisition of all flow cytometry samples prepared at Tulane National Primate Research Center. The data is distributed to the investigators via a secure server; investigators are responsible for their own data analysis.

Project Progress (one paragraph)

The Flow Lab performs stains and sample processing for absolute cell counts and viability assays. The analysis of these volumetric assays is performed by the Proprietar and the results are reported to the investigators. Service totals for 2013 for Flow Cytometry are as follows: Proprietary Info Proprietary Info

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

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Project Title Immunology Assay Core Laboratory
Unit/Division Immunology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES

PI, with institutional affiliation

Excluded by Requester — C Immunology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
- C VETERINARY MEDICINE
- C VETERINARY MEDICINE
- C IMMUNOLOGY
- C MICROBIOLOGY
- C VETERINARY MEDICINE
- C MICROBIOLOGY

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
- A University of Colorado
- A Private Source

Project Description (limited to one paragraph)

The Immunology Assay Core provides immunology services to specific research projects of in-house and outside investigators as requested. Current services include sample preparation under standardized procedures for optimal assay analysis, planning and performance of ELISPOT assays, data processing and presentation, intracellular cytokine staining, and preparation of recombinant vaccine viral stocks for use as antigenic stimulants in these assays. Based upon the particular project and collaborator's needs, Proprietary systems as well as the Proprietary systems are used for ELISPOT and/or ELISA assays in conjunction with Proprietary Info for result analysis. The core continues to provide MHC Class I tetramers to investigators. The Immunology Assay Core also provides MHC Typing service to investigators. Currently 10 alleles are available to test Rhesus monkeys for MCH class I and MHC class II genes. Continuing to expand our services, development of multicolor staining includes *in vivo* BrdU injection and staining to monitor the cell turnover of all subsets of cells involved in the immune response. This assay once validated transitions to the Flow Cytometry Core for general use.

Project Progress (one paragraph)

Total numbers for each allele of MHC typing include: A*01= Propr ietary A*02= Prop rieta A*08= Pro prie A*11= Prop rieta B*01 = Prop rieta B*03 = Propr ietary B*04= Prop rieta B*08= Prop rietar B*17= Prop rieta DRB*w201 = Prop rieta for a total of Propri etary I

The total numbers of Multicolor assays include: Multicolor Flow Cytometry Preps= Propri etary I (Number of total fluorochromes processed) and total numbers of NHP injected with BrdU = Prop rieta (Based on body weight measured in kilograms).

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Innate Immunity in Pediatric Macaques Infected with *Mycobacterium Tuberculosis*
Unit/Division Immunology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? NO
PI, with institutional affiliation

Excluded by Requester

C Immunology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester

C COMPARATIVE PATHOLOGY
C IMMUNOLOGY
C MICROBIOLOGY
C COMPARATIVE PATHOLOGY
C VETERINARY MEDICINE
C BACTERIOLOGY AND PARASITOLOGY
C BACTERIOLOGY AND PARASITOLOGY
C MICROBIOLOGY

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Very young children are especially vulnerable to *Mycobacterium tuberculosis* (*Mtb*) infection and present with more rapid and disseminated tuberculosis (TB) than older children and adults. Although this high susceptibility was initially thought to reflect under-developed adaptive and innate immunity, but much remains to be elucidated the specific aspect immunologic immaturity plays in TB susceptibility because there are few infant human studies of *Mtb* infection and no established infant TB animal models.

Project Progress (one paragraph)

To determine if infant rhesus macaques show increased disease susceptibility to *Mtb* infection compared to adult macaques, Proprietary Info rhesus macaques were infected with a low dose of *Mtb*, (CDC-1551) which induces latent or asymptomatic infection to adult macaques, by aerosol. The low dose produced significant disease in infant macaques within Pro weeks after infection manifested by weight loss, mild fever, and moderately increased C-reactive protein levels. This is in contrast to adults where higher doses are required to produce active TB. *Mtb*-infected infant macaques also presented persistently elevated monocyte turnover throughout the experiment. We also observed dramatic extrapulmonary spread of TB to tissues such as liver, kidney, cerebral cortex, meninges, and bone marrow. This is the first observation of an infant TB animal model via natural infection route reflecting characteristics of infant TB in humans such as disseminated and meningeal TB. Thus, the *Mtb*/infant macaque model will be applied to understand the high susceptibility of young children to TB and seek therapeutic approach and effective vaccines for pediatric use.

Funding Sources (include name of the source, PI and the FULL grant number)

LSUHSC COBRE (PI: Excluded by Requester NIAID-AI087302 Excluded by Request and NIAID-AI091501 Excluded by Requester and NHLBI-HL106790 (PI: Excluded by

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Lung Macrophages in Rhesus Macaques
Unit/Division Immunology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES
PI with institutional affiliation

Excluded by Requester C Immunology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C COMPARATIVE PATHOLOGY
C IMMUNOLOGY
C MICROBIOLOGY

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Private Source
A

Project Description (limited to one paragraph)

Alveolar macrophages (AM) obtained by bronchoalveolar lavage (BAL) are commonly used to study lung macrophage-mediated immune responses. Questions remain, however, about whether AM fully represent macrophage function in the lung. This study was performed to determine the role of interstitial macrophages (IM) of lung tissue that may contribute to lung immunity and that are not present in BAL sampling.

Project Progress (one paragraph)

In vivo BrdU injection was performed to evaluate the kinetics and monocyte/tissue macrophage turnover in Indian rhesus macaques (*Macaca mulatta*). Lung macrophage phenotype and cell turnover were analyzed by flow cytometry and immunohistochemistry. AM and IM in lungs of rhesus macaques comprised about Propr ietar of immune response cells in the lung. AM represented a larger proportion of macrophages, approximately Proprieta and exhibited minimal turnover. Conversely, IM exhibited higher turnover rates that were similar to those of blood monocytes during steady state homeostasis. IM also exhibited higher staining for TdT-mediated dUTP nick end labeling (TUNEL), suggesting a continuous transition of blood monocytes replacing IM undergoing apoptosis. Although AM appear static in steady state homeostasis, increased influx of new AM derived from monocytes/IM was observed following BAL. Moreover, *ex vivo* LPS stimulation significantly increased intracellular expression of TNF-α in IM but not in AM. These findings indicate that the longer-lived AM obtained from BAL may not represent the entire pulmonary spectrum of macrophage responses, and shorter-lived IM may function as the critical mucosal macrophage subset in the lung that helps to maintain homeostasis and protect against continuous pathogen exposure from the environment.

Funding Sources (include name of the source, PI and the FULL grant number)

NIAID-AI097059 (Excluded by Requester NIAID-AI087302 Excluded by Requester and NIAID-AI091501 Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Neuropathogenesis of SIV in Macaques
Unit/Division Immunology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? YES
PI. with institutional affiliation
Excluded by Requester C Immunology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Eastern Virginia Medical Center
A Private Source

Project Description (limited to one paragraph)

Undetectable levels of virus in the plasma of HIV infected patients can be achieved on seemingly effective antiretroviral therapy. However, patients that have terminated treatment, either because of intolerance or noncompliance, experience a rapid resurgence of viral burden, underscoring the role of reservoirs where the virus hide and persist. One such cellular reservoir is monocyte/macrophage lineage cells. The currently accepted "Trojan horse" hypothesis of HIV entry into the brain assumes that continuous 'seeding' of the brain by virus-infected monocytes is required to establish and maintain persistent viral infection in the brain. We have turned our attention to identifying viral and cellular mechanisms in the brain that establish HIV persistence through successful infection of perivascular macrophages during acute infection. Therefore, we propose to use a SIV/macaque model of neuroAIDS (rhesus monkeys that are SIV infected with or without CD8 lymphocyte depletion) to study the mechanism of SIV virus reservoir in the CNS.

Project Progress (one paragraph)

Perivascular macrophages (PVM) represent a major cell type infected with HIV or simian immunodeficiency virus (SIV) in primate brains. Treatment targeting these cells may enable therapeutic eradication of HIV from the brain. The identification of unique phenotypic markers for PVM in humans and monkeys is important for the understanding of their biology in HIV infection and may facilitate selective targeting of these cells. In this study, we demonstrate that the mannose receptor CD206 is expressed by PVM but not by parenchymal microglia in the normal brain, and that CD206 expression remains restricted to PVM in the HIV-encephalitic brain. CD206+ cells including multinucleated giant cells were frequently detected within perivascular spaces at the core of small encephalitic lesions. To further confirm the perivascular location and phagocytic capacity of CD206+ cells in the brain, we injected liposome-encapsulated bisphosphonates intracisternally in SIV-infected monkeys to deplete PVM. CD206+ cells were depleted from their perivascular location because they are phagocytic and take up the liposomes. *In vivo* labeling with bromodeoxyuridine in normal uninfected and SIV-infected macaques in combination with CD206 immunostaining revealed a CD206+-to-CD206– shift within pre-existing PVM during SIV infection. These findings identify CD206 as a unique marker of human and macaque PVM, and underscore the utility of this marker in studying the origin, turnover and functions of these cells in AIDS.

Funding Sources (include name of the source, PI and the FULL grant number)

Pilot Subproject (Excluded by Request) NIAID-AI087302 (Excluded by Requester) and NIAID-AI091501 (Excluded by Requester)

DIVISION OF MICROBIOLOGY

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Gastrointestinal Disease In Captive Rhesus Macaques Microsporidiosis Genome Analyses and Diagnostics
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI. with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A US Department of Agriculture
	A Private Source
	A
	A Food and Drug Administration
	A Private Source
	A
	A Oregon State University, OR, USA,
	A Private Source
	A Texas A&M University
	A University of California San Diego
	A Private Source

Project Description (limited to one paragraph)

Obligate intracellular pathogens are ubiquitous, but many questions remain about how they evolved. Microsporidia comprise a large phylum of obligate intracellular eukaryotes that are fungal-related parasites responsible for widespread disease, and here we address questions about microsporidia biology and evolution. We sequenced three microsporidian genomes from two species, *Nematocida parisii* and *Nematocida sp1*, which are natural pathogens of *Caenorhabditis* nematodes and provide model systems for studying microsporidian pathogenesis. We performed deep-sequencing of transcripts from a time course of *N. parisii* infection. Examination of pathogen gene expression revealed compact transcripts and a dramatic takeover of host cells by *Nematocida*. Phylogenomic analysis of the Microsporidia was utilized to refine microsporidian phylogeny and identify evolutionary events of gene loss, acquisition, and modification. In particular, we found that all microsporidia lost the tumor suppressor gene Retinoblastoma, which could accelerate the parasite cell cycle, and microsporidia acquired transporters that could import nucleosides to fuel rapid growth. Also, microsporidian hexokinases gained secretion signal sequences, and in a functional assay these were sufficient to export proteins out of the cell; thus hexokinase may be targeted into the host cell to reprogram it toward biosynthesis. Similar molecular changes appear during formation of cancer cells and may be evolutionary strategies adopted independently by microsporidia to proliferate rapidly within host cells. In addition, analysis of genome polymorphisms revealed evidence for a sexual cycle that may provide genetic diversity to alleviate problems caused by clonal growth. Together these events may explain the emergence and success of these diverse intracellular parasites.

Project Progress (one paragraph)

During the previous year, diagnostic PCR and ITS RNA gene amplicon sequencing were applied for identification of *Encephalitozoon* cuniculi genotype 2 as a cause of microsporidial encephalitis in a horse in Ireland. In addition, *Encephalitozoon hellem* was identified in European goldfinches in a private aviary. These species of microsporidia are

also identified as causes of opportunistic infections in humans and support zoonotic or anthroponotic transmission of microsporidiosis.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Immune Responses to Microsporidia
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) scientist associated with the project

Excluded by Requester C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A George Washington University Medical Center
A Private Source
A Einstein College of Medicine

Project Description (limited to one paragraph)

Microsporidia continue to cause opportunistic enteric and systemic infections in immune-compromised individuals worldwide and also cause persistent infections in otherwise healthy mammalian hosts. Macrophages can be activated during innate and adaptive immune responses to kill intracellular microsporidia yet some organisms escape to continue infection. Earlier studies by others demonstrated that *Encephalitozoon spp.* inhibited apoptosis in non-phagocytic host cells, and the purpose of this study was to determine if microsporidia can also inhibit apoptosis in phagocytic cells such as macrophages.

Project Progress (one paragraph)

THP1-differentiated macrophages infected with live *Encephalitozoon cuniculi* or *Vittaforma corneae* inhibited staurosporine-induced apoptosis three days later as determined by lower levels of TUNEL staining and caspase 3 activity compared with uninfected control macrophages induced with staurosporine. Conversely, THP1 macrophages incubated with dead microsporidia and treated with staurosporine three days later exhibited significantly higher levels of apoptosis than THP1 macrophages treated only with staurosporine. PCR apoptosis pathway micro-array analysis corroborated these bioassay findings. Anti-apoptosis genes including BLC2 and TP53 were significantly up-regulated in macrophages infected with microsporidia for three days while pro-apoptosis genes such as FADD, CASP3, CD40LG, LTA, and several TNF-family genes were up-regulated in the macrophages incubated with dead organisms. Interestingly, the inhibition of apoptosis was more pronounced with *E. cuniculi*, which replicates within parasitophorous vacuoles, than *V. corneae*, which replicates in close association with endoplasmic reticulum in the cytoplasm. These results open the door to consider targeting apoptosis pathways for controlling microsporidia infections.

Funding Sources (include name of the source, PI and the FULL grant number)
IWOP-12 was supported by grants from the National Institutes of Health (R13 AI098295-01A1), Private Source
Private Source

The authors gratefully acknowledge funding from the USA National Institutes of Health (AI37188 to Excluded b RR017386 to Excluded by Requester and RR00164 and AI071778 to Exclu that supported research results reported in this chapter

Work on these pathogens was supported by NIH grants AI 31788, AI093315 and AI093220 Excluded by and OD011104 Excluded by Re

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Pathogen Detection and Quantification Core
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A Private Source
A LSU Health Sciences Center Physiology
A Private Source
A
A
A
A University of Colorado Neurology, HSC, CO
A Private Source
A Tulane University Surgery, LA
A Eastern Virginia Medical School
A LSU Dept. of Gene Therapy, LA
A Private Source
A University of California, Davis, CA
A Private Source
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A University of Pittsburgh, PA,
A Private Source
A Univ of CA/Davis Anthropology, CA
A Private Source
A
A

Project Description (limited to one paragraph)

The mission of the PDQC is to provide diagnostics support for the Specific Pathogen-Free (SPF) nonhuman primate breeding colonies at the TNPRC as well as support to research investigators. All NHP are evaluated at least twice annually as part of the preventive medicine surveillance program and animals transferred to the primate center undergo a 90-day quarantine that requires diagnostics testing. The core was established in 2003 and is comprised of two units. The Diagnostics Unit performs Multiplexed Fluorometric Immunoassay™ (MFIA; Charles River) for SPF4 (+1) diagnostics (SIV, SRV, STLV, B Virus, + measles) on the majority of rhesus macaques at the center and has applied the MFIA-expanded panel testing for SPF9+ diagnostics (the SPF4+ panel viruses and SFV, CMV, RRV, SVV, SV-40, and LCV) for a smaller cohort. T8 diagnostics are available, and multiplex cytokine testing supports research investigators. The Real-Time PCR Unit performs SRV provirus PCR diagnostics for the SPF4 colony, and SFV and RRV PCR will soon be added to the SPF9+ testing capabilities. Quantitative PCR is available for SIV RNA and DNA research studies.

Confirmatory testing is performed by Charles River or the National B Virus Laboratory, and the PDQC participates in a multi-center "challenge panel test" that assesses quality assurance.

Project Progress (one paragraph)

Areas of growth over the previous fiscal year in the PDQC include expanded SPF diagnostics testing and implementation of the Proprietary Info for improved efficiency of qPCR. In addition, the PDQC began banking serum from conventional-colony animals for controls in future challenge panel testing that is conducted among the national primate research centers for quality assurance of diagnostic testing reliability. DNA from all rhesus macaques is also being processed by the PDQC for archiving by members in the Division of Veterinary Medicine for future genome sequencing and ancestry/pedigree testing.

Pathogen Detection and Quantification Core (PDQC)

	Serum processing	TB Primagam	TB STAT-PAK	TB ELISA	MFIA	MIFA-E	MFIA (Investigators)	Bioplex Assay	Bioplex Instr. Only
Diagnostics Unit									
2012-2014	Proprietary Info								
2013-2014 (projected*)									

	SRV	SIV	384-well QuantStudio	open-array QuantStudio
RT-PCR Unit				
2012-2014	Proprietary Info			
2013-2014 (projected*)				

* 2013-2014 fiscal year statistics were projected on the basis of testing performed during the first 6 months of the year.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Antisense Epitopes as Novel Markers of Latently Infected Cells
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Private Source
A University of Alabama School of Medicine

Project Description (limited to one paragraph)

Based on published data on HIV transcription, we hypothesized that during infection of resting CD4 T cells and macrophages, transcription of the antisense strand is maintained, even when transcription of the sense strand is essentially shut down. Further, we hypothesized that these antisense transcripts might be translated and epitopes derived from them might label latently infected cells. We have begun to collect preliminary data to address these hypotheses.

Project Progress (one paragraph)

Preliminary data on this project falls into two categories, *in vitro* and *in vivo*. *In vivo*, we have identified SIV infected macaques and HIV infected patients that mount T cell responses against antisense encoded epitopes, verifying their existence. *In vitro*, we developed a novel RT-PCR assay to specifically identify antisense transcripts. We found that these transcripts are polyadenylated, indicating a potential for translation. Most importantly, we found that these antisense transcripts are enriched in macrophages and non-activated CD4 T cells. We are now developing a quantitative approach to assaying antisense transcripts in these cells. Finally, we are developing an *in vitro* model of SIV latency, which was previously lacking. This will enable us to test our hypothesis.

Funding Sources (include name of the source, PI and the FULL grant number)

The study was funded by the Private Source focused on helping facilitate the discovery of an effective AIDS vaccine. PI: Excluded by Requester

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Functional Consequences of CTL Escape in SIV Nef
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Wisconsin National Primate Research Center
	A	Wisconsin National Primate Research Center

Project Description (limited to one paragraph)

Rare individuals control HIV replication. Understanding how they do this could lead to novel therapeutics and vaccine candidates. Similarly, a small percentage of rhesus macaques control simian immunodeficiency virus (SIV) replication. In both humans and macaques, these individuals are enriched for particular MHC-I alleles, suggesting overlapping mechanisms of viral control. There is one key difference, however. Control of HIV is associated with immune targeting of the Gag protein, while control of SIV is associated with immune targeting of the SIV Nef protein. Here, we sought to understand how some macaques are better able to control SIV via Nef targeting. We hypothesized that immune targeting of Nef leads to evolution of Nef variants with impaired functions. To test this, we study the patterns of T cell targeting of Nef and the subsequent viral evolution in the Nef protein in individuals that express MHC-I alleles associated with control. We then functionally characterize the discovered Nef variants to determine whether they are impaired or not.

Project Progress (one paragraph)

We have found that macaques that express the MHC-I allele Mamu-B*17 target two distinct epitopes in Nef during acute SIV infection. The virus routinely evolves to evade these responses. Using deep sequencing, we identified a set of distinct evolutionary patterns in Nef that result from the T cell targeting. We then engineered the mutations into the SIV virus and assayed their functional profiles. We found that the primary variant arising in one of the epitopes significantly reduced Nef's capacity to downregulate MHC-I molecules, a key function. This rendered infected cells more visible to T cells targeting other epitopes. Variation in the other epitope was more broad and was associated with reduced capacity to downregulate three molecules, ~~CD4, Tetherin and CD28.~~

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title A New Chimeric SIVmac251/SIVmac239 Virus for Vaccines
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester	A	University of Pennsylvania

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology
	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	
	A	
	A	

Project Description (limited to one paragraph)

Simian Immunodeficiency viruses currently used in macaque AIDS pathogenesis and vaccine studies have limitations in sensitivity to neutralizing antibody (Nab), and the innate factor TRIM5a. SIVmac239 is highly resistant to both Nab and TRIM5a. In contrast SIVe660 is moderately sensitive to Nab but moderately susceptible to TRIM5a [in some reports]. We sought to develop a new SIV challenge virus that is moderately susceptible to Nab and highly resistant to TRIM5a, both characteristics of HIV-1.

Project Progress (one paragraph)

The uncloned laboratory strain SIVmac251-CX-1 is moderately sensitive to neutralization when compared to resistant SIVmac239 and highly sensitive TCLA SIVmac251. Using molecularly cloned env-pseudotyped viruses derived from SIVmac251-CX-1, 251env clone 63 was identified as being moderately sensitive to Nab. Our goal was to replace Nab resistant mac239 env with mac251.clone63 env into the TRIM5a resistant SIVmac239 background. Our approach to generate the SIV239.env 251 chimeric virus used yeast homologous recombination to produce env minus pREC-nfl_SIV239_Δenv/URA3. The corresponding SIV251 region (nt6604-nt8765) was then amplified to replace URA3 and generate the pREC_nfl_SIV239_SIV251env vector. To produce infectious virus, the pREC_SIV239_SIV251 was co-transfected with the complementary vector, pREC_SIV239_5'LTRgag/pol into 293T cells, and transfection supernatant was inoculated in CEMx174 cells for virus propagation. In vivo infectivity of the resultant chimera was shown by intravenous inoculation of Propr[illegible] rhesus macaques with 100 TCID50 of SIVmac239.env251. The chimeric virus reached a high plasma virus peak at Pro[illegible] days post-infection and set points by the chimeric virus were within the range of parental virus. Extensive neutralization characterization assays against tier 1 (SIVsmE660/BR-CG7G), tier 1A (TCLA-SIVmac251), tier 2(SIVscE660/BR-CG7v), and tier 2B (SIVmac239CS) stocks typed the novel hybrid as a tier 2 SIV, i.e. moderately susceptible to Nab. This new chimeric virus offers a unique approach to SIV challenge systems that may be more appropriate for vaccine studies requiring a moderately Nab sensitive challenge virus that is resistant to TRIM5a.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester P01 AI071739

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title DNA Vaccine for Induction of Mucosal Immunity
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI with institutional affiliation

Excluded by Requester	A	University of Pennsylvania

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Veterinary Medicine
	C	Director
	C	Microbiology
	C	Comparative Pathology
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	

Project Description (limited to one paragraph)

The hypothesis is that with the inclusion of mucosal chemokines with intramuscular-administered DNA plasmid immunizations, a stronger mucosal immune response will be induced and that this response will correspond to increased efficacy against SIV challenge.

Project Progress (one paragraph)

Proprietary Info female Indian origin Rhesus macaques (Macaca mulatta) were immunized with SIV DNA + Teck chemokine, Flu DNA +/- Meck chemokine or Clostridium difficile (C.Diff) DNA +/- Meck chemokine. Systemic, mucosal and biopsy samples were collected throughout the immunization period to monitor the immune response. Twelve weeks after the last immunization the 8 SIV+Teck animals as well as the Flu – Meck (n=4) and C.Diff – Meck (n=4) were vaginally challenged with SIVsmE660 once a week for up to 8 challenges. All animals were infected. Plasma samples for determination of plasma virus loads were submitted to the TNPRC RT-PCR unit of the TNPRC. Results showed no significant protection over controls.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester P01 AI071739

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Efficacy and Toxicity of CSIC and Retrocyclin in the SIV Vaginal Challenge Model
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A University of Florida
A University of Pittsburgh
A University of Pittsburgh
A Private Source

Project Description (limited to one paragraph)

The overall objective of this study is to evaluate the toxicity and efficacy of two microbicides – an HIV entry inhibitor (RC-101) and an HIV non-nucleoside reverse transcriptase inhibitor (CSIC) separately and in combination against SHIV162p3 and RT-SHIV virus challenge respectively. There are five specific aims to achieve this objective. Aim 1 assessed the vaginal and systemic toxicity of RC-101 and CSIC. Aim 2 will determine the minimal infectious dose of RT-SHIV by the vaginal route. Aims 3 and 4 will determine the efficacy of each microbicide individually and in combination against RT-SHIV challenge.

Project Progress (one paragraph)

The toxicity of the CSIC and RC-101 rings were tested individually as were rings with no drugs which served as controls for the vaginal microbicide-containing rings. With the CSIC rings, a small amount of the drug was observed systemically at two time points in Propr ietar animals. This toxicity study was repeated in Pr op nimals and no evidence of toxicity was found, but systemic absorption was observed. Otherwise, no toxic effects of the drugs within the vaginal vault or systemically were found. We tested Pr op animals to determine the minimum infectious dose of RT-SHIVand SHIV162p3 in the absence of Depo-Provera. *This dose to infect all multiple exposures of 10,000 TCID50 of RT-SHIV and 500 TCId50 of SHIV162p3.* Studies on aim 3 have been done to test the efficacy of RC-101 against a SHIV162p3 challenge. Propr treated animals and Pro pri control are infected after 3 SHIV 162p3 challenges. The 2-drug combination ring was tested in an efficacy experiment against an RT-SHIV vaginal challenge after depo-provera treatment. Although delays in RT-SHIV acquisition were observed, no significant differences were seen between experimental and control groups.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Reques U19 AI082623

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Highly Effective Control of AIDS Virus Challenge in Macaques
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	A	Yale University

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Yale University
	A	NIAID/NIH
	A	NIAID/NIH
	A	Private Source
	A	NIAID/NIH
	A	Private Source
	A	
	A	

Project Description (limited to one paragraph)

Previously, we have shown partial to full sterilizing immunity in Propr ietary male Rhesus macaques (*Macaca mulatta*) vaccinated with VSV/Semliki Forest Virus/SIVsmE660 env/gag and rectally challenged with SIVsmE660. These animals completely resisted viral infection and had plasma virus loads that remained undetectable after in vivo depletion of CD8 cells. These Propr ietar animals received an additional immunization boost using VSV/SIVsmE660 env only and were followed by rectal challenge with SIVsmE660 2 years after the original immunization/virus challenge. All Pro priet animals resisted infection with plasma virus loads below detectable limits.

Project Progress (one paragraph)

To further test this promising vaccine, a new group of Propri etary I Rhesus macaques (Pro pri males and Pro pri emales) was obtained to test three immunizations with VSV vector expressing only the env protein of SIVsmE660. These animals were challenged with SIVsmE660 to determine if the env protein alone is sufficient to provide sterilizing immunity. Systemic and mucosal samples were collected to obtain a better understanding of the immune responses in these animals to immunization and challenge. The animals were then given the same high-dose mucosal challenge used in the previous studies. All vaccinated animals became infected with the challenge virus. While average peak viral loads in animals were slightly lower than seen in previous controls, the viral set-points were not significantly different. These data indicate that Gag, or the combination of Gag and Env antigens in the vaccine are critical for generation of apparent sterilizing immunity to challenge. Additionally we have continued to use the single genome analysis (SGA) technique to characterize the founder viruses from rhesus macaques vaccinated with VSV vaccines and challenged intra-rectally. We compared and contrasted the founder viruses env sequences originating from animals vaccinated with VSV-HA vaccine and from the Propri etary I animals that showed partial protection-with VSV-E660-Gag-Env vaccine. We reported a strong tendency to toward single founder viruses in partially protected groups.

NIH, Excluded by Reque R01 AI045510

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Isolation of a New HIV-2 Group in the US
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Marx, Preston, PhD	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Schieffelin, John, PhD	A	Tulane University SoM
Fair, Joseph, PhD	A	Private Source
Garry, Robert, PhD	A	Tulane University SoM
Kahn, Shiek Humarr	A	Private Source
Moses, Leena, PhD	A	Tulane University SoM
O'Connor, David H, PhD	A	Wisconsin National Primate Research Center
Lauck, Michael, PhD	A	Wisconsin National Primate Research Center

Project Description (limited to one paragraph)

The goal is to assess the risk of emergence of new HIV groups from simian immunodeficiency virus (SIV) – infected persons in Sierra Leone. It is well established that HIV-2 emerged through cross-species transmission of SIV in sooty mangabeys (sm) to humans who were exposed through hunting, preparation of bush meat or household pets. Our hypothesis is that SIVsm human infections have a low intrinsic pathogenicity after direct cross-species transmission from the natural monkey hosts to humans. These primary SIV infections do not spread from person to person at a level sufficient to sustain the emergence of new epidemic groups, comparable to HIV-2 groups A and B. The hypothesis predicts that SIVsm will replicate to significant levels during acute human infections but will be suppressed in the chronic stage.

Project Progress (one paragraph)

There has been one case of HIV-2-F in the United States documented that originated in the area of Sierra Leone that was surveyed. The epidemiology and pathogenesis of HIV-2-F disease in human populations is unknown although compelling phylogenetic data show that it originated from a strain of SIV found in sooty mangabeys in northern Sierra Leone. Data on the prevalence of HIV-2 in human populations are presently lacking as the last survey was made 18 years ago and HIV-2-F may represent an emerging AIDS. To this end we have screened over Propri persons in Northern Sierra Leone for prevalence of HIV-2-F infections. Samples collected will be analyzed for HIV-2 type F DNA sequences. Dried blood spots on cards and RNA-later preserved specimens will be analyzed. A questionnaire was administered to collect demographic information and treatment history in those testing positive. To date we have found the prevalence of HIV in the targeted sample population to be Proprietary Inf Interestingly, when compared to the last published data on HIV-2 in the region in 1997, prevalence has increased by a factor of Pro pri from Proprietary Info of HIV positive persons were newly identified cases. Of those previously testing HIV positive, only Propr ietary were currently on treatment compared to Propr ietary Info ART coverage in HIV positive persons in low and middle-income countries globally.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Exclude d by Reg R01 AI076067

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Modeling the Molecular Evolution of SIV to HIV using Humanized Mice
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Microbiology
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Colorado State University

Project Description (limited to one paragraph)

SIV in West African sooty mangabeys (sm) is well established as the source of HIV-2 human infections. SIV acquisition occurs from SMs through exposure from hunting, preparation of bush meat or household pets. Our hypothesis is that SIVsm human infections have a low intrinsic pathogenicity after direct cross-species transmission from the natural monkey hosts and that serial passage of SIVsm in humans was necessary for the emergence of epidemic forms of HIV-2. We also theorize that serial passage was inadvertently carried out through transfusions and needle reuse in pre-and post-colonial Africa. The goal of the experiments is to establish a new model to test the theory for human serial passage of SIV.

Project Progress (one paragraph)

In collaboration with Excluded by Requester we used the BLT mouse model prepared by co-transplantation of human fetal liver, thymus and hematopoietic stem cells. The mice were inoculated with SIVsm041, a primary SIVsm isolated from its natural host and maintained in sooty mangabey peripheral blood mononuclear cells. The goal is to determine if we could obtain SIVsm041 replication in inoculated BLT mice. SIVsm replication was observed and follow-up experiments involving serial passage are in progress using this novel approach.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by R01 AI076067

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Pathogenesis of Natural SIV and STLV Infections in Humans
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester	C	Director

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology
	C	Microbiology

Other affiliate scientists with Institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	Indiana Univ Center for Bioethics, IN
	A	Private Source
	A	

Project Description (limited to one paragraph)

The overall objective of the project is to assess the risk of emergence of new HIV groups from simian immunodeficiency virus (SIV) – infected persons in The Republic of Congo. It is well established that HIV-1 emerged through cross-species transmission of SIV in chimpanzees (cpz) to humans who were exposed through hunting, preparation of bush meat or household pets. Our hypothesis is that SIVcpz human infections have a low intrinsic pathogenicity after direct cross-species transmission from the natural chimpanzee hosts to humans. These primary SIV infections do not spread from person to person at a level sufficient to sustain the emergence of new epidemic groups, comparable to HIV-1 groups M, O, or HIV-2 groups A and B. The hypothesis predicts that SIVcpz will replicate to significant levels during acute human infections but will be controlled in the chronic stage. The project head in Congo Excluded by coordinated and oversaw a team for collecting blood from HIV reference centers in Brazzaville. Blood was collected and antibody assays to detect SIVcpz and other strains of SIV.

Project Progress (one paragraph)

Results thus far indicate Proprietary Info who may have antibody against SIVcpz-like viruses. This result is being followed up. Positive samples will also employ PCR-based testing and genome sequencing to identify particular strains of SIV. Some testing will be done on sight, but the majority of laboratory work will be done on specimens sent to the USA.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Req R01 AI076067

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Serial Passage of HIV-2F in Pigtail Macaques to Investigate
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) Scientist associated with the project

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Wisconsin National Primate Research Center
A Wisconsin National Primate Research Center

Project Description (limited to one paragraph)

Human immunodeficiency type 2 (HIV-2) emerged from simian immunodeficiency virus (SIVsm) that naturally infects sooty mangabeys in West Africa. While the simian origin of HIV-2 is well established, how the virus adapted to humans is poorly understood. The bulk of HIV-2 morbidity and mortality is caused by 2 strains HIV-2 groups A and B; however new pathogenic groups of HIV-2 continue to emerge (HIV-2F, 2008 and HIV-2H, 2004) underscoring the need for deeper understanding of the mechanisms behind the adaptation of these SIVs to humans. This study aims to test the serial passage theory of HIV emergence and elucidate mechanisms of HIV adaptation to a new host using the newly emerged, pathogenic HIV-2F virus in an *in vivo* pigtail macaque (PTM) model.

Project Progress (one paragraph)

Propri etary pigtail macaque was inoculated with HIV-2F infected tissue culture supernatant followed by serial passage into Propri etary additional PTMs. Blood, lymph node, endoscopy and vaginal wash samples were collected at each passage. An HIV-2F specific quantitative PCR (qPCR) assay was developed (LOQ=1.9 log VC/mL) and used for plasma virus load (PVL) quantification. Proprietar Info PTMs were infected reaching peak plasma virus loads between 6.0 and 7.2 log viral copies/ml. KF25, passage one, cleared the virus by day 42 post inoculation (PI) and remains qPCR negative to day 344 PI. KF26 and KF24, passages two and three, cleared the virus following acute infection by days 42 and 60 respectively. However HIV-2F rebounded in the Proprietary passage animals at days 150 and 120, respectively, and remains sustained between 5.6 and 3.2 log VC/mL indicating serial adaptation. Sequencing the pig-tailed adapted virus is in progress.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Exclude d by Re R01 AI076067

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Virus Characterization, Isolation, and Production Core
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Comparative Pathology
	C	Microbiology
	C	Veterinary Medicine
	C	Bacteriology and Parasitology
	C	Immunology
	C	Director
	C	Comparative Pathology
	C	Comparative Pathology
	C	Microbiology
	C	Comparative Pathology
	C	Comparative Pathology
	C	Microbiology
	C	Microbiology
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Colorado State University
	A	Physiology, LSU Health Sciences Center
	A	University of Pittsburgh
	A	Private Source
	A	
	A	University of Wisconsin
	A	Tulane University
	A	Private Source
	A	
	A	

Project Description (limited to one paragraph)

The purpose of the core is the production and cryopreservation of virus stocks to be used by NIH funded investigators. The core is designed to avoid duplication of effort and cost in the preparation of virus stocks, particularly SIV and SHIV. The viral stocks were all quantified by TCID50 in the appropriate cell line. Thus, the core prevents the unnecessary duplication of effort and expense among investigators at the TNPRC. The core maintains records on the pedigree of all virus stocks.

Project Progress (one paragraph)

In 2012-2014, 77 virus stocks were stored in Liquid Nitrogen and 84 in ultra-low temperature freezers at the TNPRC. An Excel database with details on the frozen stocks was maintained and includes: date frozen, titration date, TCID50, the number of vials of each virus, and the exact storage location. The core supplied 189 vials of different viral stocks in 2012 and 158 vials in 2013. Of these stocks, 197 vials were prepared as a result of specific investigator request. Several stocks of four different viruses were also prepared and/or added to the core in 2013. They include HIV-2F, SIVmac239, SIVmac251, and SIVmac251env/SIVmac239 hybrid.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Prime-boost Vaccination Against *Mycobacterium Tuberculosis*
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Bacteriology and Parasitology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	LSU/Louisiana Vaccine Center

Project Description (limited to one paragraph)

The major goal of this pilot grant is to test the efficacy of a recombinant BCG strain known as the 3d-BCG, which carries three deletions in the anti-oxidative burst and anti-apoptotic functions encoded by virulent mycobacteria. This modified BCG strain is pro-apoptotic and is unable to withstand host oxidative burst, thus showing better clearance in animal models. As expected, a high-degree of protection is observed in murine TB model, when vaccinated with 3d-BCG, relative to BCG. We will test 3d-BCG in the NHP model of TB at the TNPRC. As a follow-up we will study if boosting the immune response generated by 3d-BCG with pox-virus expressing specific mycobacterial antigens will enhance protection.

Project Progress (one paragraph)

Propri etary I animals were vaccinated with 3d-BCG and Prop rietar of these were boosted while the Proprietary Info were not. Boost was performed six weeks post vaccination. At 12 weeks post vaccination all Propr animals were challenged with a highly lethal dose of Mtb, one which in a comparable experiment resulted in the rapid death of a Proprie tary Inf of all animals within six weeks. We found that all of the vaccinated animals were protected from lethal challenge and exhibited latent TB infection. We were unable to discriminate between the vaccinated/non-boost and vaccinated/boost groups due to small sample size. Antigen-specific immune response measurements are currently being conducted.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester Private Source

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
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Project Title Host-targeted Interventions of Category A, B and C Bunyaviruses
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Microbiology
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Our project focuses on medically important Category A, B, and C bunyaviruses that cause hemorrhagic fever, cardiopulmonary manifestations, and encephalitis in humans. Most bunyaviruses are arboviruses with a life cycle involving replication in warm-blooded vertebrate species and arthropod vectors in nature. Species central to this project include Crimean Congo Hemorrhagic fever virus (CCHFV), Rift Valley fever virus (RVFV), and Sin nombre virus (SNV). These viruses are emerging zoonotic viruses that threaten human populations due to changing geographic and environmental interaction between human and natural reservoirs harboring these viruses. The goals of the project are to identify cellular target gene(s) from a restricted starting set of candidate cytoplasmic host factors that may be required for bunyavirus replication.

Project Progress (one paragraph)

We used a variety of techniques to examine the interaction of SNV and RVFV with intracellular pathways including confocal microscopy, immuno-precipitation, and quantitative PCR. We used U133 Affymetrix microarrays to identify human cellular genes that are up- or down-regulated in response to infection by SNV, CCHFV, and RVFV. Using a large variety of complementary molecular approaches we determined that the replication of these viruses involves engagement with cytoplasmic RNA metabolism pathways. We carried out knockdown of genes in these pathways using RNA silencing to identify genes necessary for efficient virus replication. We identified three candidate human genes, DDX60L, eIF4E-BP2, and LSM14A,that appear to be required for efficient bunyavirus replication. We are testing the hypothesis that these genes are required for viral transcription and/or genome replication. It is significant that these genes and their products are potential targets for "broad spectrum" anti-viral molecules. Consequently, we plan to carry out small molecule screening to identify molecules that may transiently inhibit these cellular factors.

Funding Sources (include name of the source, PI and the FULL grant number)

WRCE, Excluded by 5U54AI057156-09

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Platform for Defining the Host Response to RNA Virus Infection
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI. with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Los Alamos National Laboratories
	A	University of Texas Medical Branch

Project Description (limited to one paragraph)

The Bunyaviridae is the largest family of RNA viruses, containing more than 350 named isolates. Key members of the family constitute a set of problematic virulent zoonotic viruses. These are human pathogens that cause encephalitis, hemorrhagic fever, or cardiopulmonary disease. Work in our lab includes Crimean Congo Hemorrhagic fever virus (CCHFV), Rift Valley fever virus (RVFV), Sin Nombre virus (SNV), and La Crosse virus (LACV), which are four medically important, diverse, Category A, B, and C Agents members of the nairo-, phlebo-, hanta- and orthobunyavirus genera of the family, respectively. The goal of this project is to identify key cellular genes and functional pathways that are significantly up- or down-regulated following infection by bunyaviruses that can be used for the construction of multiplexed platform that defines the human and macaque cellular response to bunyavirus infection.

Project Progress (one paragraph)

We used U133 Affymetrix chips and transcriptome analysis to define constellations of host genes, pathways, and networks up and down regulated by these bunyaviruses. Relevant host cells were infected with CCHFV, SNV, or RVFV at an MOI = 0.1, and RNA was isolated and analyzed at various time points after infection. Expression of individual cellular genes was then ranked by fold-difference relative to uninfected control samples for each of the three viruses following conservative baseline normalization. The data indicate that a majority of up- and down-regulated genes were similarly affected by all three viruses. As might be expected, many of the genes in this set are dedicated to antiviral/antimicrobial response and inflammation, while the role of others in response to bunyavirus infection is less clear. However, we identified 27 genes that appear to be uniquely responsive (or uniquely unresponsive) to individual viruses. We are using these latter genes to construct a panel for quantifying the expression of key cellular genes and generating virus-specific response signatures. We are constructing parallel platforms to assess both human and macaque cellular response.

Funding Sources (include name of the source, PI and the FULL grant number)

NIAID, Excluded by Requester Ph.D., RO1-AI074011

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title An Antibody Immunoprotectant for Category B Toxins
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI with institutional affiliation
Excluded by Requester A Mapp Biopharmaceutical
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester Wadsworth Center
A Iowa State University
A University of California, Davis
A Mapp Biopharmaceutical

Project Description (limited to one paragraph)

The potential for intentional dissemination of naturally occurring infectious and toxic agents adds a serious new dimension to the threats traditionally posed by these agents. These bioterrorism threats have greatly increased our sense of urgency for developing defenses against Select Agent toxins. The Category B toxins, which consist of *Clostridium perfringens* epsilon toxin (ETX), ricin, and staphylococcal enterotoxin B (SEB), are all extraordinarily potent, and are derived from common, readily-accessible plants (ricin) and bacteria (SEB and ETX). These toxins are relatively easily produced, and can be delivered in a stable aerosol form. There are currently no preventatives or therapeutics for exposure to these toxins. We have identified monoclonal antibodies (mAbs) that individually protect against lethal ETX, ricin, and SEB challenge in animal models. The goal of this project is development of a broad-spectrum antibody cocktail against the Category B toxins (CBT-ab), manufactured in a rapid and cost-effective plant system, for prevention and post-exposure treatment of intoxication. The synergistic effect of pursuing a single product (the mAbs will be manufactured individually and then combined into the final product) against these three toxins will manifest as savings in costs and time.

Project Progress (one paragraph)

The individual mAbs identified for each toxin are currently being tested individually to determine the dose response and therapeutic window using the ETX, ricin, and SEB mouse models available. Studies with mice receiving treatment prophylactically and therapeutically were initially used as a screening system prior to nonhuman primate studies. Thereafter, the antibody selected for SEB was further evaluated in a nonhuman primate aerosol model of SEB intoxication for mitigation of the health effects caused by the toxin. An initial pharmacokinetic profile indicated plasma levels peaked at approximately 30 minutes after injection. Thereafter, the mAb was administered approximately 2 hours after animals were exposed to three times the 50% lethal dose of purified SEB by small particle aerosol. Results showed that animals were completely protected (100% survival) from SEB-induced lethality. The treatment group appeared to experience a lower rate of clinical/enteric effects than unprotected animals.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID, Excluded by Request R01 AI098774

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development of Ricin Antitoxin for Treatment
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	

Project Description (limited to one paragraph)

Ricin is one of the most potent biological toxins known, and is classified by the CDC as a category B blothreat. Much attention has been recently focused on the potential threat of actual ricin use. Ricin toxin is a lectin derived from the beans of the castor plant; in its purified form it is a powerful toxin that can cause significant health effects upon exposure. When aerosolized, ricin is exquisitely toxic, can cause death at very low doses, and is subsequently considered a biological threat agent. An antitoxin, which is an ovine-derived affinity-purified Fab^2 prime, has been developed as a potential antidote to ricin inhalation. The antitoxin has shown to be effective against ricin intoxication in preliminary mouse studies. This research project assesses the therapeutic potential of this particular ricin antitoxin in the nonhuman primate model of aerosol intoxication.

Project Progress (one paragraph)

Preliminary efficacy 'sighting' studies of ovine F(ab')2 α-ricin antitoxin were conducted in the rhesus macaque model of inhalational ricin intoxication. These dose ranging studies and therapeutic window were performed for the purpose of design of a definitive efficacy study. Using small groups of animals (n=2 or 3) a single dose of antitoxin (range of dose 26.8-107.2 mg/kg) was administered via the intravenous route to each animal. A range of time intervals between exposure to ricin and the administration of the antitoxin was investigated (actual range 0-16 hours post-exposure). A target lethal dose of inhaled ricin (3x LD50; 17.4 μg/kg) was used as the challenge for all animals in the experiments. A dose of 53 mg/kg antitoxin protected animals (n=2) from death when administered at 0 hours post-exposure although some resolving pathology was evident at necropsy on day 90. When treatment was delayed to 12 hours post exposure protection at this dose (53 mg/kg) was only partial with 1 out of 2 animals surviving. A higher dose of antitoxin was required (107 mg/kg) to protect all animals in the group (n=3) from death when administered 12 hours post toxin exposure. These animals showed signs of resolving pathology on necropsy. Only partial protection (1/2 animals surviving) was shown at the highest dose of antitoxin (107 mg/kg) when administered at 16 hours post-exposure. The limit of the therapeutic window of protection using the highest dose of antitoxin (107 mg/kg) was 12 hours post-exposure based upon these limited data.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester,Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Evaluation of Live Attenuated Brucella Vaccines in NHP
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI. with institutional affiliation

Excluded by Requester	A	Texas A&M University

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	InCell Corporation
	A	Texas A&M University

Project Description (limited to one paragraph)

Brucella melitensis is a bacterial pathogen that causes the severe disease brucellosis in many types of wild and agricultural animals. The bacterium transfers effectively to humans that come into contact with diseased animals through a number of routes of entry (ingestion, inhalation, etc.). *B. melitensis* is also considered as a bacterium that could be used for nefarious purposes as a weapon to deliberately infect people. A new vaccine designed to combat brucellosis infections has recently been developed; preliminary testing in mice and goats have indicated that this product effectively protects against infection. This vaccine will be tested in nonhuman primates by vaccinating and then experimentally exposing the vaccinated animals to the bacteria. Prior to testing the vaccine in this manner, we characterized the aerosol brucella (brucellosis) nonhuman primate model by describing the clinical and pathological outcome using a number of experimental aerosol doses. Prior studies using this model have shown that a relatively high infective inhaled dose is required (10E+06 CFU) to induce a disease similar to human brucellosis. A clear confirmation of lethal dose and resulting pathology from a range of doses is needed prior to evaluation of candidate vaccine being tested using the model. Thereafter, we will use the primate brucellosis model to evaluate the attenuated experimental brucella vaccine (Replicate II). This will be performed by immunizing primates, assessing the immunogenicity in the vaccinated animals, and challenging with fully virulent *B. melintensis* by the aerosol route. Results of these studies will provide data for further development of this experimental vaccine for prophylactic protection in the event of a deliberate release of brucella bacteria.

Project Progress (one paragraph)

Initial development efforts at defining a nonhuman primate model of brucellosis via inhaled aerosol exposure were successful and yielded a very useful test system for advanced evaluation of the candidate vaccine. An efficacy study was performed using rhesus macaques. The efficacy study was performed entirely under BSL-3 laboratory/animal housing conditions because of the nature of the vaccine. Upon challenge, immunized animals were extensively sampled through timed blood draws and continuous physiological (telemetry) measurement. The vaccine failed to protect against infection, with similar bacterial loading in the critical target organ systems (spleen, liver) as the unvaccinated controls. Interestingly, bacteria was absent from sampled mucosal surfaces (e.g., vaginal vault) compared to the control animals that showed significant bacterial loads in these locations.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester U54 AI057156

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Infectious Disease Aerobiology Core
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI. with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Bacteriology; and Parasitology
	C	Immunology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	
	A	Tulane University School of Medicine
	A	Private Source
	A	LSU Health Sciences Center
	A	National Institutes of Health
	A	Private Source
	A	University of Texas Medical Branch
	A	University of Texas Medical Branch
	A	Private Source
	A	
	A	

Project Description (limited to one paragraph)

The infectious disease aerobiology core has continued to expand and extend its capabilities as it relates to experimental aerosol infection in the current year. The core has expanded its technical capabilities required for bioaerosol characterization and aerosol challenge using a diverse number of infectious agents and newly-designed equipment that has augmented capability. The exposure capabilities operated under the core continues to maintain two distinct facilities at the TNRPC with both laboratories operating under CDC-approved select agent registered biosafety level 3 (BSL-3) containment. The core has also added the unique capability of determining microbial susceptibility over long periods of time through the use of a small toriod (rotating drum) that operates within the Class III BSC. This addition to the core equipment has facilitated studies in viral susceptibility and represents one of the only laboratories in the nation that can claim the capacity to perform such studies. The core is directed by Excluded by Requester and is staffed by Excluded by Requester who is the core aerosol engineering technician.

Project Progress (one paragraph)

In the past year, the core has maintained a significant effort in aerosol-related infection in conjunction with both intramural and NIH-funded extramural investigators. In 2013, the core performed Proprie individual nonhuman primate exposures using the following pathogens: *Bacillus anthracis*, staphylococcal enterotoxin B (SEB), ricin toxin, Venezuelan Equine Encephalitis virus, Eastern Equine Encephalitis, *Burkholderia pseudomallei*, and *Mycobacterium tuberculosis*. The core also performed a number of aerosol infections with species corollary to the nonhuman primate using agents such

as *Burkholderia pseudomallei* and *Mycobacterium tuberculosis*. In addition to the animal exposures and treatments, the core performed a number of microbial characterization assessments with a variety of pathogenic organisms and toxins as well as therapeutic biologics and pharmaceuticals. Studies focused on characterization of infectious bioaerosols continued to be a major portion of the research activities taking place within the core.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Monoclonal Immunoprotectants for Select Agent Toxins
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester	A	Mapp Biopharmaceutical

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	Iowa State University
	A	University of California, Davis
	A	Private Source

Project Description (limited to one paragraph)

This research program couples a broadly applicable antibody discovery technology with a rapid, scalable manufacturing platform; human monoclonal antibody (Mab) immunoprotectants against two Category B Select Agents, *Clostridium perfringens* (CP) epsilon toxin (ETX) and staphylococcal enterotoxin B (SEB). This project will serve as a proof-of-concept for these platforms which should be generalizable for the development of human Mab immunoprotectants against other bio-warfare agents, as well as newly emerging and re-emerging infectious diseases. Initially, a panel of human anti-ETX and anti-SEB Mabs were screened *in vitro*. The best neutralizers were then evaluated in mouse models of ETX and SEB intoxication. The three best Mabs against each toxin were mass produced in a *Nicotiana benthamiana* manufacturing system and the lead Mab for ETX and SEB was selected based on *in vivo* activity, expression, and stability data. Thereafter, each was scheduled to be tested in a nonhuman primate model of intoxication for the generation of preliminary proof of concept therapy data.

Project Progress (one paragraph)

The individual mAbs identified for each toxin are currently being tested individually to determine the dose response and therapeutic window using the ETX and SEB mouse models available. Studies with mice receiving treatment prophylactically and therapeutically were initially used as a screening system prior to the nonhuman primate studies. Thereafter, the antibody selected for SEB was further evaluated in a nonhuman primate aerosol model of SEB intoxication for mitigation of the health effects caused by the toxin. An initial pharmacokinetic profile indicated plasma levels peaked at approximately 30 minutes after injection. Thereafter, the mAb was administered approximately 2 hours after animals were exposed to three times the 50% lethal dose of purified SEB by small particle aerosol. Results showed that animals were completely protected (100% survival) from SEB-induced lethality. The treatment group appeared to experience a lower rate of clinical/enteric effects than unprotected animals.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID, Excluded by Reques U01 AI082276

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Therapeutic Human Monoclonal Antibodies against SEB
Unit/Division Microbiology
Type of Project Research
Percent PS1 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	A	Private Source

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	

Project Description (limited to one paragraph)

Staphylococcal enterotoxin B (SEB) is a prototype enterotoxin produced by many isolates of *S. aureus*. SEB causes polyclonal activation of T lymphocytes resulting in massive release of pro-inflammatory mediators and culminating in severe toxic shock. SEB is considered by the CDC as a category B select agent. SEB is also a major cause of food poisoning and toxic shock syndrome. Currently, there are no therapeutics available against SEB for human use. This research is aimed at preclinical development of fully human therapeutic anti-SEB monoclonal antibodies (hMabs). By using a human combinatorial antibody library and a phage display approach, a cohort of fully human antibodies against SEB were identified. Lead hMabs with neutralizing activity against SEB intoxication and other related superantigens have been identified based upon extensive studies using *in vitro* proliferation assays and an *in vivo* mouse model of SEB intoxication.

Project Progress (one paragraph)

The optimized hMabs are in the process of testing in a humanized transgenic mouse model and rhesus aerosol challenge model for toxic shock to identify the final preclinical therapeutic candidate against SEB intoxication. The envisioned clinical applications of the developed antibody will be both prophylactic to provide passive immunity to individuals at high risk via an imminent bioterror attack, and as a therapeutic antidote for treatment of individuals already exposed to SEB.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID, Excluded by Requester U01 AI078023

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Thermostable Vaccines for Biodefense
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A Soligenix Corporation
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Ricin intoxication through inhalation at the appropriate dose causes indiscriminate cell death, tissue damage, organ failure, and ultimately death in a wide range of mammals. There are no known medical interventions for amelioration of effects from ricin intoxication or prevention of these effects through effective vaccination. The leading vaccine product for ricin toxin, RiVax, is a subunit vaccine that is adsorbed to aluminum (alum) that has shown efficacy in murine models, but has not protected as completely in recent trials involving rhesus macaques. The lack of protective efficacy in the initial macaque trials are thought to be a function of lack of immunogenic adjuvant (alum) and relationship to the type of immune response required to protect against this type of toxic insult. It is thought that the immune response in the nonhuman primate did include generation of adequate amounts of the neutralizing antibody towards ricin consistent to what was observed in the mouse model.

Project Progress (one paragraph)

In the present study, we intend to test a formulation of the ricin vaccine that has been combined with a novel adjuvant (Toll like receptor-4 agonist) in a thermostable formulation (lyophilized) in an attempt to stimulate a robust immune response in the nonhuman primate that would be consistent with generation of neutralizing antibodies at the level associated with protection from lethal aerosol challenge. Animals will be vaccinated a number of times (one prime, two boosts) with either the newly formulated vaccine, reference vaccine (RiVax), or sham vaccinated (saline), and then challenged by small particle aerosol to purified ricin toxin. Because this is a lethal model, survival from challenge will be the primary endpoint of the vaccine experiment. A number of secondary endpoints, including biotelemetry, will be used to augment the survival data.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID, Excluded by Requester U01 AI082210-TNPRC-A

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Treatment for Pulmonary Anthrax
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with Institutional affiliation
Excluded by Request A Planet Biotechnology, Inc.
Principal Core (TNPRC) Scientist associated with the project
Excluded by Request C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Inhalation anthrax is a systemic disease caused by airborne exposure to *Bacillus anthracis* spores. *B. anthracis* is considered a priority pathogen and a disease agent with the most potential to be used as a biological weapon. Antibiotics are the only FDA-approved drugs for treatment of inhalational anthrax, but antibiotics have limitations. The project focuses on testing of PBI-220, a therapeutic protein presently intended for patients symptomatic for inhalational anthrax. PBI-220 is an immunoadhesion, a fusion of CMG_2 (the Protective Antigen (PA) receptor) and the IgG-F^c domain. PBI-220 has already been shown to be efficacious in a rabbit model of inhalation anthrax, is currently being evaluated in the cynomolgus macaque disease model. Time to treatment with PBI-220 varied from 0 hours postexposure to treatment upon the detection of PA in the blood of exposed animals.

Project Progress (one paragraph)

We have completed numerous evaluation studies utilizing the cynomolgus macaque model of inhalation anthrax. Time to treatment with PBI-220 has varied from 0 hours to the point where bloodborne PA was detected in the exposed animal. The therapeutic showed remarkable efficacy without adjunctive antibiotic therapy at a one-time intravenous dose of PBI-220 at 20 mg/kg at blocking onset of anthrax disease. Presence of bloodborne PA was between 30-36 hours postexposure. Animals treated immediately after PA detection were protected at a survival rate of 57% (4/7 animals surviving). Surviving animals were rechallenged approximately six weeks later, and survived challenge with no therapeutic intervention, demonstrating the development of a normal immune response to bacterial challenge concomitant to therapeutic treatment with PBI-220.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID, Excluded by Request R44 AI053005

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Vaccine Development for Alphaviruses
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A University of Texas Medical Branch
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Venezuelan Equine Encephalitis (VEE) is a vectorborne viral disease caused by Venezuelan Equine Encephalitis virus, a pathogenic alphavirus. Initially we recapitulated the viral disease in an experimental nonhuman primate model (*M. fascicularis*) (n=3). This morbidity model emulated the clinical syndrome and showed the hallmarks of natural disease noted in human infections. The model was established to provide an advanced monitoring system for testing the efficacy of candidate vaccines developed against VEE. The VEE vaccines under development are based upon constructs containing a picornavirus internal ribosomal entry site (IRES) to replace the subgenomic promoter for expression of the VEE virus (VEEV) structural proteins. This approach highly attenuates the virus and prevents mosquito infection, but preserves immunogenicity. Evaluation of the VEE viral vaccines using the nonhuman primate morbidity model is one of many viral vaccine evaluations involving the pathogenic alphaviruses that is associated with this research project.

Project Progress (one paragraph)

The VEE nonhuman primate model was used to test two versions of the vaccine (VEE/IRESv1, v2) in separate experiments. Animals were implanted with remote radiotelemetry for continuous monitoring of clinical signs (core temperature, respiratory rate, heart rate, ECG) and samples were taken for antibody, and viremia assays following vaccination and after challenge. Groups of animals (N=16) vaccinated with a single dose of 5.5log by either the subcutaneous (SQ; VEE/IRESv1) or intradermal (ID; VEE/IRESv2) route, or sham vaccinated with saline. Approximately 45 days postvaccination, all animals were challenged by small particle aerosol with approximately 7.0log of wild-type VEEV. The highest neutralizing antibody titers were generated by the VEE/IRESv2 vaccine group, with slightly lower mean titers by VEE/IRESv1 (ID) and VEE/IRESv1 (SQ) groups. Little or no virema was noted after vaccination, and clinical response after vaccination as measured by implantable telemetry was unremarkable. Upon challenge with WT VEEV, no vaccinated animals developed viremia, elevation in core temperature, or any other clinical hallmarks indicative of VEE disease up to +45 days postinfection. In contrast, sham-vaccinated controls developed viremia acutely (+1-3d PI) and showed dramatic changes in core temperature, heart rate, and electrocardiogram measurements. The VEE/IRES vaccine candidates are safe, highly immunogenic, and protect nonhuman primates from a robust experimental challenge model using WT VEEV. Refinements in vaccine dose, as well as route of vaccination may be explored to evaluate the long term immunity associated with this vaccine product.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester U54 AI057156

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Vaccine Development for *Burkholderia pseudomallei*
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A University of Texas Medical Branch
Principal Core (TNPRC) Scientist associated with the project
Excluded by C Microbiology
Other affiliate scientists with Institutional affiliation (doctoral level only)
Excluded by Requester A Tulane University School of Medicine

Project Description (limited to one paragraph)

This research is directed towards the development of vaccines for the category B agents *Burkholderia pseudomallei* and *Burkholderia mallei.* There is an urgent and acknowledged need to develop better prophylactic countermeasures through the use of vaccines and immune stimulants for both melioidosis and glanders. We believe that it is appropriate to consider these pathogens in parallel in this project because they are closely related at a genetic level, and there is a possibility that common approaches to these diseases can be identified. The aims of this project are to, 1) identify optimal delivery systems and protein carriers, 2) develop optimized protein–polysaccharide conjugation methods, 3) compare efficacy of homologous versus heterologous protein–polysaccharide conjugates, and 4) identify biomarkers and mechanisms of vaccine-mediated protection in acute disease models, including the laboratory mouse, the humanized SCID mouse, and nonhuman primate (rhesus) models.

Project Progress (one paragraph)

Studies during this period (2012-13) include 1) determination of infective dose of *Burkholderia mallei* by aerosol to induce glanders disease in the nonhuman primate. This includes determination of bacterial efficiency experiments (*in vitro*) in anticipation of the animal exposures. To date, aerosol efficiency determination experiments were completed and the results of this work was integral in determination of achievable target dose in the initial animal infection experiments. Nonhuman primate aerosol exposures to *B. mallei* were performed following the determination of bacterial efficiencies that were determined with the strain selected for this group of experiments (China 7). The initial exposures recapitulated the nonhuman primate model of glanders (*B. mallei* infection) in order to support the vaccine efficacy study that is presently underway.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID, Excluded by Requester U54 AI057156

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title VLP Vaccine Development for Alphaviruses
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Microbiology
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A National Institutes of Health

Project Description (limited to one paragraph)

Viruses of the genus Alphavirus, Family *Togaviridae*, are single-stranded RNA viruses that are transmitted via insect vectors such as mosquitoes. Western Equine Encephalitis virus (WEEV), Eastern Equine Encephalitis virus (EEEV), and Venezuelan Equine Encephalitis virus (VEEV) are three such zoonotic alphaviruses that cause a potentially fatal encephalitic illness in the horse. For each of these alphaviruses, transmission to humans is possible. Human infection with VEEV results in flu-like symptoms including high fever and muscle aches. People with weakened immune systems and the young and elderly can become severely ill and die from the disease. WEEV is relatively uncommon and often only causes a subclinical infection in humans. EEEV causes a more virulent disease, and has previously resulted in fatal cases of encephalitis in children, coinciding with outbreaks of EEEV in horses. The VLP vaccines for WEEV, EEEV, and VEEV were previously tested in mice and elicited a robust immune response. The major aim of this study is to test the immunogenicity of alphavirus VLP vaccines when delivered to NHPs.

Project Progress (one paragraph)

Initially, animals were exposed by aerosol to Western Equine Encephalitis Virus (McMillian) for confirmation of WEE disease model. Thereafter, we determined the immunogenicity and protective efficacy of the VLP vaccine formulations against infectious challenge against the respective alphaviral species (WEE or EEE). Cynomolgus macaques were immunized with either WEE or EEE VLP vaccines, respectively. Groups were challenged with a lethal dose of either EEE or WEE via aerosol; the VLP formulations generated a robust immune response and provided protection in vaccinated groups.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/Vaccine Research Center, Excluded by Requester U12XS337 NIH/VRC

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Epidemiology of Rhesus Enteric Calicivlruses
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Private Source
A Southwest National Primate Research Center

Project Description (limited to one paragraph)

A novel group of enteric caliciviruses was described by our group in rhesus macaques (Rhesus Enteric Calicivlruses or ReCVs). ReCVs are evolutionarily and biologically closely related to human noroviruses (NoV), exhibit similar genetic, serotypic and histo-blood group antigen binding properties, and in contrast to human NoVs can be propagated in vitro. At least four ReCV genogroups with phylogenetic distances comparable to those of human NoV have been described. While molecular characterization of ReCVs has been completed, studies that focus on epidemiology, pathogenesis and clinical relevance of these viruses are ongoing.

Project Progress (one paragraph)

Serum samples from Propr ietar animals were collected from six different species of NHPs involving three NPRCs. The sera were tested for the presence of virus-neutralizing antibodies against G1.1 (serotype 1) ReCV. Seroprevalence rates were particularly high in rhesus and cynomolgus macaques (~80%) while pig-tailed macaques, baboons, common marmosets and chimpanzees showed much lower or no ReCV seroconversion. This could be due to species-specific genetic resistance factors, differences in distribution of dominant serotypes and/or differences in husbandry practices at different NPRCs. Over Proprietary Info rhesus-stool samples collected at Tulane NPRC contained ReCV-specific RNA. The rate of ReCV seroprevalence, fecal shedding and diarrhea in juvenile macaques coupled with the capability of these viruses to induce symptomatic infection in seronegative animals indicate that hypothesis-driven studies should be performed to address the applicability of the model to human disease as well as to disease control and prevention in NHP colonies.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Exclude d by Re U24 RR018111

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Functional Analysis of Phage-displayed Coronavirus Proteins
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester A University of Agriculture, China

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A US Department of Agriculture
A Private Source

Project Description (limited to one paragraph)

Transmissible gastroenteritis virus (TGEV) is a highly contagious coronavirus with enteric tropism, characterized by up to 100% mortality of its natural host (suckling newborn piglets). Akin to other coronaviruses, TGEV consists of surface (S) envelope glycoprotein, positive sense oriented ssRNA genome and three other structural viral proteins (M, N and sM). Despite that several of the live/attenuated TGEV vaccines are already available for prevention of TGEV outbreaks in the U.S. and other countries, there is a need to improve the safety and efficacy of such vaccines.

Project Progress (one paragraph)

In this study, the TGEV M protein was used in biopanning involving the 12-mer phage display random peptide library. Three phages expressing the M protein peptides were generated. A phage-based immunosorbent assay (phage-ELISA) capable of differentiating TGEV from other coronaviruses was developed using the phage displayed M peptide as an antigen. The phage-ELISA was more sensitive ($p<0.01$) than antibody-ELISA, although less sensitive than reverse transcription polymerase chain reaction (RT-PCR). A chemically synthesized, phage displayed M peptide (HALTPIKYIPPG) that had the best reactivity with TGEV M protein in ELISA was used for antiviral assays. Plaque-reduction assay revealed that the M peptide was able to abrogate TGEV infection *in vitro* ($p<0.01$), following the virus-peptide pretreatment. When TGEV M peptide was used in combination with porcine aminopeptidase N-derived peptide (FKPSSPPSITLW), further decrease of TGEV infectivity was measured ($p<0.01$). Indirect immunofluorescence and real-time RT-PCR confirmed the inhibitory effects of the both phage-displayed peptides. These results indicate that phage displayed TGEV M peptides might be exploited for commercial preparation of coronavirus-specific diagnostics and antivirals in future – provided their further characterization and optimization.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester,Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Immunogenetics of Gluten Sensitivity in Rhesus Macaques
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No

PI, with institutional affiliation

Excluded by Requester	C	Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Veterinary Medicine
	C	Comparative Pathology
	C	Comparative Pathology
	C	Comparative Pathology
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	Tulane University School of Medicine
	A	Stanford University, CA
	A	Stanford University, CA

Project Description (limited to one paragraph)

Celiac disease (CD) is an autoimmune disorder caused by intolerance to dietary gluten. A chronic diarrheal disease called "Gluten-Sensitive Enteropathy" (GSE) was recently described in a subset of captive rhesus monkeys fed gluten-containing chow. The presence of TG2 and anti-gliadin serum antibodies, decreased absorption of nutrients, decreased xenobiotic metabolism, small intestinal villous atrophy and inflammation, chronic diarrhea, weight loss, cancer predisposition and immunogenetic (*MHC II*-linked) association were all reported in gluten sensitive rhesus macaques. In gluten sensitive macaques and in human celiac patients, GSE can be induced by dietary gluten; withdrawal of dietary gluten typically results in both species in health improvement.

Project Progress (one paragraph)

Interleukina (IL)-17 and IL-22 function as innate regulators of mucosal integrity. Impaired but not well-understood kinetics of the IL-17/22 secretion has been described in celiac patients. In this study, IL-17 and IL-22-producing intestinal cells were evaluated upon their *in vitro* stimulation with mitogens in class II major histocompatibility complex-defined, gluten-sensitive rhesus macaques. Biopsies were collected from the distal duodenum during the stages of disease remission and relapse. Regardless of dietary gluten content, IL-17 and IL-22-producing cells consisted of CD4+ and CD8+ T lymphocytes as well as of lineage-negative (Lin-) cells. Upon introduction of dietary gluten, the ability of intestinal T cells to secrete IL-17/22 started to decline ($p<0.05$), which was paralleled with gradual disruption of epithelial integrity. These data indicate that IL-17/22-producing cells play an important role in maintenance of intestinal mucosa in gluten-sensitive primates.

Funding Sources *(include name of the source, PI and the FULL grant number)*

NIH, Excluded by Requester 1 DK076653
NIH, 01 DK076653-02S1
NIH, R01 DK063158

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Infection and Immunity Induced by Rhesus Enteric Caliciviruses
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Microbiology

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C Comparative Pathology
C Veterinary Medicine
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Private Source
A Division of Viral Diseases, CDC

Project Description (limited to one paragraph)

A novel group of enteric caliciviruses was described by our group recently in rhesus macaques (Rhesus Enteric Caliciviruses or ReCVs). ReCVs are evolutionarily and biologically closely related to human noroviruses (NoV), exhibit similar genetic, serotypic and histo-blood group antigen binding properties, and in contrast to human NoVs can be propagated in vitro. At least four ReCV genogroups with phylogenetic distances comparable to those of human NoV genotypes have been described. While molecular characterization of ReCVs was already completed, studies that focus on epidemiology, pathogenesis and clinical relevance of these viruses are still ongo

Project Progress (one paragraph)

In this study, the tissue culture-adapted Tulane virus (TV), a GI.1 ReCV was used to inoculate juvenile rhesus macaques (Macaca mulatta). TV-inoculated macaques developed diarrhea, fever, virus shedding in stools, inflammation of duodenum and 16-fold increase of TV-neutralizing (VN) serum antibodies but no vomiting a. [1]No VN-antibody responses could be detected against a GI.2 ReCV strain FT285, suggesting that TV and FT285 represent different ReCV serotypes. Examination of duodenum biopsies of the TV-inoculated macaques showed lymphocytic infiltration of the lamina propria and villous blunting. TV antigen positive cells were detected in the lamina propria and were CD20 antigen positive (B cells). In most of the TV positive cells, viral antigens co-localized perinuclearly with calnexin - an endoplasmic reticulum protein. These results indicate that ReCV model might be further used to study questions related to enteric calicivirus replication and immunity.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester R21 AI54146

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Molecular ABO Phenotyping of Cynomolgus Macaques
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No

PI, with institutional affiliation

Excluded by Requester	A	University of California, Davis

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	
	A	University of California, Davis
	A	University of California, Davis
	A	California National Primate Research Center
	A	University of California, Davis

Project Description (limited to one paragraph)

Macaques are commonly used in biomedical research as animal models of human disease. The ABO phenotype of donors and recipients plays an important role in the success of transplantation and stem cell research of both human and macaque tissues. Traditional serological methods for ABO phenotyping can be time consuming, provide ambiguous results and/or require tissue that is unavailable or unsuitable.

Project Progress (one paragraph)

In this study, a novel method was developed to detect the A, B, and AB phenotypes of macaques using real-time quantitative polymerase chain reaction. This method enables simple and rapid screening of these phenotypes without the need of fresh blood or saliva. Although regionally variable, the distribution of the A, B, and AB phenotypes in captive cynomolgus macaques closely resembled the distribution in rhesus macaques. Blood group B, predominates in cynomolgus macaques and its frequency distribution is linked with probability of major incompatibility of 41%. No silencing mutations have been identified in exon 6 or 7 in macaques that could be responsible for the O phenotype, that, although rare, have been reported. The excess homozygosity of rhesus and cynomolgus macaque genotypes in this study, that assumes the absence of the O allele, suggests the possibility of a not well-understood mechanism that prevents the expression of the A and B transferases.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester R24 RR005090
NIH, Excluded by Re R24 RR025871
Excluded by Requester.Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Role of Rhesus Rotavirus Gene 4 in Biliary Atresia
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by [redacted] A Cincinnati Children's Hospital Medical Center

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Cincinnati Children's Hospital Medical Center
A Cincinnati Children's Hospital Medical Center
A Cincinnati Children's Hospital Medical Center

Project Description (limited to one paragraph)

Biliary atresia (BA) is the leading indication for liver transplantation in the pediatric population. The murine model of BA supports viral etiology, because infection of neonatal mice with rhesus rotavirus (RRV) results in biliary obstruction. Viral infection targets the biliary epithelium and development of the model is viral strain dependent. No study has yet determined whether human cholanglocytes are also susceptible to rotavirus infection. An *in vitro* human model was established using an immortalized human cholangiocyte cell line and primary human cholangiocytes obtained from explanted livers to determine human cholangiocyte susceptibility to rotavirus infection.

Project Progress (one paragraph)

In this study, replication and binding assays were performed on immortalized mouse (mCL) and human (H69) cells using six different strains of rotavirus. Primary human cholangiocytes were isolated from cadaveric livers, characterized in culture, and infected with RRV, which causes BA in mice, and another simian strain, TUCH, which does not cause BA in mice. Immortalized mouse and human cholangiocytes demonstrated similar patterns of infectivity and binding with different rotavirus strains. Both cell lines produced a significantly higher viral yield with RRV infection than with the other strains tested. In primary human cholangiocytes, which maintained their epithelial characteristics, as demonstrated by cytokeratin staining, RRV replicated to a yield 1000-fold higher than TUCH. Both immortalized and primary human cholangiocytes are susceptible to RRV infection in a fashion similar to murine cholangiocytes. These findings suggest that rotavirus could have a role in pathogenesis of human BA.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester R03 DK087974
NIH, [redacted]01 DK091566

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title The Rhesus Macaque Gut Microbiome in Health and Disease
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester	A	Southeastern Louisiana University

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Southeastern Louisiana University
	A	Southeastern Louisiana University

Project Description (limited to one paragraph)

Composition of gastrointestinal (GI) microflora plays an important role in mammalian host health. In past studies, a high incidence of chronic enterocolitis associated with the presence of opportunistic and obligate pathogens has been recorded from colonies with captive rhesus macaques. The data collected by our group and others indicate that in these colonies, chronic diarrhea is one of the most significant causes of morbidity. In this ongoing project the focus is on the microbial composition of stool samples obtained from captive macaques as a predictive indicator of health and disease. The specific goal is to characterize the composition and changes in microbial communities during chronic bacterial enterocolitis and gluten-sensitive enteropathy in order to be able to improve the measures leading to prevention of these diseases.

Project Progress (one paragraph)

Stool samples collected from Pro prie rhesus macaques (including the Pro priet with chronic enterocolitis and Pro pri healthy controls) were analyzed by targeting the V4 region of the 16S rRNA gene. The Fuzzy C-means clustering method reliably separated the two groups. Stool sample analysis revealed greater taxa richness in healthy controls than in enterocolitis group (96.12 ± 11.69 vs. 69.7 ± 7.67). Greater over-dispersion was demonstrated in enterocolitis than in control group (p=0.004). The compositional differences of bacterial genera between the two groups were also identified: The enterocolitis group had greater relative abundances of *Blautia, Ruminococcus, Dorea, Subdoligranulum, Lachnospira, Eubacterium,* and *Coprococcus*, and lower abundances of *Sutterella, Fibrobacter, Parabacterlodes, Paludibacter,* and *Treponema* genera. Identified differences could be exploited in future studies and surveys with emphasis on diagnostics and pathogenesis. In summary, initial phase of our project demonstrated the successful application of the Dirichlet multinomial method for evaluation of rhesus macaque GI microbiome.

Funding Sources (include name of the source, PI and the FULL grant number)

SLU, Excluded by Requester Internal Funding

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Animal Models to Design and Evaluate Improved VZV Vaccines
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester A University of Arkansas for Medical Sciences

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Microbiology
C Comparative Pathology
C Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

The simian varicella and SIV NHP infection models, utilizing simian varicella virus (SVV) and simian immunodeficiency virus (SIV) were used to evaluate recombinant varicella rSVV- SIV vaccine candidates. SVV expressing SIV env and gag antigens were constructed. The hypothesis tested was that a live, attenuated rSVV-SIV vaccine will induce immune responses against SIV in the rhesus macaques and provide protection against SIV challenge. Our initial study demonstrated that rSVV-SIV vaccination induced low levels of neutralizing antibodies and cellular immune responses to SIV in immunized rhesus macaques and significantly reduced viral loads following intravenous challenge with pathogenic SIVmac251-CX-1.

Project Progress (one paragraph)

Further laboratory analysis showed additional immunological parameters that define correlates of protection in these animals. Flow cytometry evaluated levels of stimulated memory lymphocyte subpopulations using CD3, CD4, CD8, CD28, CD95 and KI67 antibodies. Intracellular cytokine assays tested functional characteristics of cryopreserved PBMCs following vaccination and challenge. Samples 14 days following immunization, day of SIV challenge, and day 231 post SIV challenge were evaluated. Samples were stimulated with SIV peptides, stained with CD3, CD4, and CD8 surface markers and IL-2, TNF-alpha, and and IFN-gamma. Results showed that vaccinated animals had more polyfunctional CD4+ and CD8+ T cell SIVgag-specific responses compared with SIV env-specific responses. Importantly vaccinated and SIV challenged animal showed a significantly increased population of proliferating CD4+ T cells inversely correlated with viral load. Increases in cellular proliferation and antigen specific polyfunctional cytokine responses in CD4 T helper cells may be crucial to control viral loads in vaccinated and SIV challenged macaques.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester RO1 AI52373-01

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Identification and Preclinical Testing of Microbicides for HPV
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	A	University of Wisconsin

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology
	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	University of New Mexico
	A	Private Source

Project Description (limited to one paragraph)

Human papillomavirus (HPV) is one of the most common sexually transmitted infections and a significant cause of cervical, anal, and other cancers worldwide. HIV positive men and women have a higher prevalence of HPV infections and HPV-associated disease and cancers than HIV negative individuals. Rhesus papillomavirus virus type 1 (RhPV-1), isolated from a metastatic rhesus penile cancer shares many genetic and phenotypic similarities to the highly carcinogenic human isolate HPV type 16. Our working hypothesis, based on data of incidence of HPV infections in young women, was that RhPV1 inoculation of female rhesus macaques will result in infection, will produce either intermittent or persistent viral DNA shedding by 2-4 months post infection and have a high probability of developing low-grade pathology (atypical squamous cells of unknown significance -ASC-US, low-grade squamous intraepithellal lesion-LGSIL, or cervical intraepithellal neoplasia-CIN), associated with papillomavirus infection, and as defined by standard Pap smears and colposcopic examination. A small, Propr ietar animal pilot study was previously conducted in female rhesus macaques with inoculation of 10^9 RhPV1 virus genome equivalents (vge). Results showed RhPV infection and persistence of laboratory derived RhPV1 virions in host target cells, rhesus macaque genital epithelium.

Project Progress (one paragraph)

A larger study of Proprie tary Inf female rhesus was conducted to characterize inoculum dose response with inoculation of Pro prie animals each with 10^7, 10^8, or 10^9 vge RhPV1 as well as a Pr on animal control group inoculated with 10^9 non-replicating RhPV1. Monthly evaluations were performed, similar to the pilot study, for antibody titers, viral replication and production of cervical lesions using blood, cervical and anogenital sampling, Pap smear, and cervical colposcopy. After ten months, all Pro rie animals were intravenously inoculated with 100 $TCID^{50}$ SIVmac239 and monitored clinically for an additional Propri etary months for RhPV1 and SIV viral loads. Results showed RhPV DNA shedding through Pr op months post RhPV1 infection was greatest in the 10^9 high-dose group with positive results in Proprietary Info pilot study animals and Proprietary Info dose response animals. Clinical evidence of RhPV1 virus-specific progressive cellular changes were observed for Proprietary Info of the high-dose 10^9 RhPV1 inoculated pilot study animals and Proprietary Info of the comparable 10^9 RhPV1 inoculated dose response study animals. Animals receiving the lower dose RhPV1 inoculum (10^7 and 10^8) were neither consistently infected nor showed progression to disease. SIV viral loads and kinetics of co-infection were similar in all RhPV1 dose groups, with the exception of two possible MHC controller animals, CK69 and FD92. SIV co-infection reduced RhPV1 ELISA antibody positive animals from Proprietary Info in a three month period, suggesting loss of CD4 cells and critical immune functions by SIV infection. Progression of cervical cytological changes in

Proprietary Info high-dose RhPV1 infected animals following SIV co-infection suggests that SIV immunodeficiency may contribute to RhPV1 progressive disease.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester R21/R33 A0171947

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Molecular Pathogenesis of Varicella Zoster Virus Infection
Unit/Division Microbiology
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester

A University of Colorado Health Sciences Center
C Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A University of Colorado Health Sciences Center
A University of Colorado Health Sciences Center
A University of Colorado Health Sciences Center
A Private Source
A University of Colorado Health Sciences Center

Project Description (limited to one paragraph)

Simian varicella virus (SVV) infection of primates resembles human varicella-zoster virus (VZV) infection. After primary infection, SVV becomes latent in ganglia and reactivates after immunosuppression or social and environmental stress. Previous work describes infections of both rhesus and cynomolgus macaques with SVV and experimental SVV reactivation. Tissue samples from these experiments have been and continue to be analyzed to understand mechanisms of reactivation.

Project Progress (one paragraph)

An additional group of Proprietary rhesus macaques were inoculated with SVV intrabronchially, followed through their acute infection and monitored for latency. At four-five months post inoculation (p.i.) and time of latency, all animals were exposed to a single dose (200 cGy) of x-rays, while the control animal remained untreated. The next day the Proprietary animals were then started on daily immunosuppressant medicines: 80µg/kg/day tacrolimus, orally, and 2 mg/kg/day prednisone, IM, while the control animal remained untreated. Animals were monitored for four months for SVV reactivation with samples taken. We are currently analyzing samples for viral expression, lymphoid and cytokine responses.

Funding Source (include name of the source, PI and the FULL grant number)

NIH, Excluded by Requester P01 AG032958

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

DIVISION OF REGENERATIVE MEDICINE

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Genetically Engineered CTL Against HIV Env
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	C	Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Microbiology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Private Source
	A	Infectious Disease, RWMC, RI
	A	Infectious Disease, RWMC, RI
	A	Private Source
	A	

Project Description (limited to one paragraph)

Infection with HIV-1 results in CD4+ T cell depletion and the subsequent loss of immune function results in AIDS. Although HAART lowers plasma viremia, it requires life-long drug therapy. However, some patients control viral replication without HAART. To increase the immunosurveillance of HIV; autologous T cells will be genetically engineered to express CD4-chimeric antigen receptors (CARs) and bolster/redirect CTL towards an HIV-specific target (in collaboration with Excluded by Requester). First-generation vectors used the CD4 extracellular domain to target HIV Env and the T-cell receptor zeta (TCRζ) intracellular signaling domain to activate T cells. These T cells killed infected cells *in vitro*, but failed to control viremia in clinical trials. These studies will improve the CD4-TCRζ by adding intracellular signaling domains (ie, CD28, 4-1BB, OX40) or shRNA against inhibitor signals (ie, PD-1 or CTLA-4). Additionally, to protect transduced cells from viral challenge, we will co-transduce cells with the membrane-associated C46 (maC46) fusion inhibitor. When tethered to susceptible cells, maC46 binds HIV and blocks viral replication – demonstrating protection and a strong selective advantage in transduced cells (published previously in collaboration with Excluded by Requester). We will use a novel *in vivo* CTL assay to demonstrate functional activity.

Project Progress (one paragraph)

CD4-TCRζ and CD4-28ζ CAR were pseudotyped with GaLV and the maC46 vector with amphotropic Env. We stimulated rhesus PBMCs with αCD3αCD28 and co-transduced T cells with CD4-CAR and maC46 vectors. To evaluate the CTL activity of the dTc, we measured 1) HIV Env-specific cytotoxicity using a novel real-time cytotoxicity assay as changes in electrical impedance and 2) cytokine production using IFN-γ ELIspot. HEK 293T cells were transiently transfected with an HIV-1 Env expression plasmid and plated with transduced T cells at effector:target ratio of 1:1. Gene transfer frequency was up to 60-70% of rhesus CD3+CD8+ T cells individually and 35% of co-transduced cells. CD4-CAR T cells specifically killed 293T-Env+ cells and showed increased frequency of IFN-γ spot-forming cells. In conclusion, we showed that genetically modified T cells were redirected to target HIV Env+ cells. Control of viremia without HAART would revolutionize treatment for HIV patients.

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Sustained Expression of Peptide Inhibitor In MSCs
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester	C	Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Regenerative Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Medicine, Tulane University
	A	Pharmacology, Tulane University
	A	Private Source
	A	
	A	Medicine, Tulane University

Project Description (limited to one paragraph)

Infection with human immunodeficiency virus (HIV) results in CD4+ T cells depletion and the subsequent loss of immune function has led to the death of over 25 million people from AIDS. In combination, antiretroviral therapies control viremia; however, drug regimens are complex and expensive, require life-long intervention with potential side effects. We have shown that expression of the membrane-associated and secreted C46 peptides (members of the new fusion inhibitor class of antiretroviral drugs) efficiently block infection of new cells by interfering with the function of HIV-1 gp41. To evaluate the therapeutic potential of the Secreted Anti-Viral Entry inhibitory (SAVE) peptide in transduced mesenchymal stem cells (MSCs), we measured the inhibition of HIV infection *in vitro* with C46-transduced MSCs.

Project Progress (one paragraph)

We transduced rhesus BM-MSC with retroviral (RV) and lentiviral vectors (LV) expressing GFP, maC46 (M218 [RV]), or the secreted C46 (T-60 [RV] and T-42 [LV]). Fluorescent microscopy and flow cytometry demonstrated that up to 69% of LV-transduced MSCs cells expressed GFP. qPCR revealed that up to 25% of the rhesus MSCs were transduced with the T-60 and M218 vectors. C46 was detectable by western blot using 2F5 antibody. Single round infection assay showed that conditioned medium from C46 and SAVE transduced rhesus BM-MSC blocked the infection of HIV pseudovirus by 60-75% *in vitro*. The transduced rhesus BM-MSCs maintained osteogenic, adipogenic, and chondrogenic differentiation potential. Thus, SAVE peptides expressed by MSCs may provide sustained *In vivo* drug delivery to AIDS patients and, in combination with other anti-retroviral therapies, provide long-term viral inhibition and clinical efficacy.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Biology of Nonhuman Primate Marrow Stromal Cells
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? NO
PI with institutional affiliation

Excluded by Requester C Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Veterinary Medicine
C Regenerative Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

The overall aim of the project is to develop procedures whereby adult stem cells from the bone marrow stroma can be used for trials of gene therapy in non-human primates. The adult stem cells, referred to as mesenchymal stem cells or marrow stromal cells (MSCs), are of interest for cell and gene therapy because they can readily be obtained from a patient, expanded in culture, genetically engineered with or without the use of viruses, and then returned for therapy of the same patient. They are also of interest because they home to damaged tissues and differentiate to replace the damaged cells in the tissues. The cells are currently being tested in many small animal models of human diseases and several promising clinical trials with the cells have been initiated in rare diseases in children. However, extensive trials of the cells in non-human primates are clearly essential for some of the currently proposed applications to common diseases such as osteoporosis, cardiac failure, Parkinsonism, leukodystrophies, and Alzheimer's disease. The ongoing research comparing primate MSCs to human MSCs has begun to focus on the characterization of the biologic properties of MSCs and their applications for disease treatment.

Project Progress (one paragraph)

The therapeutic efficacy of human adipose-derived MSCs (ASCs) from older donors was directly compared to cells from younger donors for disease prevention. Mice were induced with chronic experimental autoimmune encephalomyelitis (EAE) using the MOG35-55 peptide and treated before disease onset with ASCs derived from younger (<35 years) or older (>50 years) donors. ASCs from older donors failed to ameliorate the neurodegeneration associated with EAE, and mice treated with older donor cells had increased CNS inflammation, demyelination, and splenocyte proliferation *in vitro* compared to the mice receiving cells from younger donors. Therefore, the results of this study demonstrated that donor age significantly affects the ability of human ASCs to provide neuroprotection, immunomodulation, and/or remyelination in EAE mice.

Funding Sources (include name of the source, PI and the FULL grant number)

NINDS/NIH R21 NS059665 Excluded by Requester
NCRR/NIH R24 RR022826

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Immunopathologic Alterations in Rhesus Macaques with Globoid Cell Leukodystrophy
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? NO
PI, with institutional affiliation

Excluded by Requester	C	Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Comparative Pathology
	C	Veterinary Medicine
	C	Director
	C	Regenerative Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Globoid cell leukodystrophy, or Krabbe's disease, is a severe disorder of the central and peripheral nervous system caused by the absence of galactocerebrosidase (GALC) activity. We have previously determined that rhesus macaques affected with Krabbe's disease demonstrated marked increases in the levels of expression of iNOS, TNF-alpha, and IL-1 in the affected white matter, colocalizing with globoid cells, activated microglia, and astrocytes. Cytokine mRNA levels revealed markedly increased gene expression of CCL2 in the brain of affected macaques. CCL2-expressing cells were detected throughout the affected white matter, colocalizing with GFAP cells and astrocytes. We are presently investigating the role of the innate immune system in the progression of disease. Our data demonstrates that TLR2 is upregulated on macrophages and microglia early in the disease process before other cells in the brain become activated and continues to rise in the brains of affected individuals coincident with the progression of brain pathology. Based on *in vitro* data, TLR2 signaling is activated by a product released or produced by psychosine-treated oligodendrocytes. It is hoped that identifying signaling mechanisms involved in the upregulation of inflammation and disease progression will identify potential targets for therapeutic intervention.

Project Progress (one paragraph)

This study explored a novel explanation for the development of the pathological changes in the early stages of GLD associated with TLR2 upregulation in the hindbrain and cerebellum as a response to dying oligodendrocytes. TLR2 upregulation on microglia/macrophages coincided with morphologic changes consistent with activation at 2 and 3 weeks of age. After TLR2 was upregulated on activated microglia/macrophages, astrocytes became activated and cytokines/chemokines were markedly upregulated. Because oligodendrocyte cell death is an important feature of GLD, the ability to respond to oligodendrocyte cell death by TLR2 reporter cells was tested. These reporter cells demonstrated the ability to respond *in vitro* to medium conditioned by psychosine-treated oligodendrocytes, indicating the likelihood that oligodendrocytes release a TLR2 ligand during apoptosis. TLRs are a member of the innate immune system and initiate immune and inflammatory events; therefore, the identification of TLR2 as a potential driver in the activation of CNS glial activity in GLD may provide important insight into the pathogenesis of the disease.

Funding Sources (include name of the source, PI and the FULL grant number)

NCRR/NIH R24RR022826 (Excluded by Requester
DPCPSI/NIH T32 OD011124 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title Nonhuman Primate Model for Krabbe's Disease
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? NO
PI, with institutional affiliation

Excluded by Requester	C	Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Veterinary Medicine
	C	Comparative Pathology
	C	Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	University of Illinois
	A	San Raffaele Telthon Institute, Italy
	A	LSU Health Sciences Center

Project Description (limited to one paragraph)

The long-term goal of this proposal is to maintain and study our colony of nonhuman primates affected with Globoid Cell Leukodystrophy (GLD; Krabbe's disease), which represents the only colony of nonhuman primates in the world in which an inherited lysosomal disorder has been recognized, propagated, and is available for study. Harem breeding groups containing a carrier (heterozygous) male and a combination of carrier and normal females are established based on pedigree data from the carrier colony as well as the availability of normal females who can be placed with carrier males. Ultrasounds are performed to confirm pregnancies. Hair samples are collected from new infants for genetic screening. Beginning in 2010, carrier yearlings began to be derived to establish an SPF (negative for SIV, STLV-1, SRV, and B-virus) carrier colony using management procedures employed to establish three other SPF colonies at TNPRC.

Project Progress (one paragraph)

During 2012, there were Pr op pregnancies Pro pri from carrier x carrier matings and Pro prie from carrier x normal matings) which resulted in Pro prie ive births and Pr op tillbirths. There wer Prop rieta ffected infants born Pro prie carriers, and Prop rieta normal Propri etary of the affected infants were assigned to a research project involving gene therapy. Propri etary affected died shortly after birth so no follow up beyond necropsy could be done. The other affected infant's disease progression was monitored via clinical and behavioral evaluations monthly until its death at 50 days of age. Due to funding, all breeding groups were disbanded in 2013 and monkeys are being maintained in same-sex groups or compatible pairs. The cell and tissue banking program continues with all carrier and affected animals providing samples (peripheral blood, bone marrow mononuclear cells, mesenchymal stem cells, skin fibroblasts) that are available to investigators for their research. The colony currently consists o Prop rieta arrier animals Prop rieta re conventional and Pro prie SPF Pro prie breeding age males, Pro pri breeding age females, and Prop rieta juveniles.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NCRR R24RR022826 Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Stem Cell Production Core
Unit/Division Regenerative Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? NO

PI with institutional affiliation

Excluded by Requester	C	Regenerative Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Regenerative Medicine
	C	Regenerative Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	LSU Health Sciences Center
	A	University of Iowa
	A	Private Source
	A	Oregon National Primate Research Center
	A	LSU Health Sciences Center
	A	Texas A&M
	A	LSU Health Sciences Center

Project Description (limited to one paragraph)

Mesenchymal stem cells or marrow stromal cells (MSCs) are a subset of adult stem cells from bone marrow. These cells are of medical and therapeutic interest because they have been shown to differentiate into osteoblasts, adipocytes, chondrocytes and myocytes. In addition these cell types have been shown to squelch inflammatory response associated with disease processes. Due to their biologic properties, these cells have the potential to be useful for the treatment of a large number of genetic diseases. Excluded by Requester has successfully defined the requirements for the expansion and characterization of rhesus macaque MSCs isolated form either the bone marrow or adipose tissue. The Stem Cell Production Core Facility (SCPC) focuses on generation, maintenance and distribution of nonhuman primate MSCs. MSCs are regularly isolated from rhesus macaque bone marrow and adipose tissue samples. We presently have a bank of MSC cell lines generated from over Proprietary rhesus macaques of varying age prepared and ready for distribution.

Project Progress (one paragraph)

Due to their biologic properties, these cells have the potential to be useful for the treatment of a large number of genetic diseases. Excluded by has successfully defined the requirements for the expansion and characterization of rhesus macaque MSCs isolated form either the bone marrow or adipose tissue. The Stem Cell Production Core Facility (SCPC) focuses on generation, maintenance and distribution of nonhuman primate MSCs. MSCs are regularly isolated from rhesus macaque bone marrow and adipose tissue samples. The SCPC presently has a large impact not only on the Regenerative Medicine Program, but on other divisions such as Comparative Pathology within the TNPRC, but also Departments and Centers within the Tulane Health Sciences Center and the Pennington Biomedical Research Center and other research labs nationally.

Funding Sources (include name of the source, PI and the FULL grant number)

DPCPSI/NIH T32 OD011124 Excluded by Requester

Publications Resulting from this Project *(only include publications with a PMCID number)*

Excluded by Requester

DIVISION OF VETERINARY MEDICINE

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Behavioral Management Program
Unit/Division Veterinary Medicine
Type of Project Management
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester
C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester
C Veterinary Medicine
C Veterinary Medicine
C Regenerative Medicine
C Immunology
C Microbiology
C Bacteriology & Parasitology
C Comparative Pathology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

The Unit of Behavioral Management (formerly named the Unit of Environmental Enrichment) aims to optimize the psychological health of the nonhuman primates maintained for breeding and research at the TNPRC. Key to program success is the integration of the Enrichment Unit with the Units of Clinical and Research Medicine and Animal Resources, the Quality Assurance Program and the Institutional Animal and Care Committee. Also notable is the degree to which the program is guided by objective metrics, retrospective and prospective assessments, and results of research projects (examples provided below). The program is overseen by a behavioral scientist and implemented by dedicated enrichment technicians as well as animal care technicians. The program includes numerous elements, including conspecific social contact, primate/human positive interaction and training, feeding enrichment, structural enhancements, manipulable objects, and enrichment devices.

Project Progress (one paragraph)

In 2013, over Propr ietary singly housed individuals were introduced into pairs or small groups. Excluding animals with current scientific, clinical, or behavioral justifications for single housing, 92% of the TNPRC colony is socially housed. Over Propriet ary Info individuals were transferred with familiar companions from large social groups to caging for research assignment, avoiding the use of single housing. Approximatel Pro priet nfant fosterings were implemented in order to reduce the use of nursery rearing. Social management of breeding groups was guided by behavioral observations and by retrospective assessments of introduction and reintroduction outcomes. Animal caging was repurposes as climbing structures in field cages to increase environmental complexity and attempt to habituate animals to housing in caging. The use of positive reinforcement training was augmented via additional support to research projects and an intensive program to teach positive reinforcement training to animal care staff so that these techniques can be incorporated into routine husbandry procedures. Animals arriving into quarantine were provided desensitization to habituate them to the facility. A large number of foraging devices have been added to cages in the transitional housing facilities.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Social Housing and SIV Disease
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Nonhuman primates used in biomedical research can be provided the best quality of life if their management takes their disease status into consideration. For example, it is important to understand how to best meet the social needs of primates throughout the progression of the Simian Immunodeficiency Virus disease. This study aims to 1) characterize the changes in psychological wellbeing associated with Simian Immunodeficiency Virus disease progression, 2) determine the correspondence between measures of wellbeing and disease-related changes in physiology, and 3) identify any threshold behavioral or physiological values that should be used to trigger either increased scrutiny of compatibility or alterations in the social setting of research subjects.

Project Progress (one paragraph)

Subjects included adult, Indian-origin rhesus macaques assigned to research protocols involving SIV infection and anticipated development of SIV disease (i.e. not subject to vaccines, other prophylactic measures, or experimental treatments). Using behavioral, physiological, immunological and clinical data, changes within individuals are assessed. In addition, effects of pair- versus single housing is being compared. Videotaped data collection begins prior to social introduction and SIV inoculation in order to document baseline profiles in single housing, and is repeated after introduction into pair housing and prior to infection. Within pairs, both members are inoculated on the same day. After inoculation, data are collected intensively for the first month. After the first month, a steady scheduling of less intensive data collection is followed until the endpoints approved by the Animal Care and Use Committee are reached. A total of 300 hours of data have been collected ove[Pro prie] subjects and coding is underway.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Blocking Virus Spread By DCs with Carrageenan-Based Compounds
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Population Council
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Private Source

Project Description (limited to one paragraph)

Microbicides may prevent HIV and sexually transmitted infections (STIs) in women; however, determining the optimal means of delivery of active pharmaceutical ingredients remains a major challenge. We previously demonstrated that a vaginal gel containing the non-nucleoside reverse transcriptase inhibitor MIV-150 partially protected macaques from SHIV-RT (simian/HIV reverse transcriptase) infection, and the addition of zinc acetate rendered the gel significantly protective. Herpes simplex virus-2 (HSV-2) infection increases HIV susceptibility. We previously established a rhesus macaque model of vaginal HSV-2 pre-exposure followed by co-challenge with HSV-2 and simian/HIV (SHIV-RT).

Project Progress (one paragraph)

The activity of MIV-150 without the addition of zinc acetate was tested when delivered from either ethylene vinyl acetate (EVA) or silicone intravaginal rings (IVRs). MIV-150 was successfully delivered and was detected in vaginal fluids and tissues by radioimmunoassay in pharmacokinetic studies. Moreover, EVA IVRs significantly protected macaques from SHIV-RT infection. Our results demonstrate that MIV-150-containing IVRs have the potential to prevent HIV infection and highlight the possible use of IVRs for delivering drugs that block HIV and other STIs. To test a CG gel containing MIV-150 and zinc acetate (MZC), which provided naïve animals full protection from SHIV-RT for at least 8 hours (h), MZC (vs. CG) was applied daily for 14 days (d) followed by co-challenge 8h later. MZC prevented SHIV-RT infection (Propr ietary nfected, p=0.04 vs Propr ietar n CG controls), but only reduced HSV-2 infection by 20% Propr Infected vs Prop in CG, p=0.6). In HSV-2-infected animals, Propri etary I of the gel-treated animals seroconverted, and Proprietary Info had measurable HSV-2-specific T cell responses. This study shows the promise of MZC to prevent immunodeficiency virus infection (even in the presence of HSV-2) and reduce HSV-2 infection after exposure to a high-dose inoculum. Additionally, it demonstrates the potential of a macaque co-infection model to evaluate broad-spectrum microbicides.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester,Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title HIV-envelope-specific DARP in-based Microbicide Strategies
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Population Council
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Private Source

Project Description (limited to one paragraph)

We tested the efficacy of a new HIV gp120-specific DARPIns in prevention of vaginal transmission of SHIV. Using 15 rhesus macaques, we tested the ability of the DARPin D12, a small molecule inhibitor of HIV infection that binds to gp120, to prevent SHIV SF162P3 infection when formulated in a vaginal carrageenan gel at 4mg/ml. The control gel contained a DARPin with no anti-HIV activity, E3.5. We tested two different times of gel application: 4 hours vs. 8 hours before challenge. The rationale for these timings comes from previous work showing that when carrageenan gels are applied vaginally close to the time of challenge with SHIV-RT, carrageenan exerts a barrier effect which hinders detection of protection. However, we have never tested carrageenan gels against SHIV SF162P3 and wanted to make sure that we applied the product close enough to the time to challenge to see an effect by the D12 gel. Thus we chose 4 hours and 8 hours for the gel application times in DepoProvera treated macaques (30mg intramuscular injection) with challenge 5 weeks after the DepoProvera.

Project Progress (one paragraph)

At this time, the gels have been applied, the animals challenged, and blood samples collected up to 6 wks post-challenge. Nested PCR for SIV gag in PBMCs at week 2 post-challenge showed that Proprietary four hour D12 gel animals and Proprietary eight hour D12 gel animals were positive vs. Proprietary four hour E3.5 control gel animals and Proprietary eight hour E3.5 control gel animals. Thus, it does not appear that the D12 gel offered any protection from SHIV SF162P3. In plasma samples collected 1 hour after gel application, no D12 binding activity was detected, indicating that D12 did not become systemic. Importantly, no vaginal swab samples could be collected around the time of challenge as this would perturb the mucosa and potentially impact infection. Unlike in the SHIV-RT model, there was no barrier effect of carrageenan against SHIV SF162P3.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester PI 1R01 AI084133-01

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 -- April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Imaging
Unit/Division Veterinary Medicine
Type of Project Management
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester	C	Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Veterinary Medicine
	C	Regenerative medicine
	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Director
	C	Comparative Pathology
	C	Veterinary Medicine
	C	Microbiology
	C	Bacteriology & Parasitology
	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Veterinary Medicine
	C	Microbiology
	C	Comparative Pathology
	C	Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	LSUHSC
	A	Private Source
	A	
	A	
	A	LSUHSC
	A	LSUHSC
	A	Private Source

Project Description (limited to one paragraph)

Radiology support is provided with a Proprietary Info compatible digital radiography unit. In addition, images are stored on a Proprietary Info distributed imaging server. Images are accessed at workstations in animal procedure areas and at veterinarians' desktop computers. Ultrasonographic examinations and procedures are performed using one of three Proprietar Info or a portable Proprietary Info ultrasound machine. Color doppler capability is present on three of the four machines. MRI is performed on the TNPRC campus on a contract basis utilizing a private imaging company.

Project Progress (one paragraph)

In 2012, Prop rieta radiographs were taken. 8 MRIs and Propr ietary ultrasounds were performed. In 2013, Propri etary radiographs and Propri etary ultrasounds.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by *PI* 1 R01 HL106786
NIH Excluded by 1R01 AI094595
NIH Excluded by Requester *PI* 5 R01 HL106790-03
NIH Excluded by *PI* 5 R44 AI053005-06
NIH Excluded by Request *PI* 5R01 AI089323-03
Excluded by Requester,Private Source
Excluded by Requester,Private Source
NIH Excluded by Request *PI* OD011104-52
NIH Excluded by *PI* P60 AA09803
NIH Excluded by Requester *PI* R01 AI084765-01
NIH Excluded by R01 AI084793
NIH Excluded by *PI* R01 AI097059
NIH Excluded by *PI* TNPRC Pilot OD011104-52
NIH Excluded by Re *PI* TNPRC Pilot OD011104-52
NIH Excluded by *PI* U24 OD011109-11
NIH Excluded by *PI* U42 OD010568-12
Excluded by Requester,Private Source

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Impact of ART on DC and Treg Responses in Oral Tissues
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A Population Council
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Private Source

Project Description (limited to one paragraph)

The goal of antiretroviral therapy (ART) is to suppress virus replication to limit immune system damage. Some have proposed combining ART with immune therapies to boost antiviral immunity. For this to be successful, ART must not impair physiological immune function. We studied the impact of ART (tenofovir and emtricitabine) on systemic and mucosal immunity in uninfected and simian immunodeficiency (SIV)-infected Chinese rhesus macaques.

Project Progress (one paragraph)

Subcutaneous ART was initiated 2 weeks after tonsillar inoculation with SIVmac239. There was no evidence of immune dysregulation as a result of ART in either infected or uninfected animals. Early virus-induced alterations in circulating immune cell populations (decreased central memory T cells and myeloid dendritic cells) were detected, but normalized shortly after ART initiation. ART-treated animals showed marginal SIV-specific T-cell responses during treatment, which increased after ART discontinuation. Elevated expression of CXCL10 in oral, rectal, and blood samples and APOBEC3G mRNA in oral and rectal tissues was observed during acute infection and was down regulated after starting ART. ART did not impact the ability of the animals to respond to tonsillar application of polyICLC with increased CXCL10 expression in oral fluids and CD80 expression on blood myeloid dendritic cells. Early initiation of ART prevented virus-induced damage and did not impede mucosal or systemic immune functions.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester PI 5U19 AI065412-05

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Macaque Explant Model for Microbicides Testing
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Private Source
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Louisiana State University Ag Center

Project Description (limited to one paragraph)

The Population Council's leading microbicide gel containing 14mM zinc acetate dihydrate (ZA) and 50μM MIV-150 in carrageenan (MIV-150/ZA/CG) affords ~90% protection against SHIV-RT challenge 24h after gel administration (repeated and single dosing). Repeated application of ZA/CG gel provides significant (~70%) protection against vaginal SHIV-RT challenge. Thus, In addition to the NNRTI activity of MIV-150, ZA also contributes to the protection. We hypothesized that ZA modulated innate immune factors to limit immunodeficiency virus infection.

Project Progress (one paragraph)

In vitro models consistently show that cell-associated HIV infection is more efficient than cell-free. Therefore, it would be beneficial for a microbicide product to have activity against cell-associated virus. The Population Council's lead MIV-150/zinc acetate/carrageenan (MZC) gel provides macaques complete protection against cell-free SHIVRT infection when applied vaginally up to 8h post challenge and inhibits SHIVRT infection in macaque vaginal explants *in vitro* and *ex vivo*. To investigate MZC gel and other formulations activity against cell-associated infection of the mucosa, we established a cell-associated SHIVRT infection model of macaque vaginal survival biopsies and necropsy tissues. Co-culture of 10^3 SHIVRT infected macaque PBMCs and vaginal explants resulted in reproducible tissue infection as determined by increasing p27 over the co-culture period. Infection was inhibited with 3TC. Supernatants from mitomycin C-treated PBMCs cultured alone had undetectable p27 throughout the culture. Tissue challenge with the cell-associated SHIVRT (vs. cell-free) resulted in high infection with early peak. Exposure to the MZC gel (up to 1:300 dilution) at the time of cell-associated challenge completely blocked infection in explants. The MZC gel (up to 1:100 dilution) also strongly reduced tissue infection by the cell-associated inoculum when challenged 24h or 4d later. Conclusions: We established a robust cell-associated infection model of macaque vaginal explants to evaluate activity of microbicide formulations. The promising MZC gel effectively inhibits cell-associated infection in this model. These data support the planned clinical evaluation of the MZC gel in humans.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester.Private Source

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Mucosal Dendritic Cell-T Cell Milieu and SIV Spread
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Population Council
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Private Source

Project Description (limited to one paragraph)

Integrin α4β7 (α4β7) mediates the homing of CD4+ T cells to gut-associated lymphoid tissues (GALT) which constitutes a highly favorable environment for HIV expansion and dissemination. HIV and SIV envelope proteins bind to and signal through α4β7 and during acute infection SIV preferentially infects α4β7high CD4+ T cells. We postulated that the frequency of these cells could influence mucosal transmission and acute viral load (VL).

Project Progress (one paragraph)

We found that the frequency of memory CD4 T cells that expressed high levels of α4β7 (α4β7 memory CD4 T cells) in blood before challenge correlated strongly with susceptibility to infection and acute VL. Notably, not only at the time of challenge, but also their frequency 3 weeks before challenge correlated with infection. This association extended to the rectal tissue as we observed a strong direct correlation between the frequency of α4β7 memory CD4 T cells in blood and rectum before and after challenge. The frequency of α4β7 myeloid DCs and α4β7 CD80 DCs also correlated with infection and acute VL, while blood CCR5 and CD69 CD4 T cells could not be associated with infection. Our results suggest that animals with higher frequency of α4β7 CD4 T cells in circulation and in rectal tissue could be more susceptible to SIV rectal transmission.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester *PI* 5R37 AI040877-14

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Phenotypic and Genotypic Determinants of SHIV Pathogenesis
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI with institutional affiliation
Excluded by Requester A Aaron Diamond AIDS Research Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

We previously reported that adoption of an "open" envelope glycoprotein (Env) to expose the CD4 binding site for efficient receptor binding represents an early event in the process of coreceptor switch in two rapid progressors (RP) infected with SHIVSF162P3N.

Project Progress (one paragraph)

Here we extended these studies to Propr ietary additional RP monkeys with coreceptor switch and Proprie tary Inf without to confirm and identify additional factors that facilitated the process of phenotypic conversion. We found that regardless of coreceptor switching, R5 viruses in SHIVSF162P3N-infected RP macaques evolved over time to infect macrophages more efficiently. This was accompanied by increased sCD4 sensitivity, with structural changes in the CD4 binding site, the V3 loop and/or the fusion domain of their Envs that are suggestive of better CD4 contact, CCR5 usage and/or virus fusion. However, sCD4-sensitive variants with improved CD4 binding were observed only in RPs with coreceptor switch. Furthermore, cumulative viral load was higher in RPs with than in those without phenotypic switch, with the latter maintaining a longer period of seroconversion. Our data suggest that the increased virus replication in the RPs with R5-to-X4 conversion increased the rate of virus evolution and reduction in the availability of target cells with optimal CD4 expression heightened the competition for binding to the receptor. In the absence of immunological restrictions, variants that adopt an "open" Env to expose the CD4 binding site for better CD4 use are selected, allowing structural changes that confer CXCR4-use to be manifested. Viral load, change in target cell population during the course of infection and host immune response therefore are interdependent variables that influence R5 virus evolution and coreceptor switch in SHIVSF162P3N-infected rhesus macaques. Because an "open" Env conformation also renders the virus more susceptible to antibody neutralization, our findings help to explain the infrequent and late appearance of X4 virus in HIV-1 infection when the immune system deteriorates.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester PI 5R37 AI041945-14

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title R5 SHIV/Macaque Model for the Evaluation of T and B Cell-based HIV-1 Vaccine
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Aaron Diamond AIDS Research Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Private Source
A

Project Description (limited to one paragraph)

Infection of rhesus macaques (RMs) of Indian origin with SIV or SHIV provide powerful tools to study HIV-1 transmission and disease, and for testing the efficacy of novel drugs, vaccines and prevention strategies. In developing alternative nonhuman primate AIDS models for the CCR5 (R5)-tropic SHIVSF162P3N, we characterized virus transmission and infection in Chinese origin RMs. Virologic, immunologic and pathogenic evaluations of R5 SHIVSF162P3N infection in Chinese RMs challenged intrarectally (ir) or intravaginally (ivg) were performed and compared to those previously observed in Indian origin rhesus exposed to the same inoculum dose and via similar route. R5 SHIVSF162P3N transmits efficiently across mucosal surfaces in Chinese RMs. The magnitude and kinetics of early virus dissemination following intrarectal inoculation in the Chinese macaques were similar to those observed in Indian rhesus, but a trend towards increased SHIVSF162P3N vaginal infectivity and rapid virus spread was seen in the Chinese macaques compared to the Indian origin animals. Once infected, however, set-point viremia in the ir- and ivg-infected Chinese rhesus was significantly lower and the animals survived longer compared with infected Indian rhesus. The R5 SHIVSF162P3N/Chinese rhesus macaque infection model is suitable for studies of mucosal HIV-1 transmission and protection, but the high frequency of spontaneous control of chronic viremia and reduced virulence with SHIVSF162P3N in this macaque subspecies may limit its utility in studying HIV-1 pathogenesis and in evaluating vaccines and antiretrovirals that rely on reduction in chronic viral load or AIDS development as an experimental endpoint.

Project Progress (one paragraph)

We observed progression to AIDS in rhesus macaques infected intrarectally with molecular clones of the pathogenic R5 SHIVSF162P3N isolate. Expansion to CXCR4 usage was documented in Propr ietary diseased macaque that mounted a neutralizing antibody response and in Proprietar y Info that failed to do so, with the latter displaying a rapid progressor phenotype. V3 loop envelop glycoprotein gp120 sequence changes that are predictive of a CXCR4 (X4)-using phenotype in HIV-1 subtype B primary isolates, specifically basic amino acid substations at positions 11 (S11R), 24 (G24R) and 25 (D25K) of the loop were detected in the Propr ietar infected macaques. Functional assays showed that envelopes with V3 S11R or D25K mutation were dual-tropic, infecting CD4+ target cells that expressed either the CCR5 or CXCR4 coreceptor. And, consistent with findings of coreceptor switching in macaques infected with the pathogenic isolate, CXCR4-using variant was first detected in the lymph node of the chronically infected rhesus monkey several weeks prior to its presence in peripheral blood. Moreover, X4 emergence in this macaque coincided with persistent peripheral CD4+ T cell loss and a decline in neutralizing antibody titer that are suggestive of immune deterioration, with macrophages as the major virus-producing cells at the end-stage of disease. The data showed that molecular clones derived from the R5 SHIVSF162P3N isolate are mucosally transmissible and induced disease in a manner similar to that observed in HIV-1

infected individuals, providing a relevant and useful animal infection model for in-depth analyses of host selection pressures and the env evolutionary changes that influence disease outcome, coreceptor switching and vaccine escape.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIAID Excluded by Requester PI 5R01AI084765-02

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Surgery
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester	C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C Comparative Pathology
	C Veterinary Medicine
	C Regenerative Medicine
	C Veterinary Medicine
	C Veterinary Medicine
	C Bacteriology & Parasitology
	C Veterinary Medicine
	C Veterinary Medicine
	C Veterinary Medicine
	C Immunology
	C Director
	C Comparative Pathology
	C Veterinary Medicine
	C Microbiology
	C Comparative Pathology
	C Bacteriology & Parasitology
	C Veterinary Medicine
	C Microbiology
	C Veterinary Medicine
	C Microbiology
	C Veterinary Medicine
	C Comparative Pathology
	C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A LSUHSC
	A NIH
	A Private Source
	A
	A UCLA School of Medicine
	A LSUHSC
	A LSUHSC
	A Private Source
	A

Project Description (limited to one paragraph)

TNPRC surgery facilities provide support for all research projects requiring major or minor survival surgery as a component of the research and for cases that require surgery as an element of the treatment of clinical conditions in breeding colony and research animals. Major surgery is performed in either of two surgery rooms in the surgical facility. Minor surgical and technical procedures are performed in clinical procedure rooms of animal housing buildings as well as in the surgical facility. The facility is under the direct supervision of a veterinarian, who is assisted by the surgery supervisor and two surgery technicians. Procedures performed are those approved by the IACUC or for medical management of non-research and research animals. Currently all surgical procedures performed at the TNPRC involve a veterinarian. Trained veterinary technicians are present during every surgical procedure. Veterinarians provide support to new investigators performing surgical procedures in rodents until the investigator becomes competent in specific techniques.

Project Progress (one paragraph)

In 2012, Proprietary major survival surgeries, Proprietary minor surgeries/procedures, and Proprietary endoscopic procedures were performed in support of research or clinical care. In 2013 we performed Proprieta major survival surgeries, Proprietary minor surgeries/procedures and Proprietary endoscopic procedures.

Funding Sources (include name of the source, PI and the FULL grant number)

CFAR Excluded by Requester PI 5-P30-AI-045008-12
CFAR Excluded by Requester 5-P30-AI-045008-12
Excluded by Requester,Private Source
DoD Defense Threat Reduction Agency (naval research) Excluded by Requester
Excluded by Requester,Private Source
NIH Excluded by Reque PI OD011104-52
NIH Excluded by PI P01 AG032958
NIH Excluded by Requester PI P20 GM103458-09
NIH P60 AA09803
NIH Excluded by Requester R01 A1099795
NIH R01 AI076067
NIH Excluded by Requester PI R01 AI084765-01
NIH Excluded by R01 AI084816
NIH Excluded by Requester R01 AI097059
NIH PI R01 AI100724-01
NIH R01 DA030053-01
NIH R01 DK0838929-01A2
NIH Excluded by PI R01 NS048952
NIH Excluded by Requester R21 AI091501
NIH Excluded by R21 AI106540-01A1
NIH/NIAID Excluded by PI R37 AI040877-13
NIH Excluded by TNPRC Pilot OD011104-52
NIH Excluded by Requester U19 AI057234 S2
NIH Excluded by Requ U24 OD011109-11
NIH Excluded by Requester PI U42 OD010568-12
NIH U54 AI057156-08
NIH Excluded by Requester U54 AI057156-09
Excluded by Requester,Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development of Therapies for Preexposure Prophylaxis (PreP) for Prevention of HIV Infection
Unit/Division Veterinary Medicine
Type of Project Research
Percent PS1 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by Requester A Private Source

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Veterinary Medicine
C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Private Source
A
A

Project Description (limited to one paragraph)

GSK1265744 (744) has exhibited potent antiviral activity following short-term monotherapy in infected patients. The physicochemical properties of 744 permit a long-acting parenteral (LAP) formulation in a nanoparticle suspension (200 mg/mL). Following a single injection of 744LAP in healthy volunteers, a drug half-life of 21-50 days was noted, supporting monthly or quarterly dosing in humans. While oral and topical pre-exposure prophylaxis (PrEP) studies have demonstrated a degree of protection against HIV-1 transmission, efficacy results have been largely attributed to the lack of adherence to the prescribed regimen. With its PK profile, 744LAP offers an opportunity to address this deficiency in our current approach to PrEP.

Project Progress (one paragraph)

Propri etary I male rhesus macaques were injected intramuscularly with 744LAP (50 mg/kg) at two time points, one week prior to the first virus exposure and four weeks later. Propri etary I other male macaques were untreated and served as placebo controls. Pro prieta animals were challenged intrarectally each week with SHIV162p3 (50 TCID50) for up to Propri etary I exposures. Infection status was monitored by real-time PCR amplification of viral gag sequences from plasma samples obtained weekly. The infection status of each monkey has been evaluated through three weeks after the last virus challenge. Proprietar y Proprietary Info macaques became infected after a median of two rectal exposures (range 1 to 7). Of the Propri etary I 744LAP-treated macaques, Propri etary I has detectable systemic viremia. In these protected animals, the plasma concentrations of 744 throughout the period of virus challenges were comparable to those observed in human volunteers. All protected macaques will be monitored for at least 7 more weeks before sacrifice to look for additional evidence of SHIV infection. Our results show that 744LAP, at clinically relevant concentrations, can protect macaques against repeated intrarectal challenges with SHIV, and they support further preclinical evaluations to determine the minimum protective dose of 744LAP and to perform similar virus-challenge experiments in female macaques. 744LAP appears to be a promising next-generation PrEP agent suitable for monthly or quarterly injections.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Establishment of SPF Rhesus Colony for Non-AIDS
Unit/Division Veterinary Medicine
Type of Project Management
Percent P51 dollars - 0.651%
AIDS? No

PI, with institutional affiliation

Excluded by Requester	C	Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C	Comparative Pathology
	C	Veterinary Medicine
	C	Regenerative Medicine
	C	Regenerative Medicine
	C	Bacteriology & Parasitology
	C	Bacteriology & Parasitology
	C	Immunology
	C	Director
	C	Comparative Pathology
	C	Microbiology
	C	Microbiology
	C	Microbiology
	C	Comparative Pathology
	C	Comparative Pathology
	C	Bacteriology & Parasitology
	C	Microbiology
	C	Microbiology
	C	Comparative Pathology
	C	Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	LSUHSC
	A	Univ of Buffalo
	A	Private Source
	A	Univ of Pittsburgh
	A	Private Source
	A	
	A	Univ of Pittsburgh
	A	PrimGen (PreLabs)
	A	Univ of Texas Medical Br Galveston
	A	Univ of Pittsburgh
	A	University of Colorado, Denver
	A	Univ of Pittsburgh
	A	Univ of Pittsburgh
	A	ADARC
	A	Private Source
	A	
	A	LSU HSC
	A	TUSPH&TM

Excluded by Requester

A Univ of Pittsburgh
A Private Source
A Mississippi State University
A Univ of Colorado Denver
A Private Source
A Univ of North Carolina Charlotte
A Private Source
A LSUHSC
A Tulane University
A Univ of Pittsburgh
A Univ of Pittsburgh
A LSU
A Private Source
A University of Massachusetts Medical School
A Private Source
A LSUHSC
A Univ of Pittsburgh
A Private Source
A

Project Description (limited to one paragraph)

The presence of retroviral infection in nonhuman primate research animals makes them unsuitable for a number of research studies. In addition, the presence of B-virus in nonhuman primates used in research is a significant occupational safety and health concern. The specific pathogen free (SPF) program was created to provide rhesus monkeys seronegative for SIV, SRV, STLV-1, and B-virus. The majority of the animals assigned to the SPF breeding program are in the NCRR/OAR AIDS colony which limits assignment of animals to AIDS research programs. The base grant supported SPF colony described here allows allocation of SPF animals to other than AIDS studies.

Project Progress (one paragraph)

In 2012 the colony census was Propri etary I animals Propri etary Chinese-origin rhesus and Propri etary ndian-origin rhesus). In 2012, a total o Pro prie animals were made available for assignment to core and affiliate researchers. The colony currently consists of Propri etary I animals (Chinese-origin rhesus and Indian-origin rhesus). In 2013, a total of Propr ietar animals were made available for assignment to core and affiliate researchers. In addition, piggybacked use of animals in the breeding colony occurred. Tissues, including blood, feces, saliva, and bone marrow, were provided to investigators to support their research programs. Behavioral/observational data were also collected to support research and management programs. All piggyback use of animals is noninvasive or minimally invasive and allows animals to remain in their social groups with no impact to production.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title *In vitro* HIV/SIV assays using rhesus macaque blood
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation

Excluded by A Private Source

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A	Aaron Diamond AIDS Research Center
	A	Private Source
	A	
	A	
	A	
	A	

Project Description (limited to one paragraph)

Our objective is to understand the interaction, function and regulation of human immunodeficiency virus type 1 (HIV-1) and the human immune system using the NHP model. The rhesus macaque has similar immune system like human. This model had been used for over two decades to understand pathogenesis and immune functions of HIV-1 infection of humans. As a result of this work, potent anti-viral drugs, immune enhancing proteins, entry inhibiting drugs and microbicides were discovered. Despite of these discoveries and gained knowledge, HIV-1 still drags on devastating many communities around the world. Therefore there is an urgent need to develop safe vaccines; topical barriers and microbicides that can efficiently protect or reduce sexually transmitted HIV-1 infection. In vitro, using rhesus macaque tissues, we will continue to advance our understanding of pathogenesis in relation to the immune system. Furthermore, we will continue to test new promising anti-HIV-1 blockers, immune modulators, microbicides, and challenge viruses that truly resemble HIV-1 infection. Promising vaccines, microbicides, immune modulators and entry inhibitors that are screed in vitro will further be tested in a relevant animals model, such as the rhesus macaque model for their potency before advancing to humans.

Project Progress (one paragraph)

In 2012, blood samples were collected from Pro pri aive TNPRC breeding colony animals. In 2013, blood samples from Propr ietary naive breeding colony animals were collected. An additional blood sample was collected from Pr op animal from another research project (#3548) in 2012.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester Private Source

NIH Excluded by Requester PIR01 AI084765-01

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title NIA: Aging Colony Maintenance
Unit/Division Veterinary Medicine
Type of Project Management
Percent P51 dollars - 0.879%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A National Institute on Aging

Project Description (limited to one paragraph)

The NIA set aside program maintains aged rhesus monkeys at several facilities to provide for allocation to NIA-funded investigators.

Project Progress (one paragraph)

In 2012 the animal census of the NIA colony was Pro prie which was comprised of Indian-origin rhesus macaques of both sexes ranging in age from 16.56 to 27.71 years of age. The animals were housed among their breeding colony cohorts in several enclosures or were pair housed with a compatible conspecific in indoor housing. During 2012, tissues from Proprie tary Inf animals were sent to support NIA-supported programs. The current census of the NIA colony is Pro priet animals, which is comprised of Indian-origin rhesus macaques of both sexes ranging in age from 15.47 to 23.75 years of age. The animals are housed among their breeding colony cohorts in several enclosures or they are pair housed with a compatible conspecific in indoor housing. During 2013, tissues from Propr ietary animals were sent to support NIA-supported programs. In 2013, progress continued to convert the NIA colony to SPF status (negative for SIV, SRV, STLV1, BV, measles, and TB) by replacing conventional animals that died with SPF animals 15 years or older. The rest of the TNPRC colony is SPF. As a result of the young demographic in the newly derived TNPRC SPF colony, it will take time to mature to the minimum age required for inclusion in the NIA colony.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Optimal Dose of 7DW8-5 as an Adjuvant for AdPfCA, a Candidate Malaria Vaccine
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No

PI with institutional affiliation
Excluded by Requester A Private Source

Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Aaron Diamond AIDS Research Center

Project Description (limited to one paragraph)

A key strategy to a successful vaccine against malaria is to identify and develop new adjuvants that can enhance T-cell responses and improve protective immunity. Upon co-administration with a rodent malaria vaccine in mice, 7DW8-5, a recently identified novel analog of α-galactosylceramide (α-GalCer), enhances the level of malaria-specific protective immune responses more strongly than the parent compound. In this study, we sought to determine whether 7DW8-5 could provide a similar potent adjuvant effect on a candidate human malaria vaccine in the more relevant non-human primate (NHP) model, prior to committing to clinical development. The candidate human malaria vaccine, AdPfCA (NMRC-M3V-Ad-PfCA), consists of two non-replicating recombinant adenoviral (Ad) vectors, one expressing the circumsporozoite protein (CSP) and another expressing the apical membrane antigen-1 (AMA1) of *Plasmodium falciparum*. In several phase 1 clinical trials, AdPfCA was well tolerated and demonstrated immunogenicity for both humoral and cell-mediated responses.

Project Progress (one paragraph)

Proprietary Info rhesus macaques received prime and boost intramuscular (IM) immunizations of AdPfCA alone or with an ascending dose of 7DW8-5. Our results indicate that 7DW8-5 is safe and well-tolerated and provides a significant enhancement (up to 9-fold) in malaria-specific CD8+ T-cell responses after both priming and boosting phases, supporting further clinical development.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by PI AI070258
Excluded by Requester Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Spectral Trans through Red Cages on Circadian Met and Phys in Nude rats
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No

PI. with institutional affiliation
Excluded by Requester C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A Private Source
A Tulane Med School
A Tulane Med School
A Private Source

Project Description (limited to one paragraph)

Light entrains normal circadian rhythms of physiology and metabolism in all mammals. Previous studies from our laboratory demonstrated that spectral transmittance (color) of light passing through cages affects these responses in rats. Here, we addressed the hypothesis that red tint alters the circadian nocturnal melatonin signal and circadian oscillation of other metabolic and physiologic functions.

Project Progress (one paragraph)

Female nude rats (Hsd:RH-Foxn1(rnu); n = Pro priet per group) were maintained on a 12:12-h light (300 lx; 123.0 µW/cm(2); lights on 0600):dark regimen in standard polycarbonate translucent clear or red-tinted cages. After 1 wk, rats underwent 6 low-volume blood draws via cardiocentesis over a 4-wk period. Plasma melatonin levels were low during the light phase (1.0 ± 0.2 pg/mL) in rats in both types of cages but were significantly lower in red-tinted (105.0 ± 2.4 pg/mL) compared with clear (154.8 ± 3.8 pg/mL) cages during the dark. Normal circadian rhythm of plasma total fatty acid was identical between groups. Although phase relationships of circadian rhythms in glucose, lactic acid, pO2, and pCO2 were identical between groups, the levels of these analytes were lower in rats in red-tinted compared with clear cages. Circadian rhythms of plasma corticosterone, insulin, and leptin were altered in terms of phasing, amplitude, and duration in rats in red-tinted compared with clear cages. These findings indicate that spectral transmittance through red-colored cages significantly affects circadian regulation of neuroendocrine, metabolic, and physiologic parameters, potentially influencing both laboratory animal health and wellbeing and scientific outcomes.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester PI R25 OD010934

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Spectral Trans through Tint Cages on Circadian Met and Phys in Nude rats
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No

PI, with institutional affiliation

Excluded by Requester C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A Private Source
A Tulane Med School
A Tulane Med School
A Private Source

Project Description (limited to one paragraph)

Light is potent in circadian, neuroendocrine, and neurobehavioral regulation, thereby having profound influence on the health and wellbeing of all mammals, including laboratory animals. We hypothesized that the spectral quality of light transmitted through colored compared with clear standard rodent cages alters circadian production of melatonin and temporal coordination of normal metabolic and physiologic activities.

Project Progress (one paragraph)

Female nude rats (Hsd:RH-Foxn1(rnu); n = Pr op er group) were maintained on a 12:12-h light:dark regimen (300 lx; lights on, 0600) in standard translucent clear, amber, or blue rodent cages; intensity and duration of lighting were identical for all groups. Rats were assessed for arterial blood levels of pO(2) and pCO(2), melatonin, total fatty acid, glucose, lactic acid, insulin, leptin, and corticosterone concentrations at 6 circadian time points. Normal circadian rhythms of arterial blood pO(2) and pCO(2) were different in rats housed in cages that were blue compared with amber or clear. Plasma melatonin levels (mean ± 1 SD) were low (1.0 ± 0.2 pg/mL) during the light phase in all groups but higher at nighttime in rats in blue cages (928.2 ± 39.5 pg/mL) compared with amber (256.8 ± 6.6 pg/mL) and clear (154.8 ± 9.3 pg/mL) cages. Plasma daily rhythms of total fatty acid, glucose, lactic acid, leptin, insulin, and corticosterone were disrupted in rats housed in blue or amber compared with clear cages. Temporal coordination of circadian rhythms of physiology and metabolism can be altered markedly by changes in the spectral quality of light transmitted through colored standard rodent cages.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester *DVM, PI* R25OD010934

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Spectral Trans through Tinted Cages on Circadian Met and Phys in SD rats
Unit/Division Veterinary Medicine
Type of Project Research
Percent PS1 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A Private Source
A Tulane Medical School
A Tulane Medical School
A Private Source

Project Description (limited to one paragraph)

The suprachiasmatic nucleus is synchronized by the light:dark cycle and is the master biologic clock that serves as a pacemaker to regulate circadian rhythms. We explored the hypothesis that spectral transmittance (tint) of light through caging alters circadian rhythms of endocrine and metabolic plasma constituents in nonpigmented Sprague-Dawley rats.

Project Progress (one paragraph)

Rats (Crl:SD; n = Pro priet er group) were housed in a 12:12-h light:dark environment (300 lx; 123.0 µ W/cm(2); lights on, 0600) in either clear-, amber-, blue-, or red-tinted rodent cages. Blood was collected at 0400, 0800, 1200, 1600, 2000, and 2400 and measured for melatonin, total fatty acids, pH, glucose, lactic acid, corticosterone, insulin, and leptin. As expected, plasma melatonin levels were low during the light phase but higher during the dark phase in all groups; however, when compared with the clear-cage group, rats in amber-, blue-, and red-tinted cages had 29%, 74%, and 48%, respectively, greater total daily melatonin levels due to an increased duration and, in some cases, amplitude of the nocturnal melatonin signal. No differences were found in dietary and water intake, body growth rates, total fatty acids, pH, or glucose among groups. Disruptions in circadian rhythms, manifesting as alterations in phase timing, amplitude, or duration, occurred in the melatonin, lactic acid, corticosterone, insulin, and leptin levels of rats in tinted compared with clear cages. Therefore, the use of variously tinted animal cages significantly alters circadian rhythms in plasma measures of metabolism and physiology in laboratory rats, thus potentially altering the outcomes of scientific investigations.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester PI R25OD010934

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title SPF Rhesus Monkey Colony for AIDS Research
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes

PI, with institutional affiliation

Excluded by Requester	C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester	C Comparative Pathology
	C Comparative Pathology
	C Veterinary Medicine
	C Regenerative Medicine
	C Regenerative Medicine
	C Bacteriology & Parasitology
	C Immunology
	C Comparative Pathology
	C Microbiology
	C Microbiology
	C Microbiology
	C Comparative Pathology
	C Comparative Pathology
	C Bacteriology & Parasitology
	C Microbiology
	C Microbiology
	C Comparative Pathology
	C Comparative Pathology
	C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A Private Source
	A
	A
	A LSUHSC
	A Baylor
	A Univ of Pittsburgh
	A Private Source
	A
	A Univ of Texas Medical BR Galveston
	A Private Source
	A
	A University of Colorado, Denver
	A University of Pittsburgh
	A Private Source
	A
	A
	A
	A TUSPH&TM

Excluded by Requester

A Private Source
A Univ of Colorado Denver
A Private Source
A
A LSUHSC
A Tulane University
A Univ of Pittsburgh
A LSU
A Private Source
A
A
A
A
A
A

Project Description (limited to one paragraph)

The presence of retroviral infection in nonhuman primate research animals makes them unsuitable for a number of research studies. In addition, the presence of B-virus in nonhuman primates used in research is a significant occupational safety and health concern. The specific pathogen free (SPF) program was created to provide rhesus monkeys seronegative for SIV, SRV, STLV-1, and B-virus. Two grants (U24, U42; ORIP) provide funding for derivation of the AIDS SPF, Indian origin, M. mulatta colony. Initially animals were derived from the TNPRC conventional breeding colony. Animals are negative for SIV, STLV-1, SRV, and B-virus. The expanded SPF colony is negative for the aforementioned 4 viral agents an in addition are negative for SV40, RRV, LCV, CMV, and SFV. All animals from the AIDS SPF colonies are limited to assignment to AIDS research projects.

Project Progress (one paragraph)

The 2012 animal census of the colony was approximately Proprietary which met projections. Proprietary Info of the animals were assigned to the expanded SPF program. In 2012, Prop rietar SPF rhesus were made available for assignment to affiliate and core investigators. The current census of the colony is approximately Propri which meets projections Proprietary of the animals are assigned to the expanded SPF program. In 2013 Propri etary SPF AIDS rhesus were made available for assignment to affiliate and core investigators. In addition, piggybacked use of animals in the breeding colony occurred. Tissues, including blood, feces, saliva, and bone marrow, were provided to investigators to support their research programs. Behavioral/observational data were also collected to support research and management programs. All piggyback use of animals is noninvasive or minimally invasive and allows animals to remain in their social groups with no impact to production.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester, PI U42 OD010568
NIH Excluded by U24 OD011109

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Treatment with Vivitrol to reduce self-biting behavior in adult rhesus macaques
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Self-injurious behavior (SIB) may be defined as any self-directed behavior that results in tissue injury. The condition occurs in approximately 5-13% of the captive rhesus macaque population with self-biting being the most common expression of the behavior. Additionally, SIB is a significant human health problem, which interestingly occurs in 4% of the general public. Currently, there are no widely accepted treatments for human or nonhuman primate SIB. However, studies with human and nonhuman primates have shown that therapeutic drugs used to treat alcoholism and drug abuse, such as oral naltrexone hydrochloride, are effective in reducing the occurrence of SIB. To date, there have been no studies examining the value of Vivitrol, a long-acting 30 day injectable naltrexone, for the treatment of human or nonhuman primate SIB. A focused study using Vivitrol for SIB may open the exploration of a novel use for Vivitrol in both research facilities and the general public.

Project Progress (one paragraph)

Following a 4-week pharmacokinetic study Proprietary Info subjects with a history of self-injurious behavior were enrolled in a treatment study. In the first four week phase baseline behavior was established. Two injections of Vivitrol were administered with a four week interval between injections. This phase was followed by an additional 4 week post-treatment baseline period. All observations were made through video recording and coding (Observer 9XT) according to an established ethogram. Blood samples were collected at the time of each Vivitrol injection and at seven day intervals until the end of the study for therapeutic range data analysis. In comparison to the baseline phase, both the frequency and the total time spent self-biting fell significantly in the treatment phase and time spent self-biting remained significantly reduced in a post-treatment phase despite undetectable levels of the blood in plasma.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester R25 RR024231

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Tulane Resource Allocation Committee
Unit/Division Veterinary Medicine
Type of Project Management
Percent P51 dollars - 0.651%
AIDS? No

PI, with institutional affiliation

Excluded by Requester — C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C Comparative Pathology
C Veterinary Medicine
C Comparative Pathology
C Comparative Pathology
C Veterinary Medicine
C Veterinary Medicine

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester
A LSU HSC
A Private Source

Project Description (limited to one paragraph)

The Tulane Resource Allocation Committee (TRAC) membership is composed of core and affiliate scientists who are responsible for the equitable allocation of animal resources. The twelfth year of operation of the TRAC saw continued refinement of operations of the committee, development of policy statements, and better reporting and analysis of allocation data. Analysis of breeding colony demographic, morbidity, and mortality data as well as allocation data assist in colony management decision-making.

Project Progress (one paragraph)

In 2012, a total of Pro pri investigator applications were received requesting a total of Prop rietar animals. Approximately Propriet ary Info of animal allocation was to affiliate (outside) investigators and Proprie tary to core investigators. At the end of 2012, Proprie tary Inf investigator requests for Pro animals remained deferred.
In 2013, a total of Pro priet investigator applications were received requesting a total of Prop rietar animals. Approximately Proprieta ry Info of animal allocation has been to affiliate (outside) investigators and Proprieta to core investigators for the last reporting period. At the end of 2013 Propr ietary core investigator request for Pr op animals remained deferred at the PI's request.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Videotaped Behavior as a Predictor of Clinical Outcomes in Rhesus Macaques
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Excluded by Requester
C Veterinary Medicine
C Veterinary Medicine
C Veterinary Medicine
C Comparative Pathology

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester A Mannheimer Fdn, Inc

Project Description (limited to one paragraph)

Understanding nonhuman primate behavior in the context of a biomedical research setting is beneficial for a multitude of reasons including improved health assessment. Rhesus macaques (*Macaca mulatta*) are known to mask their clinical signs in the presence of observers, making it difficult to interpret the severity of their condition on cage-side observation. The purpose of this study was to better understand the behavior of critically-ill rhesus macaques and determine if specific behavior(s) or subtle behavioral changes can be used to aid in improving the determination of the prognosis.

Project Progress (one paragraph)

Videotaped recordings of Pro prie critically ill subjects were collected after the subjects were removed from the outdoor breeding colony for diagnostic workup and treatment. Subjects were categorized according to clinical outcome: survivors (n= Prop rieta and those that were euthanized per existing clinical endpoints (n= Pro prie Behavior was compared between these groups in several contexts relating to the presence or absence of the veterinarian performing cage-side examinations: 1) prior to cage-side examination, 2) during cage-side examination, and 3) after cage-side examination, in order to compare the ability of these different settings to detect differences between groups and to characterize any masking of behaviors during direct observation. Prior to cage-side examination, levels of a number of behaviors (e.g. self-grooming and anxiety behaviors) were higher in surviving subjects than euthanized subjects. Few significant contrasts were detectable during or after the examination. During examination, the higher level of illness-related behaviors was the only difference found in euthanized subjects. However, not all animals requiring euthanasia showed these signs when an observer was present, as these signs were significantly suppressed during direct observation. Furthermore, these animals spent more time in an alert posture during observation than outside of it. Findings indicate that direct observation of critically ill rhesus macaques may not enable the most accurate assessment of illness severity and that the use of video to assess behavior may be helpful for predicting prognosis.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title *In Vivo* Suppression of SIV-mediated immune activation
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Boston Children's Hospital
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

PH-797804 is a potent inhibitor of a major cell enzyme called p38 mitogen-activated protein kinase (p38-MAPK). This enzyme is responsible for initiating cell activation in lymphocytes. Because immune activation is believed to drive SIV and HIV replication, we will test this immune suppressant in nonhuman primates infected with SIV to see if it results in decreased viral levels in blood, activation of immune cells and delay in progression to disease. Excluded by lab has shown that in a cell culture model of SIV infection, inhibition of a specific cellular pathway involved in the signaling of inflammation with a novel drug being tested in clinical trials for the inhibition of other inflammatory processes can markedly reduce activation of immune cells. Prop rhesus macaques (RM) will be infected rectally with SIV mac 251. Propri etary I will be treated orally with PH-797804 for Pro prietweeks on and Pro priewks off for up to 3 cycles. Two RM will not be treated to prove that the treatment reduces activation and viremia. Gene expression profiles and expression of surface molecules linked to immune activation in RM PBMC, lymph nodes and rectal mucosal biopsies and serum levels of inflammatory cytokines and chemokines will be evaluated.

Project Progress (one paragraph)

Proprie tary Inf RM have been infected with SIV mac251. Several samples have been collected but no results are available at this time.

Funding Sources (include name of the source, PI and the FULL grant number)

NIAID Excluded by Requester 1 R21 AI106540-01A1

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Oral Vaccination for AIDS Prevention in Rhesus Macaques
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI with institutional affiliation
Excluded by Requester
A Boston Children's Hospital
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

This proposal is designed to extend our ongoing studies by investigating immunization approaches aimed at maximizing immune responses to oral or intestinal SIV vaccination in primates. As a source of viral antigen during vaccination, we will use a SIV construct previously used in our SIV and SHIV vaccine studies: a genetically inactivated proviral genome that produces non-infectious viral particles. We achieved significant systemic and mucosal cellular responses with a SIV DNA-rMVA approach after oral cavity and intestinal immunizations. These immunizations had two important impacts on SIV exposure and infection: 1. the intestinal immunization provided significant protection from infection but no protection from disease progression; 2. the oral cavity immunization provided significant protection from disease with no AIDS development observed during the post-challenge follow up and with more than 50% of the animals controlling virus replication to undetectable blood levels after experiencing a peak of viremia, and apparently clearing the infection. The goals of this proposal are: 1. to evaluate whether an immunization consisting of SIVvaxmac/sm and cytokine DNA, matched rMVA, and gp140 SIVsmE543-3 Env administered in the oral cavity or intestinally, leads to persistent anti-Env IgG and IgA titers at mucosal sites of HIV exposure in humans and whether this addition improves protection from heterologous SIVmac251 infection and disease in Indian RM. 2. to more extensively evaluate the correlates of protection from infection and disease previously observed with the DNA+MVA oral and intestinal vaccinations; 3. to evaluate whether the best regimen identified in Aim 1 that protects after vaginal SIV exposure also provides a similar protection after rectal viral exposure in both male and female animals.

Project Progress (one paragraph)

No animal work has been conducted as of 1/2014

Funding Sources (include name of the source, PI and the FULL grant number)

NIH/NIDCR Excluded by Requester 2RO1DE019060-06A1

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Alcohol, SIV Infection and Host Defense
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester A Louisiana State University Health Sciences Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Louisiana State University Health Sciences Center

Project Description (limited to one paragraph)

The purposes of this study are to identify mechanisms by which alcohol impacts SIV disease transmission and progression in animals not treated or treated with ART (rhesus macaques Prop female and Pro males) with surgically implanted gastric catheters to administer either ethanol or sucrose over the las Pro years in an ongoing study involving multiple investigators. Animals were infected with SIVmac251 three months after starting alcohol and infected with *Streptococcus pneumoniae* 4 months after SIV inoculation. Some animals started to receive anti-retroviral drugs at Propr months of SIV infection.

Project Progress (one paragraph)

Macaques administered ethanol had higher plasma viremia and virus-specific cellular immune responses compared to the sucrose-controls. The emergence of virus-specific cytokine responses temporally correlated with the decline in mean plasma viral load after Pro ays post infection in all SIV infected animals. SIV envelope-specific IgG and neutralizing antibodies were similar over the disease course in both groups. To date, these studies indicate that alcohol abuse may accelerate disease progression, in part, by suppressing host defense against the infection and prolonging up regulation of virus production via increased T helper cell turnover and in response to an opportunistic infection. Also, alcohol-treated females have statistically increased SIV infection rate Proprieta compared to sucrose controls Proprie Inf Although more studies are needed, this increased rate of infection was associated with changes in the microbial flora in the genital tract observed in another cohort of animals. Studies continue to identify differences in mucosal tissues between alcohol and sucrose treated males and females. Other ongoing studies are examining the effect of alcohol on effectiveness of ART on viral load, intestinal and genital T helper cell reconstitution, lung host defense against bacterial infection, muscle protein synthesis, cytotoxicity and bone marrow progenitor cells response to SIV and lung infection. While analysis is ongoing, one interesting finding is that alcohol increases T helper cell turnover in gut mucosal tissue.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester *TNPRC P* Excluded by Requester P60 AA009803-16

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title *Moraxella osloensis* Septic Arthritis in a Rhesus Macaque
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Bacteriology & Parasitology
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

A 5.5-year-old Chinese-origin female rhesus macaque (*Macaca mulatta*) presented for hindlimb lameness. She was mother-reared in Tulane National Primate Research Center's specific pathogen free breeding colony and was seronegative for B-virus, Macacine herpesvirus 1, simian immunodeficiency virus, simian retrovirus type D, and simian T-lymphotropic virus. Her medical history included social trauma resulting in left tibia osteomyelitis and a surgically repaired right cranial cruciate ligament rupture.

Project Progress (one paragraph)

Physical examination findings on presentation included thin body condition, mild dehydration, pregnancy, and bilaterally swollen stifles that were warm to the touch, with the right more severely affected. Mild instability, decreased range of motion, and muscle atrophy were observed bilaterally. Hematologic evaluation revealed mild leukocytosis with marked neutrophilia and lymphopenia, moderate anemia, and mild thrombocytosis. Serum biochemistry revealed mild hyponatremia, hypochloremia, hypoalbuminemia, hyperglobulinemia, and moderate hypoglycemia. Arthrocentesis for culture and gram staining revealed Moraxella-like organisms. Treatment with enrofloxacin was initiated empirically and subsequently switched to cephalexin based on published case reports. Definitive diagnosis of *Moraxella osloensis* septic arthritis was made via isolation of the organism, cloning, and DNA extraction for sequencing of the 16S ribosomal DNA region. To our knowledge, this is the first reported case of *Moraxella osloensis* septic arthritis in a rhesus macaque.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester *PI* R25OD010934

Publications Resulting from this Project (only include publications with a PMCID number)

Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development and Pharmacology of Novel Lipidic rAHF
Unit/Division Veterinary Medicine
Type of Project Collaborative
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A SUNY
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Our hypotheses are that phospholipids-- specifically phosphatidylinositol (PI) and phosphatidylcholine (PS)-- associated with the C2 domain of the Factor VIII protein in the form of liposomal nanoparticles might have the ability to prolong the circulating lifetime and decrease the immunogenicity of the protein. Both particles have been shown to reduce immunogenicity of FVIII in mice. Furthermore, *in vivo* experiments have suggested they may have the capability to induce tolerance to that protein. The PS particle is rapidly cleared when injected intravenously but may be amenable to subcutaneous delivery, where it will provide a depot effect. The PI particle improved the intravenous pharmacokinetic profile of FVIII in mice. The goal of the pharmacokinetic studies is to investigate whether lipid-FVIII complexes have a longer circulating half-life in blood than free FVIII. The endpoint these studies is the concentration of FVIII protein circulating in blood as a function of time. Animals in the i.v. studies will then be administered i.v. injections of free FVIII at doses of 25 , 50, and 100 IU/kg and the PI-FVIII complex at a dose of 25 IU/kg. Blood samples will be drawn to determine FVIII, antibody titers and cytokine (TGF-β, IL-6, IL-10, IL-17) levels. The goal of the immunogenicity studies is to investigate whether lipid-complexed FVIII elicits a lower antibody-mediated immune response in animals compared to free FVIII as well as to see if administrations of FVIII-phospholipid complexes will tolerize the system to future injections of FVIII. The endpoint for immune response is measuring antibody titers to FVIII. Animals used in the above PK studies will be immunized by giving them three additional weekly injections of either free FVIII 25 IU/kg i.v., PI-FVIII 25 IU/kg i.v., free FVIII 100 IU/kg s.c., or PS-FVIII 100IU/kg s.c

Project Progress (one paragraph)

We completed the experiments and sample collections for the Free FVIII i.v. and PI-FVIII i.v. treatment groups. When analyzing the samples and data, we determined that there are no currently available assays sensitive enough to detect injected FVIII due the endogenous FVIII levels in the rhesus macaque.

In order to collect useful data, we have refocused our work to investigate the safety and efficacy of these lipidic formulations in rhesus macaques. These studies are in progress.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester *TNPRC PI* Excluded by Requester R01 HL070227

OD-011104-52

Reporting Period: May 1, 2013 – April 30, 2014

FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.

****

Project Title dmLT Adjuvanted Sublingual Vaccination with IPV in NHPs
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A Tulane University Health Sciences Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

The goal of the proposed studies is to confirm the ability of dmLT to (a) facilitate dose-sparing for IPV and (b) induce mucosal immune responses following sublingual immunization. SL immunization with IPV ± dmLT will also provide a proof-of-concept for continuing to pursue SL immunization as a viable vaccine strategy against polio. Proprietary Inf groups of NHP each, will be vaccinated sublingually (SL) or intramuscularly (IM) on three occasions with IPV or with a control antigen. The vaccines will be coadministered with or without the mucosal adjuvant dmLT. A novel SL formulation containing a mucoadhesive thermo responsive gel (TRG) will also be tested. Blood, saliva and feces from each animal will be collected 2 weeks before the first vaccine, before each immunization, 2 weeks after each immunization and monthly thereafter throughout the study period (6 months). Levels of polio-specific antibodies and polio neutralizing antibodies present in serum, saliva and feces will be analyzed. Proprietary I

Project Progress (one paragraph)

We are in the process of having animals assigned to our project, and upon assignment of animals, we will begin the study.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester Private Source

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Efficacy of Lipidic Formulations for Monoclonal Antibody Delivery
Unit/Division Veterinary Medicine
Type of Project Collaborative
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A SUNY
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Our lab has previously established the ability of O-Phospho-L-Serine (OPLS) added to a particular drug treatment to reduce the immune response to the drug in Hemophilia A mice. This technology was applied to Adalimumab (ADM) and has shown promising results (i.e. lower immune response to ADM) in Swiss Webster mice. The goal of the study is to investigate whether the reduced immune response afforded by the addition of OPLS to a drug treatment can be applied to ADM without adversely affecting how the body processes the drug in non-human primates. We hypothesize that due to the innate capability of OPLS to modify the functioning of the immune system, it will reduce the immune response to the antigen (i.e. ADM) with which it is co-administered. Pro prie healthy, juvenile, male rhesus monkeys will be divided into 2 treatment groups o Pro pri nimals each. According to treatment group, animals will be administered one PK dose of 5mg/kg followed by three weekly immunogenicity doses of 1mg/kg ADM s.c. or OPLS/ADM s.c. Blood samples will be collected at various timepoints for immunogenecity and pharmacokinetic data analyses.

Project Progress (one paragraph)

We have completed the experiment involving the free ADM treatment group and are currently analyzing samples.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester *(TNPRC PI* Excluded by Requester R01 HL070227

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Safety Assessments of Lipidic Formulations for Protein Delivery
Unit/Division Veterinary Medicine
Type of Project Collaborative
Percent PS1 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A SUNY
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

We hypothesize that since the lipidic entities in our formulations are biodegradable counterparts or derivatives of endogenous phospholipids, they are safe for clinical use. Short-term, repeated-dose safety studies will be conducted with PI, PS and OPLS alone. The goal of these studies is to establish a No Observed Adverse Effect Level (NOAEL) for each of these lipidic entities in non-human primates. Macaques will be administered 21 daily doses of either PI i.v., PS s.c., or OPLS s.c. at the clinically relevant dose. Control animals will receive daily doses of vehicle. On day 8, animals will be administered a single i.m. injection of the antigen Keyhole Limpet Hemocyanin (KLH), a standard antigen that is used to evaluate the immunocompetence of an animal. Blood samples will be collected at various timepoints. Demonstrating the safety of these formulations in nonhuman primates will bring this technology closer to fulfilling pressing medical needs in protein therapy – decreased occurrence of adverse immune responses, decreased dosing frequency, and the possibility of subcutaneous administration in lieu of the currently used intravenous route.

Project Progress (one paragraph)

We have completed the experiments involving the OPLS and control treatment groups and are currently analyzing the samples.

Funding Sources (include name of the source, PI and the FULL grant number)

NIH Excluded by Requester (*TNPRC PI* Excluded by Requester) R01 HL070227

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development of a SNP Assay for Determination of Ancestry of Rhesus Monkeys
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A ONPRC
A CNPRC
A CNPRC
A NENPRC
A YNPRC
A SWNPRC

Project Description (limited to one paragraph)

Rhesus macaques (*Macaca mulatta*) are an important primate model organism in several areas of biomedical research. The wide geographic distribution of this species has led to significant genetic differentiation among local and regional populations. These regional differences can be important factors in the selection of specific animals for particular research studies as animals from different populations can respond differently to the same experimental treatment. Consequently, in many circumstances it is valuable to be able to confirm the geographic ancestry (i.e. genetic ancestry) of individual rhesus monkeys.

Project Progress (one paragraph)

In order to facilitate the use of genetic information to identify or confirm the ancestry of individual rhesus macaques, we have developed a panel of 96 single nucleotide polymorphisms (SNPs) that effectively distinguish Indian-origin from Chinese-origin rhesus monkeys. This genetic test can be used to determine the origin of individual animals and to detect individuals that are hybrids between these two regional populations. This tool will be useful to researchers, colony managers, and others who wish to evaluate or investigate the genetic identity and ancestral origin of individual rhesus macaques, and therefore facilitate more effective and efficient use of these animals in biomedical research.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Empirical Comparison of STRs and SNPs
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation

Excluded by Requester C Veterinary Medicine

Principal Core (TNPRC) Scientist associated with the project

Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester

A ONPRC
A CNPRC
A NENPRC
A YNPRC
A ONPRC
A UC Davis
A UC Davis
A WNPRC

Project Description (limited to one paragraph)

We compared the effectiveness of short tandem repeat (STR) and single nucleotide polymorphism (SNP) genotypes for estimating pairwise relatedness, by using molecular data and pedigree records from a captive Chinese rhesus macaque population at the California National Primate Research Center.

Project Progress (one paragraph)

We find that a panel of 81 SNPs is as effective at estimating first-order kin relationships as a panel of 14 highly polymorphic STRs. We note, however, that the selected STRs provide more precise predictions of relatedness than the selected SNPs, and may be preferred in contexts which require the discrimination of kin related more distantly than first-order relatives. Additionally, we compare the performance of three commonly used relatedness estimation algorithms, and find that the Wang algorithm outperforms other algorithms when analyzing STR data, while the Queller and Goodnight algorithm outperforms other algorithms when analyzing SNP data. Future research is needed to address the number of SNPs required to reach the discriminatory power of a standard STR panel in relatedness estimation for primate colony management.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Exome Sequencing of TNPRC Rhesus Monkeys
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with Institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A University of Nebraska Medical Center

Project Description (limited to one paragraph)

A total of 78 samples of genomic DNA obtained from rhesus macaques with unusual phenotypes were analyzed. For all samples, human exome capture kits were used to pull down exons. Samples from animals TU-10 and TU-14 were sequenced at the University of Nebraska Medical Center. Samples from TU-101...TU-173 were sequenced by SeqWright Genomic Services. For all samples, an Illumina Hi-Seq 2000 was used to obtain paired-end 100 or 101 bp reads. Sequences were aligned against version 7 of the new rhesus macaque genome (created by the Excluded by Reques ab in collaboration with Excluded by Requester and Excluded by Requester t the University of Maryland).

Project Progress (one paragraph)

The GATK pipeline (Broad Institute) has been used for a preliminary analysis of high impact mutations. A number of interesting mutations are being investigated. For example, a stop-gain in exon 16 of the COL9A2 gene was observed in both TU-10 and TU-13 in the heterozygous state. This mutation was not observed in any of the other TNPRC samples. TU-10 and TU-13 are siblings. Their dam, TU-11, does not have this mutation. Hence, we conclude that their sire, not included in the samples we have analyzed, likely also has this mutation. Mutations in COL9A2 are associated with bone growth disorders including lumbar disc disease. Information on high impact mutations in primate colonies could be used to create rhesus macaque models of human genetic disease by identifying and breeding heterozygotes to produce null mutant homozygotes.

Funding Sources (include name of the source, PI and the FULL grant number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Genetics and Genome Banking Core
Unit/Division Veterinary Medicine
Type of Project Management
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester
A SWNPRC
A Baylor College Medicine
A University of Nebraska Medical Center

Project Description (limited to one paragraph)

The efforts of the Core have focused on banking of genetic resources and participating in the development and validation of Proprietary Info assays for ancestry and parentage testing, identification of genes suspected of involvement in extreme phenotypes and identification of Propr ietary by whole genome sequencing.

Project Progress (one paragraph)

Blood and tissue biopsies were collected during routine physical examinations of breeding colony animals. Blood was used for DNA extraction and for banking using archival blood cards. Biopsies were processed to establish and cryopreserve fibroblast cell lines. I. Genome banking: The Core received Pro kin biopsies from which to date Propri etary fibroblast cell lines have been generated and cryopreserved. A total of Propri etary I blood samples were obtained and preserved on archival FTA cards. From these as well as from stored blood samples Propr ietary DNA extractions were performed. Currently the genome bank contains a total of Propr ietary cell lines and archived blood samples from Propri etary I animals. DNA was also extracted from bone samples of Pro pri animals whose remains had been found in the corrals. II. Genetic management: DNA from Propri etary I animals was used to generate Propr ietary for parentage testing. Results were used for assignment of dams and sires.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Parameters of reproductive efficiency and longevity among female rhesus macaques
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Louisiana State University Ag Center

Project Description (limited to one paragraph)

We have expanded our analysis to determine if age at first reproduction is related to other reproductive characteristics and to longevity of female rhesus macaques. Data sets included only females born at the TNPRC with confirmed birth dates. Least squares statistical analyses were carried out to evaluate what factors (generation, dam birth year within generation, and AFR (early or late) are influencing this response. Cox proportional hazards survival analysis was also carried out to study the influence of generation and age at first reproduction on the survival response.

Project Progress (one paragraph)

For analysis of response traits age at first parturition was divided into two ages, early age which varied from Proprietary Info years of age and older age which varied from Proprietary Info years of age. Females that had an early first parturition had a longer first postpartum birth interval than females with a later first parturition Proprietary Info and lived a shorter time to death than later first parturition females Proprietary Info yrs). They produced more total progeny in their lifetime than later parturition females Proprietary Info but earlier age at first parturition did not differ from older age at first parturition for mean postpartum birth interval. Age at first parturition did not have an effect on first infant survival at birth, Proprietary Info of age. First parturition females whose infants lived to a year of age also had longer first postpartum birth intervals than females whose infants died before a year of age Proprietary Info vs Proprietary Info In the Cox proportional hazards regression analysis, age at first parturition had a significant influence on probability of survival but only approached significance for probability of number of offspring born in a female's lifetime.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Reproductive Efficiency of Captive Rhesus Macaque Females
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? Yes
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)
Excluded by Requester A Louisiana State University Ag Center

Project Description (limited to one paragraph)

Reproductive records Proprietary Info from Propr ietary Chinese-origin and Propri etary ndian-derived females spannin Propr ietary nerations were studied. Least-squares analysis of variance procedures were used to compare reproductive and infant survival traits while proportional hazards regression procedures were used to study female age at death, number of infants born per female and time from last birth to death.

Project Progress (one paragraph)

Generations Proprietary Info included Proprietary Info and Pro prie emales, respectively. Chinese females were older at first parturition than Indian females because they were older when placed with males, but the two subspecies had similar first and lifetime post-partum birth intervals. Females that gave birth to stillborn infants had shorter first post-partum birth intervals than females giving birth to live infants. Post-partum birth interval decreased in females from Proprieta ry Info ears of age but then increased again with advancing age. Chinese infants had a greater survival rate than Indian infants a Prop rieta , Prop rieta mo and Pro prie of age. Proprietary Info female Proprietary Info ad uncensored, or true records for age at death, number of infants born per female, and time from the birth with death whereas Prop rietar females Proprietary Info had censored records for these traits. Low and high-uncensored observations for age at death were Proprietar y Info years of age for Chinese and Proprietary Info years of age for Indian females. Uncensored number of infants born per female ranged from Proprieta Info or Chinese females and Proprieta ry Info for Indian females. Each of these traits was significantly influenced by the origin x generation interaction in the proportional hazards regression analyses, indicating that probabilities associated with age at death, number of infants born per female and time from last birth to death for Chinese and Indian females did not rank the same across generations.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)
Excluded by Requester

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Whole Genome Sequencing of Rhesus Macaques
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Other affiliate scientists with institutional affiliation (doctoral level only)

Excluded by Requester	A ONPRC
	A CNPRC
	A CNPRC
	A NENPRC
	A YNPRC
	A SWNPRC
	A SWNPRC
	A SWNPRC
	A WisNPRC

Project Description (limited to one paragraph)

This study was designed to discover within-species genetic variation among rhesus macaques (*Macaca mulatta*), investigate species' evolutionary history and begin characterizing functionally significant variation. We generated whole genome DNA sequences fo[Propri etary] unrelated rhesus macaques from eight research colonie[Propriet ary Info]ndian-origin [Pro prie]hinese-origin). [Proprietary Info] animals were sequenced to deep [Propri etary] and [Proprietary Info] genome coverage. We identified [Propri etary I] million [Proprietary Info] including singletons, which is [Proprietary Info]

Project Progress (one paragraph)

On average, Indian-origin individuals have [Prop rieta] million variants, where Chinese animals have [Prop rieta] million. We estimate current effective population size (Ne) as [Propriet] for Indian-origin animals, [Proprieta] or Chinese-origin, with both estimates higher than in humans. Analyses also reveal dramatic demographic changes over time. Ne was [Proprieta ry] until 500,000 years ago, then increased dramatically, followed by a decline that was more dramatic for Indian animals than Chinese, possibly indicating a bottleneck during migration into India. [Proprietary Info] mapped to ENCODE transcription factor binding sites (TFBS). The density of [Propri etary I] in TFBS is lower than genome-wide expectation, suggesting negative selection on TFBS. [Propriet] software identifies [Proprietar] candidate variants that may significantly affect TF binding, and thus gene expression. Our study identified novel genetic variation in rhesus macaques, shows that population sequencing is a powerful approach for in-depth demographic analysis and detects specific polymorphisms likely to influence gene expression and possibly phenotypic variation.

Funding Sources (include name of the source, PI and the FULL grant number)

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title A Macaque Model of Acute *Coxiella burnetii* Infection
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester C Veterinary Medicine
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester
C Veterinary Medicine
C Microbiology
C Bacteriology & Parasitology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Coxiella burnetii is an obligate intracellular bacterium that causes Q fever, a flu-like illness with complications including pneumonia and hepatitis in humans. We propose to re-establish and characterize the aerosol-challenge rhesus macaque model of acute Q fever by detailing physiologic, pathologic, and immunologic changes following infection. The optimum challenge dose will be confirmed based on aspects of the disease that most resemble acute human illness, such as development of fever and pneumonia, to prepare for future vaccine efficacy studies. Advanced monitoring including biotelemetry, radiology, polychromatic flow cytometry, DNA microarray, multiplex cytokine/chemokine assays, and immunohistochemistry will be used to gain a more thorough understanding of the host response and immunopathogenesis of *C. burnetii* infection than has been accomplished in previous studies.

Project Progress (one paragraph)

Pending

Funding Sources (include name of the source, PI and the FULL grant number)

NIH-NIAID WRCE Excluded by Requester P/ U54AI057166-10

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title Development of a Subunit Vaccine Against Q Fever
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI, with institutional affiliation
Excluded by Requester A Texas A&M Health Sciences Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester Veterinary Medicine
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

Q fever, caused by *Coxiella burnetii*, is most often an acute flu-like illness in humans that may be followed by pneumonia; a chronic form of the disease can also occur that results in endocarditis or hepatitis. There is currently no approved *Coxiella* vaccine in the United States. This study proposes to test the abilities of new vaccines against *Coxiella* in mouse and guinea pig animal models. Vaccinated animals will be inoculated with *C. burnetii* via intraperitoneal injection, intratrachael instillatio, or aerosol.

Project Progress (one paragraph)

Pending

Funding Sources (include name of the source, PI and the FULL grant number)

NIH-NIAID WRCE Excluded by Requester *PI* U54AI057166-10

Publications Resulting from this Project (only include publications with a PMCID number)

2013-2014 Annual Progress Report
OD-011104-52
Reporting Period: May 1, 2013 – April 30, 2014
FORMAT FOR DESCRIPTION OF EACH PROJECT PERFORMED DURING THE GRANT YEAR (Includes Research, Management, Pilot and any other type of project.) One separate page per project.
****

Project Title OMV Vaccine-Mediated Protection Against Aerosolized *B. pseudomallei*
Unit/Division Veterinary Medicine
Type of Project Research
Percent P51 dollars - 0.651%
AIDS? No
PI with institutional affiliation
Excluded by Requester A Tulane University Health Sciences Center
Principal Core (TNPRC) Scientist associated with the project
Excluded by Requester C Veterinary Medicine
C Microbiology
Other affiliate scientists with institutional affiliation (doctoral level only)

Project Description (limited to one paragraph)

B. pseudomallei is an aerosol biothreat agent of military significance. Despite enhanced research and vaccine efforts in recent years, traditional vaccine strategies employing attenuated bacterial strains, recombinant proteins, or purified polysaccharides have failed to elicit complete protection against aerosol challenge with *B. pseudomallei*. Inhalation represents the primary route of infection in a deliberate biological attack and it is imperative that vaccine candidates are efficacious against this route of challenge. We previously showed that mice immunized with non-optimized, naturally-derived outer membrane vesicles (OMVs) from *B. pseudomallei* were significantly protected against aerosol challenge with 5 LD50 of *B. pseudomallei* Excluded by Requester We propose that OMVs represent a safe, inexpensive, multi-antigen vaccine strategy against *B. pseudomallei* that promotes protective antibody and cellular-mediated immune responses. The objectives of this project are 1) to optimize the OMV vaccine by examining multiple dose, delivery, and adjuvant combinations in mice and 2) to down-select the best OMV vaccine formulation for evaluation in the non-human primate (NHP) model of pneumonic melioidosis. These studies are essential to maximize OMV vaccine effectiveness and to move forward with comprehensive efficacy studies in the NHP.

Project Progress (one paragraph)

OMV vaccines have been tested in mice with moderate success.

Funding Sources (include name of the source, PI and the FULL grant number)

Excluded by Requester Private Source

Publications Resulting from this Project (only include publications with a PMCID number)

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

Census date: 12/16/13

Genus, Species	Breeding Colony[2]				Animals not in breeding colony[3]				Total Colony Census
	M	F	U[4]	Total	M	F	U[4]	Total	
Macaca mulatta (Indian)	544	839	30	1413	89	53	0	142	1555
Macaca mulatta (Chinese)	165	255	14	434	42	2	0	44	478
Macaca fascicularis	0	0	0	0	3	0	0	3	3
Cercocebus torquatus atys	10	5	0	15	0	0	0	0	15
Cercocebus torquatus lunulatus	4	2	0	6	0	0	0	0	6
Total	723	1101	44	1868	134	55	0	189	2057

[1] None of these animals is supported by a SPF U24 or U42 grant.

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

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

[4] Sex undetermined

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

Census date: 12/16/13

Genus, Species	Breeding Colony[2]				Animals not in breeding colony[3]				Total Colony Census
	M	F	U[4]	Total	M	F	U[4]	Total	
Macaca mulatta (Indian)	777	1166	23	1966	199	263	0	462	2428
Macaca mulatta (Chinese)	0	0	0	0	14	34	0	48	48
Macaca fascicularis	0	0	0	0	9	20	0	29	29
Macaca nemestrina	0	0	0	0	19	3	0	22	22
Totals	777	1166	23	1966	241	320	0	561	2527

[1] 1,996 Indian ancestry M.mulatta colony is supported by a SPF U24 or U42 grant

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

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

[4] Sex undetermined

3. Non-primate colonies[1]

Census date: 12/16/13 (no non-primate species on P51 projects)

Genus, Species	Total number of animals
Total	

[1] Include only those animals supported partially, or in whole by the P51 base grant.

15 pages (Publications) Removed – Excluded by Requester